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ENTRY AND OPERATION STRATEGIES OF INDIAN PHARMACEUTICAL FIRMS IN AFRICA UNDER THE DYNAMICS OF MARKETS AND INSTITUTIONS

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To My Grandfather
Dr. Phulgenda Sinha

Abstract

The existing literature on the internationalization of Indian pharmaceutical firms has mainly focused on their penetration to highly regulated markets of economically advanced countries (Chapter 1). While this approach has enriched our knowledge of the strategies used by Indian firms in developed country settings, it considers the pharmaceutical markets in Sub-Saharan Africa only as an intermediate step in the broader process of internationalization. This dissertation opens the dialogue by asking, *"What are the market entry and operation strategies of Indian pharmaceutical firms in Sub-Saharan Africa?"* It employs a neo-institutional framework and looks at the problem from three different perspectives for a holistic picture of the phenomenon.

Taking an empirical approach, the thesis starts the investigation by constructing a political economy narrative to highlight the importance of institutional factors behind internationalization rooted both inside and outside India (Chapter 2). It shows that the early protectionist environment put in place by the Indian government helped build a robust indigenous pharmaceutical industry. The simultaneous arrival of TRIPS and economic liberalization created both competitive and supportive *push factors* forcing Indian firms to look for new avenues of growth beyond national boundaries. Furthermore, generic supporting policies of African countries acted as *pull factors* for Indian firms to engage in these markets. It also demonstrates the pull created by the action of international organizations and the new governance of donor-funded markets through the cases of antiretroviral and antimalarial medicines.

Next, the thesis explores the organization of the pharmaceutical market in Francophone West African countries through the case of Mali and examines the entry and operational strategies of Indian firms therein (Chapter 3). It relies on the analyses of two sets of semi-structured interviews conducted in Mali and India, a Malian pharmaceutical market authorization list, and pharmaceutical export data from the International Trade Centre. It shows that the pharmaceutical market is divided into four specific segments – government-funded public

market, donor-funded public market, formal private market and the informal market – with different regulatory characteristics governing their functioning. Indian firms are using only export to operate in Francophone West African countries, but the organization of export as well as product portfolio varies according to the segment in which a firm intends to operate.

Lastly, it studies the impact of strategic alliance of Indian firms with Product Development Partnerships (PDPs) and the regulatory framework put in place by international organizations on the market entry strategy (Chapter 4). It relies on the case study of Synriam, a new antimalarial medicine developed through the partnership between Medicines for Malaria Venture (MMV) and Ranbaxy. It shows that Ranbaxy used partnership for developing capabilities, accessing new markets and gaining legitimacy. The case also reflects that international organizations may create institutional barriers and influence the market entry strategy especially for medicines against diseases which have a substantial donor-funded market segment.

To conclude, this thesis illustrates the richness and complexities of the African pharmaceutical market and shows that market entry and operation strategies of Indian firms are influenced by the underlying institutional environment.

Keywords: Indian pharmaceutical firms; internationalization; market entry; firm strategy; Sub-Saharan Africa; pharmaceutical markets; international organizations; Product Development Partnerships

Résumé

La littérature existante sur l'internationalisation des firmes pharmaceutiques indiennes s'est principalement concentrée sur leur pénétration dans les marchés hautement réglementés des pays avancés (Chapitre 1). Bien que cette approche ait enrichi notre connaissance des stratégies utilisées par les firmes indiennes dans les pays développés, elle considère les marchés pharmaceutiques en Afrique subsaharienne seulement comme une étape intermédiaire dans le processus d'internationalisation. Cette thèse essaie de répondre à la question suivante : « quelles sont les stratégies d'entrée sur le marché et de fonctionnement des firmes pharmaceutiques indiennes en Afrique subsaharienne ? ». À travers un cadre néo-institutionnel, cette problématique est abordée selon trois perspectives différentes afin d'obtenir une image holistique du phénomène.

Notre démarche est avant tout empirique. La thèse débute par une mise en évidence l'importance des facteurs institutionnels que sous-tendent l'internationalisation à la fois à l'intérieur et à l'extérieur de l'Inde (Chapitre 2). Cela démontre que l'environnement protectionniste mis en place par le gouvernement indien a contribué à bâtir une industrie pharmaceutique solide. L'arrivée simultanée de l'Accord ADPIC et de la libéralisation économique a créé des « push factors » à la fois compétitifs et favorables, obligeant les firmes indiennes à chercher de nouvelles voies de croissance au-delà des frontières nationales. En outre, les politiques de soutien des pays africains en faveur des génériques ont induits des « pull factors » permettant aux firmes indiennes de s'engager davantage sur ces marchés. Cette thèse montre également que le « pull » a été créé par l'attraction des organisations internationales et de la nouvelle gouvernance des marchés financés par les bailleurs de fonds.

La thèse explore ensuite l'organisation du marché pharmaceutique et les stratégies d'entrée et d'exploitation des firmes indiennes dans les pays francophones d'Afrique de l'Ouest à travers le cas du Mali (Chapitre 3). Une analyse de deux séries d'entretiens semi-directifs menés au Mali et en Inde a été complétée par l'analyse d'une liste d'autorisations de mise sur le marché des produits pharmaceutiques au Mali et de données sur les exportations de produits

pharmaceutiques du Centre du Commerce International. Cette enquête montre que le marché pharmaceutique en Afrique de l'Ouest francophone est divisé en quatre segments spécifiques – le marché public financé par l'État, le marché public financé par des donateurs, le marché privé formel et le marché informel – avec des réglementations différentes régissant leur fonctionnement. Les firmes indiennes n'utilisent que l'exportation pour opérer dans ces pays, mais leur organisation ainsi que le portefeuille de produits varient selon le segment dans lequel une firme a l'intention de s'implanter.

Enfin, l'alliance stratégique des firmes indiennes avec les partenariats de développement de produits (PDP) a été étudiée tout en s'intéressant au cadre réglementaire mis en place par les organisations internationales concernant la stratégie d'entrée sur le marché (Chapitre 4). Cette recherche s'appuie sur l'étude du Synriam, un nouvel antipaludéen développé dans le cadre du partenariat entre Medicines for Malaria Venture (MMV) et Ranbaxy. Les résultats montrent que Ranbaxy a utilisé ce partenariat pour développer ses capacités, accéder à de nouveaux marchés et gagner en légitimité. Cette étude a mis également en évidence le fait que les organisations internationales peuvent créer des barrières institutionnelles et influencer la stratégie d'entrée sur le marché.

En conclusion, cette thèse illustre la richesse et la complexité du marché pharmaceutique africain et démontre également que les stratégies d'entrée sur le marché et d'exploitation des firmes indiennes sont influencées par l'environnement institutionnel sous-jacent.

Mots-clés : Firmes pharmaceutiques indiennes; internationalisation; entrée sur le marché; stratégie des firmes; Afrique subsaharienne; marchés pharmaceutiques; organisations internationales; partenariats pour le développement de produits

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List of Abbreviations and Acronyms

A2S2	Assured Artemisinin Supply System
ACT	Artemisinin-Based Combination Therapy
ARV	Antiretroviral Therapy
CMS	Central Medical Store
CRS	Catholic Relief Services
CSCOM	Centre de Santé Communautaire
DCGI	Drug Controller General of India
DNDi	Drugs for Neglected Diseases Initiative
DPM	Direction de la Pharmacie et du Médicament
FDC	Fixed-Dose Combination
IS	l'Inspection de la Santé
LNS	Laboratoire Nationale de la Santé
MDG	Millennium Development Goals
MMV	Medicines for Malaria Venture
NEML	National Essential Medicine List
PDP	Product Development Partnership
PEPFAR	President's Emergency Plan for AIDS Relief
PMI	President's Malaria Initiative
PPM	Pharmacie Populaire du Mali
PQR	Price and Quality Reporting
PSI	Population Services International
SDG	Sustainable Development Goals
WHO	World Health Organization

Introduction Générale[1]

Au cours du demi-siècle dernier, l'Inde a développé une industrie pharmaceutique robuste et compétente. Elle n'est pas seulement rentable, mais elle a aussi amené les firmes pharmaceutiques indiennes à l'avant-garde des affaires mondiales (Athreye & Kapur, 2009; Chittoor & Ray, 2007; Dhar & Gopakumar, 2009). Au départ, les firmes indiennes étaient communément appelées "pirates" et "copieurs" par les Big Pharma (Angeli, 2014; Chittoor, Sarkar, Ray, & Aulakh, 2009; Owen, 2013), mais elles sont passées du statut d'imitateurs ordinaires à celui de collaborateurs et de concurrents des multinationales des pays développés (MNC) sur le marché mondial. Aujourd'hui, l'industrie pharmaceutique indienne se classe troisième en volume et quatorzième en valeur, représentant 20% de l'offre mondiale de génériques (Department of Pharmaceuticals, 2015). Elle réalise plus de 50% de son chiffre d'affaires total en exportant vers près de 200 pays à travers le monde (Department of Pharmaceuticals, 2015; IBEF, 2017).

Sans aucun doute, les firmes pharmaceutiques indiennes représentent un cas intéressant d'expansion à l'étranger par des multinationales de pays émergents (Ramamurti, 2009). Elles ont également attiré des économistes et des chercheurs en commerce international pour étudier leurs voies et leurs motivations d'internationalisation (Dixit & Yadav, 2015; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Pradhan & Alakshendra, 2006; Yeoh, 2011). Cependant, la plupart des études se sont concentrées sur la résolution du "comment" et du "pourquoi" de l'entrée sur le marché par rapport aux pays développés. La littérature sur l'internationalisation des firmes pharmaceutiques indiennes a adopté une approche réductionniste à l'égard des marchés pharmaceutiques dans les pays en développement, en particulier en Afrique subsaharienne. En effet, l'entrée sur le marché africain est traitée comme faisant partie du

[1] Cette introduction générale en français provient du Chapitre 1. Elle présente succinctement la logique de la recherche, expose les principales questions de recherche et l'organisation de la thèse. Pour plus de détails, voir le Chapitre 1.

processus naturel où les firmes entrent d'abord dans des pays qui sont culturellement et géographiquement proches, partagent une histoire commerciale et où l'environnement réglementaire est similaire à celui du pays d'origine. Ces facteurs réduisent la distance psychique et augmentent la propension à l'internationalisation et, au fur et à mesure que les firmes acquièrent de l'expérience, elles se dirigent vers des économies plus développées avec des marchés hautement réglementés (Erramilli, 1991; Johanson & Vahlne, 1977; Johanson & Wiedersheim-Paul, 1975). Si cet argument est vrai pour de nombreuses firmes indiennes (Dixit & Yadav, 2015; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Yeoh, 2011), il n'en est pas moins très simpliste et unitaire dans son approche pour diverses raisons.

Premièrement, cette démarche ne se penche pas sur les modes opérationnels post-entrée. Les marchés sont des constructions sociales et dynamiques par nature (Coriat & Weinstein, 2005; Fligstein, 1996; Fligstein & Calder, 2015; Spillman, 1999; Storr, 2010). Ils sont en constante évolution en raison des changements de la réglementation du pays d'accueil et du pays d'origine, des nouvelles technologies de production, de l'arrivée de gros acheteurs, de l'arrivée d'une nouvelle classe thérapeutique pour le traitement d'une maladie, de l'évolution de l'épidémiologie de la maladie, etc. En réponse, les firmes doivent continuellement reconsidérer leurs stratégies pour être dans le jeu. De plus, les firmes continuent de tirer des leçons de leurs expériences antérieures sur le même marché ou en pénétrant de nouveaux marchés. En fait, la plupart des grandes firmes indiennes comme Ranbaxy étaient entrées sur le marché africain il y a des décennies (Bowonder & Mastakar, 2005), et pendant ce temps, elles ont acquis de nouvelles capacités et un nouveau savoir-faire grâce à leurs opérations dans les pays développés. Cela indique que même si une firme a utilisé un mode particulier comme les exportations pour entrer sur le marché africain des médicaments dans le passé, elle doit évoluer au fil du temps et elle peut même utiliser un ensemble de stratégies combinées (Benito et al., 2009).

Deuxièmement, le marché pharmaceutique en Afrique peut être divisé en plusieurs marchés. Le marché public comprend l'achat de médicaments à l'aide de fonds provenant de gouvernements nationaux ou de donateurs internationaux. D'autre part, le marché privé peut être soit formel - avec une réglementation bien définie - soit informel et donc non réglementé. **Chacun de ces segments de marché est soumis à des réglementations différentes et le comportement et les intérêts des acteurs de chaque segment ne sont souvent pas les**

mêmes. Les caractéristiques des firmes peuvent varier d'un segment à l'autre et une même firme peut cibler différents segments avec des stratégies différentes.

Troisièmement, le marché pharmaceutique africain est également différent en raison de l'arrivée de nouvelle structure de gouvernance des marchés financés par des donateurs et dirigés par des organisations internationales. Ces acteurs agissent en tant que « market makers » et travaillent de diverses manières pour améliorer l'accès aux médicaments. Ils recommandent (et proscrivent) les médicaments, façonnent les politiques nationales, assurent la qualité des médicaments, fournissent un financement et une assistance technique, gèrent la chaîne d'approvisionnement, négocient les prix avec les fabricants, décident qui peut être compétitif et influencent le comportement des concurrents. L'action de ces organisations peut également avoir un impact sur le comportement et la stratégie des firmes à l'égard du marché africain.

Quatrièmement, la littérature existante sur le sujet a montré de diverses façons les voies d'internationalisation et les motivations de quelques firmes indiennes bien connues comme Ranbaxy, Dr Reddy's, Sun Pharma, Wockhardt et Nicholas Piramal qui ont pénétré avec succès les marchés des pays développés (Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Mowla et al., 2014; Yeoh, 2011). Ces firmes offrent en effet un cas intrigant pour évaluer la montée en puissance des firmes multinationales des pays émergents dans une industrie à forte intensité de connaissances et de technologie, comme les produits pharmaceutiques.

L'accent mis sur une poignée de firmes qui réussissent à l'échelle mondiale soulève également la question de savoir si elles représentent l'ensemble de l'industrie pharmaceutique indienne. Des firmes comme Ranbaxy et Dr. Reddy's ont la capacité financière et technologique de prendre le risque d'entrer sur les marchés hautement réglementés des pays développés. En effet, la plupart des acquisitions récentes aux États-Unis et en Europe n'ont été réalisées que par une minorité de firmes indiennes, et même parmi elles, il y avait une forte concentration entre les principaux acteurs (D. Nayyar, 2008). Un tel traitement ignore clairement un grand nombre de petites et de moyennes firmes indiennes qui réalisent une part substantielle de leurs revenus à l'étranger, principalement sur les marchés semi-réglementés d'Asie et d'Afrique. Ces firmes manquent de capacités technologiques pour le développement de produits et sont trop petites pour avoir la capacité financière d'établir une filiale étrangère ou d'effectuer une acquisition à l'étranger (Chaudhuri, 2015a; Sampath, 2005). La plupart de ces firmes n'ont pas de pré-qualification donnée par l'OMS (ou d'autres certifications de qualité comme USFDA et MHRA) en raison de l'investissement sous-jacent et choisissent d'opérer sur le marché privé

des médicaments par le biais d'exportations et la mise en œuvre d'accords contractuels (Chaudhuri, Mackintosh, & Mujinja, 2010). Cela distingue l'Afrique des marchés des pays développés où seules quelques grandes entreprises indiennes, capables de se conformer à l'environnement réglementaire rigoureux, fonctionnent avec succès.

Enfin, au cours des deux dernières décennies, une nouvelle forme d'organisations privées à but non lucratif a émergé. Ces organisations s'engagent principalement dans le développement de nouveaux médicaments en utilisant le modèle de partenariat public-privé, pour les maladies qui affectent de manière disproportionnée les pays en développement, en particulier l'Afrique subsaharienne (Chataway, Brusoni, Cacciatori, Hanlin, & Orsenigo, 2007; Grace, 2010; Muñoz, Visentin, Foray, & Gaulé, 2014). Ces partenariats dits de développement de produits (PDP) ne disposent pas de leur propre infrastructure pour effectuer toute la recherche et le développement en interne. Ils agissent plutôt comme des sociétés pharmaceutiques virtuelles et confient tous les travaux de Recherche et Développement (R&D) à un réseau d'institutions (J. F. Li & Garnsey, 2014; Munos, 2006). Certains d'entre eux, comme la « Drugs for Neglected Diseases Initiative » (DNDi) et le « Medicines for Malaria Venture » (MMV) ont réussi à commercialiser plusieurs nouveaux médicaments en partenariat avec des sociétés pharmaceutiques (Abdulla & Sagara, 2009; Bompart, Kiechel, Sebbag, & Pecoul, 2011; J. P. Cohen, Sturgeon, & Cohen, 2014; DNDi, 2005). Il convient de noter qu'ils ne s'associent pas seulement avec des multinationales de pays développés, mais qu'ils offrent aussi des possibilités aux firmes de pays en développement tel que l'Inde et la Chine. Par exemple, DNDi, en partenariat avec Cipla, une société indienne, a lancé une nouvelle formulation d'un médicament antipaludique, "artesunate-mefloquine" (DNDi, 2012; S. Wells, Diap, & Kiechel, 2013). Ce constat ouvre un nouveau champ pour examiner l'alliance des firmes indiennes avec des organisations internationales actives dans le domaine du développement de médicaments comme une stratégie d'entrée sur le marché africain.

Les questions de recherche principales et secondaires

Dans la lignée de la discussion de la section précédente et en suivant une démarche empirique, la principale question à laquelle cette thèse entend répondre est la suivante : **quelles sont les stratégies d'entrée sur le marché et d'exploitation des firmes pharmaceutiques indiennes en Afrique subsaharienne ?** Il faut ouvrir la « boîte noire » du commerce pharmaceutique entre l'Inde et les pays subsahariens, et faire la lumière sur les divers aspects de la chaîne

d'approvisionnement - de la production à l'approvisionnement - et examiner les différentes stratégies des firmes. En tant que tel, cela ne peut être traité de manière isolée et nécessite donc d'examiner et de comprendre le contexte institutionnel et historique dans lequel les firmes pharmaceutiques indiennes ont acquis leurs compétences et se sont développées à l'échelle internationale. L'industrie pharmaceutique indienne est devenue l'un des fournisseurs de médicaments génériques les plus compétitifs et les plus abordables au monde, et cela n'aurait été possible sans les *push factors* mise en place par le pays d'origine.

De même, il est tout aussi important de comprendre l'environnement institutionnel qui agit comme un *pull factor* incitant les firmes à se développer à l'échelle internationale. Il s'agit notamment d'identifier les changements institutionnels qui ont conduit à une augmentation de la demande de médicaments génériques dans les pays africains. Les pays en développement ont des institutions très différentes des économies développées et ont été reconnues comme étant des déterminants essentiels du comportement des firmes (Dunning & Lundan, 2008; Peng, Wang, & Jiang, 2008). Dans le contexte des marchés pharmaceutiques, l'environnement institutionnel soutenant le développement de nouveaux médicaments abordables et adaptés aux populations locales des pays en développement est également influencé et façonné par les organisations internationales.

La thèse vise donc à répondre aux questions suivantes :

1. Quels sont les changements institutionnels qui ont permis aux firmes indiennes de développer leurs capacités et de se développer à l'étranger ?

2. Quels ont été les changements dans l'environnement institutionnel des pays d'accueil qui ont servi de leviers d'attraction pour les firmes indiennes ?

3. Quel est le rôle de la nouvelle gouvernance internationale des marchés financés par les bailleurs de fonds dans l'expansion des firmes indiennes sur le marché africain ?

4. Comment le marché pharmaceutique africain est-il organisé ?

5. Comment les PDP et le cadre réglementaire mis en place par les organisations internationales peuvent-ils façonner la stratégie d'une firme ?

En répondant à ces questions, cette thèse ne s'intéresse pas seulement aux changements juridiques et politiques historiques qui régissent l'industrie pharmaceutique indienne et à

l'organisation du marché pharmaceutique en Afrique, mais démontre aussi la fonction des organisations internationales dans la formation du marché et le rôle croissant des firmes indiennes. Ce n'est qu'après avoir répondu à ces questions que l'on peut établir le contexte pour étudier les stratégies d'entrée et d'exploitation des firmes indiennes.

Organisation de la thèse

Le **Chapitre 2** débute par l'enquête sur les fondements institutionnels qui ont conduit au développement d'un secteur pharmaceutique compétent en Inde. Il s'agit d'aborder un certain nombre de politiques et de réformes gouvernementales antérieures à la libéralisation, comme la Loi sur les brevets indiens de 1970 et la Loi sur la Réglementation des Échanges (FERA) de 1973, entre autres, ainsi que de la création d'installations spécialisées dans la recherche pharmaceutique, considéré comme un élément crucial pour renforcer les capacités de la production pharmaceutique indienne. Ce chapitre traite ensuite des réformes post-libéralisation et de l'arrivée de l'Accord international sur les aspects des droits de propriété intellectuelle qui touchent au commerce (ADPIC) qui ont offert des *push factors* favorisant l'expansion des firmes indiennes à l'étranger. Plus important encore, il est également discuté des *pull factors* générés par les changements institutionnels dans les pays en développement et la montée en puissance de la nouvelle gouvernance des marchés financés par les bailleurs de fonds dans le contexte de la lutte contre les trois grandes pandémies - VIH/SIDA, tuberculose et paludisme - dans les pays du Sud. Cette enquête montre en outre comment ce nouveau marché financé par les bailleurs de fonds est régi par les organisations internationales à partir de la création de marché des thérapies combinées à base d'artémisinine (ACT) pour le paludisme. Enfin, il y est démontré le rôle croissant joué par les firmes indiennes sur le marché des ACT financés par les donateurs suite à l'analyse d'une base de données sur les antipaludéens achetés par le Fonds mondial de lutte contre le sida, la tuberculose et le paludisme.

Le **Chapitre 3** met en lumière la structure institutionnelle du marché pharmaceutique africain en se concentrant sur l'Afrique de l'Ouest francophone. À partir de l'analyse du système d'approvisionnement pharmaceutique Malien, cette partie porte sur l'organisation et le cadre réglementaire régissant le fonctionnement de quatre segments de marché différents :

i. Le marché public financé par les gouvernements nationaux

ii. Le marché public financé par des bailleurs de fonds internationaux

iii. Le marché privé formel

iv. Le marché privé informel

Une telle classification est nécessaire parce que les "règles du jeu" dans chacun de ces segments sont différentes. Les firmes utilisant l'internalisation doivent donc décider quels marchés cibler et quelle stratégie adopter étant donné qu'elles peuvent changer selon le segment de marché utilisé. Ce chapitre analyse ensuite les stratégies d'entrée et d'exploitation des firmes pharmaceutiques indiennes en se focalisant sur la chaîne d'approvisionnement dans les trois premiers segments de marché cités précédemment.

Enfin, le **Chapitre 4** explore le modèle PDP de R&D pharmaceutique à travers l'étude de Synriam pour identifier les opportunités que de telles initiatives peuvent offrir aux firmes indiennes et également, pour analyser les stratégies utilisées par Ranbaxy pour commercialiser ce produit face aux contraintes réglementaires mises en place par les organisations internationales.

1. Introduction to the Problematic: Key Elements from Literature

Over the course of the last half-century, India has developed a robust and competent pharmaceutical industry. It is not only profitable but has put Indian firms at the forefront of global business (Athreye & Kapur, 2009; Chittoor & Ray, 2007; Dhar & Gopakumar, 2009). Initially, Indian firms were widely referred to as "pirates" and "copycats" by the Big Pharma (Angeli, 2014; Chittoor, Sarkar, Ray, & Aulakh, 2009; Owen, 2013), but they have risen from the position of ordinary imitators to collaborators and competitors of developed country multinationals (MNCs) in the global market. Today, the Indian pharmaceutical industry ranks third in terms of volume and fourteenth in value, accounting for 20% of the global supply of generics (Department of Pharmaceuticals, 2015). It generates over 50% of its total turnover by exporting to nearly 200 countries (Department of Pharmaceuticals, 2015; IBEF, 2017) .

Undoubtedly, Indian pharmaceutical firms present an interesting case of foreign expansion by emerging country multinationals (Ramamurti, 2009) and have attracted economists and international business researchers to study their internationalization paths and motivations (Dixit & Yadav, 2015; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Pradhan & Alakshendra, 2006; Yeoh, 2011). However, the focus of most studies has been on solving the "hows" and "whys" of market entry with respect to developed countries. The internationalization literature on Indian pharmaceutical firms has taken a reductionist approach towards pharmaceutical markets in developing countries, particularly Sub-Saharan Africa. It treats them like an intermediate step before firms can move to highly regulated markets such as the United States (US) and Europe. This simplistic take on African market has restricted our understanding of its richness engendered by the complex interactions between firms, states and international organizations.

Not only has Africa been consistently the second largest destination for Indian pharmaceutical exports (Pharmexcil, 2015, 2016, 2017) but it has also been crucial in the rise and recognition of Indian firms. In fact, the international community first acknowledged the capabilities and effectiveness of Indian firms to provide good quality and affordable generic medicines during

the HIV/AIDS crisis in the 2000s (Owen, 2013). Since then, India firms have occupied a central place in the global fight against the three major pandemics – HIV, tuberculosis and malaria – which primarily concerns the countries of the south. Indeed, studies have shown that nearly 90% of the donor-funded antiretroviral medicines are purchased from Indian manufacturers (Sagaon-Teyssier, Singh, Dongmo-Nguimfack, & Moatti, 2016; Waning, Diedrichsen, & Moon, 2010). They have acted as the lifeline to treatment for so many that the industry is often called the "pharmacy of the developing world" (Hoen, 2009; Waning, Diedrichsen, et al., 2010). This dissertation is inspired by the role of Indian pharmaceutical firms towards the global access to essential medicines and is poised to shed new light on the functioning of Indian firms within the institutional context of the African market.

The present introductory chapter is dedicated to explaining theme and outline of the thesis by providing a broader understanding of **the central problematic, i.e., the market entry and operation strategies of Indian pharmaceutical firms in Sub-Saharan Africa**. Section 1.1 elucidates the conceptual foundations of 'internationalization' and 'entry-mode' and also explains the meanings of control, risk and resource commitment. Section 1.2 provides a review of the literature regarding the internationalization of Indian firms. Section 1.3 identifies the gap in the literature and provides the rationale for research. It then outlines the main research questions and objectives that this thesis intends to answer. Section 1.4 identifies the neo-institutional theory as the theoretical framework for achieving the objectives and provides arguments in its support. Section 1.5 presents the organization of rest of the chapters.

1.1. Internationalization

Economists have long been interested in the international activity of firms and today internationalization has evolved as a research area of its own that aims to deal with the diversity and dynamics of foreign market business arrangements. In its simplest sense internationalization refers to the outward expansion of a firm's operations beyond its home country. However, a standard definition of the term remains elusive even though researchers have taken different theoretical approaches to explain the concept.

Johanson & Vahlne (1977) have conceptualized internationalization as **a sequential process of increasing involvement of a firm in a foreign market**. In their view, firms develop their operation in individual countries in a sequence of stages or establishment chain which is a

function of their market knowledge and market commitment. Welch and Luostarinen (1988) regard internationalization as **"the process of increasing involvement in international operations"**. This broader approach allows taking both inward and outward sides of internationalization into account arguing that the international growth and success is partly dependent on inward performance.

Another definition of internationalization is offered by Beamish (1990) as "…the process by which firms both increase their awareness of the direct and indirect influence of international transactions on their future, and establish and conduct transactions with firms of other countries". Irrespective of their origin and approaches, all these definitions highlight the dynamic and evolutionary nature of internationalization and a characteristic pattern of transactions beyond national boundaries. Thus, internationalization is not a static phenomenon but rather a time-dependent process where firms carry out business transactions with foreign entities.

This thesis will use the definition proposed by Beamish (1990) with minor modifications:

"Internationalization is the process by which firms both increase their awareness of the direct and indirect influence of international transactions on their future, and establish and conduct transactions with foreign firms, **states, and transnational organizations**."

First, the definition proposed by Beamish integrates internal learning of the firm with its patterns of investment (Coviello & McAuley, 1999). Second, it not only recognizes the dynamic nature of internationalization but at the same time emphasizes that relationships built by a firm through international transactions facilitate its growth and expansion to other countries (Coviello & McAuley, 1999). Finally, in the globalized world of today, firms not only transact with other foreign firms but they also frequently deal with states and transnational organizations. Including "states and transnational organizations" in this definition, permits to look beyond firm-firm interaction and takes into account the role of states and international non-governmental organizations in the internationalization process. The inclusion of states and transnational organizations is particularly crucial for pharmaceutical markets where firms increasingly negotiate and transact with such entities. In many instances, the state or international organizations are the only buyers of particular kind of medicines. The most notable being antiretroviral therapies (ARVs) for the treatment of HIV/AIDS.

1.1.1. Market Entry and Entry Modes

After having chosen a foreign market for its product or services, a firm must decide an appropriate mode of entry for organizing its business activities abroad. Thus, choosing a suitable foreign market and selecting an appropriate entry mode is an intrinsic feature of a firm's internationalization process. It is a strategic decision (Agarwal & Ramaswami, 1992; Erramilli & Rao, 1990) that determines the organizational structure of a firm to manage its foreign operations effectively (Laufs & Schwens, 2014a). It is not a surprise then that the choice of the market entry mode and foreign operation has been a fundamental theme of the international business (IB) literature (Sharma & Erramilli, 2004). The choice of foreign market entry mode determines a firm's degree of resource commitment, risk exposure, management control and return on investment (Laufs & Schwens, 2014a; Pan & Tse, 2000).

However, what is meant by entry mode? The most widely accepted definition in the international business and marketing literature is the one given by Root, who defines entry mode as: **"an institutional arrangement that makes possible the entry of a company's products, technology, human skills, management or other resources into a foreign country"** (Root, 1994). This definition is broad in its scope and encompasses production, marketing and export activities of a firm in a foreign market.

Sharma and Erramilli (2004) further simplify the understanding of entry modes by providing a straightforward and comprehensive definition. In their words,

"An entry mode is a structural arrangement that allows a firm to implement its product market strategy in a host country either by carrying out only the marketing operations (i.e., via export modes), or both production and marketing operations there by itself or in partnership with others."

This definition allows considering multiple governance structures to operate in foreign markets and not only those that require a host country-based production. This is particularly important for studying firms from developing countries of which a large number are small and medium-sized enterprises (SMEs) who often choose exports to enter a host country rather than production-based mechanisms.

After having decided to enter a host country, a firm has a wide range of mode choices to select from, and each entry mode is associated with its own set of advantages and drawbacks. These entry modes can be grouped hierarchically into non-equity and equity-based modes depending

upon if they entail capital investment in the host country or not (Erramilli, Agarwal, & Dev, 2002; Pan & Tse, 2000). Non-equity modes include exports and contractual agreements and require a smaller market commitment by the entrant firm. Whereas, equity modes include equity joint ventures & wholly owned subsidiaries and reflect much more significant and irreversible commitment to a foreign market by the entrant as they require establishing independent organizations abroad (Pan & Tse, 2000; Peng, 2014).

There can be further variations within a given mode of entry (Anderson & Gatignon, 1986; Hill, Hwang, & Kim, 1990; Pan & Tse, 2000). For example, exporting can be either indirect or direct. In the indirect exports mode, a firm has no investment presence in the host country and uses its home country intermediaries to enter its product in a foreign market. The home country intermediary may be a trading house, an export management company or an export broker with a business presence in the host country (Sharma & Erramilli, 2004). In this mode, a firm has no control over how its products are distributed or marketed in the host country, but it also minimizes host country involvement and perceived risk. On the other hand, direct exports require a firm to use either its own channels or local intermediaries (distributors/ agents) for marketing its products in the host country. The former route is known as direct exporting via the company-owned channel, and the latter is known as direct exporting via host country intermediary (Sharma & Erramilli, 2004). It offers economies of scale from home country based production and better control over distribution channels compared to indirect exports (Peng, 2014).

Contractual agreements are another sub-group of non-equity mode and include licensing, franchising and management contract. In licensing or franchising (in service firm), the entrant firm allows the host country partner or collaborator to use its proprietary technology or knowledge (patents, trademarks, and know-how among others) in return for some payment (Aulakh, Jiang, & Pan, 2010; Erramilli et al., 2002). The licensor or franchiser can also provide technical advice, training and marketing support but has minimal involvement in day-to-day operation (Erramilli et al., 2002). The advantage of this method to internationalize is a low capital investment by the entrant, but the downside is that the entrant has less control over how the technology is used and there is a risk of dissemination of proprietary knowledge.

Management contracts are another non-equity contractual agreements where the entrant firm not only leases its brand-name but also provides active managerial support through its onsite managers in exchange for some combination of royalties, management fees, and a share of

profits (Erramilli et al., 2002). It offers more strategic and operational control over day-to-day activities of the host country collaborator, but at the same time, it is more expensive than franchising or licensing due to the active presence of onsite staff (Erramilli et al., 2002).

All form of equity modes involves some form of FDI that separates them from non-equity entry modes. Joint ventures (JVs) comprise the lower end of the hierarchy of equity-based entry modes. They can be broadly categorized into the minority (less than 50 percent equity), equal (50 percent equity) and majority (more than 50 percent equity) JVs, depending upon the equity stake of the entrant firm (Pan & Tse, 2000; Peng, 2014). There can be production joint ventures, where the host partner is responsible for the production, while the entrant takes the marketing responsibilities. Likewise, in a marketing joint venture, the host partner assumes the primary responsibility of marketing and the entrant is responsible for production (Sharma & Erramilli, 2004). JVs can offer a strategic balance between risks and return in a foreign market as the entering firm shares them with the local partner and at the same time, it also permits a certain degree of operational control depending upon the nature of the JV. Further, JVs also allow the entrant firm to learn more about the host country, and it is politically more acceptable. The major drawback of JVs is the partners often have conflicting goals, and operational control can be difficult to achieve (Peng, 2014).

Finally, an entrant firm can invest in wholly owned subsidiary either by acquisition of another host country firm or through greenfield investment by starting a new firm from scratch (Pan & Tse, 2000; Sharma & Erramilli, 2004). A wholly owned subsidiary through greenfield investment grants the entrant total strategic and operational control over the activities of the new firm that can be easily aligned with the global strategy of the parent company. It also protects the entrant from the leakage of proprietary technology and know-how to competitors. Nevertheless, staring a greenfield subsidiary is a risky endeavor as the entrant bears all the expenses and moreover, it can be a lengthy process that can take years. The alternative is to acquire a local firm. Acquisitions have all the advantages of a greenfield subsidiary, and additionally, they are a faster mode of entry. However, they may result in post-acquisition integration problems.

1.1.2. Control, Risk and Resource Commitment

Anderson and Gatignon (1986) regard control as the firm's ability to influence systems, methods, and decisions in the foreign market. Similarly, Hill et al. (1990) define control as the firm's authority over operational and strategic decision making in the foreign market. Control is essential for coordinated action, implementing and revising strategies and resolving disputes between parties in a contract. It is linked to the ability to commit resources and willingness to take responsibilities and thus, is a unique and distinguishable feature of entry modes. Each of the entry modes can be arranged from a low to high degree of control, resource commitment and exposure to risk in the host country (Anderson & Gatignon, 1986; Hill et al., 1990).

Export and contractual agreements like licensing offers the lowest degree of control while wholly owned subsidiaries provide the highest level of control over foreign operations of a firm (Hill et al., 1990). In case of licensing, the control is exerted by the terms of the licensing contract, but it is not all-embracing due to the bounded rationality of the entrant. In case of a wholly owned subsidiary, certain strategic decision making and control over day-to-day operations may be delegated to the foreign subsidiary, but the parent firm holds the ultimate control. In the case of joint ventures, the level of control lies somewhere between licensing and wholly owned subsidiary and depends upon the equity share and the number of parties involved. Nevertheless, in any case, the control must be shared with the venture partners (Hill et al., 1990; Laufs & Schwens, 2014a).

The degree of control is closely associated with the resource commitment in the foreign market. The higher the level of control, the more resource the firm needs to commit (Agarwal & Ramaswami, 1992). So, in case of wholly owned greenfield subsidiary, the internationalizing firm has to bear all the cost of starting a new firm and serving the foreign market, and thus it commits more resources (Hill et al., 1990; Laufs & Schwens, 2014a). On the other hand, in case of exports and licensing the resource commitment is the lowest. The level of resource commitment in case of joint ventures lies between these two extremes depending upon the type of joint venture: minority, majority or equity joint venture.

Also, upon entering a foreign market, a firm faces both the risk of unintended knowledge diffusion (e.g., a firm-specific technology) and losing its resources if the foreign market engagement fails. If a firm commits more resources (e.g., wholly owned subsidiary), it will have a higher risk to lose them if the foreign engagement fails but, greater resource commitment

will provide safety against the diffusion of firm-specific know-how (Agarwal & Ramaswami, 1992; Hill et al., 1990).

1.1.3. Towards a Realistic Conceptualization of Foreign Operation Modes

Previous sections have helped to conceptualize the meaning of internationalization and entry modes. They have also clarified that entry mode choices are innately bound to risk, resource commitment and control of the foreign market activities. However, does the foreign market entry decision and entry mode choices represent a static phenomenon? Alternatively, is it possible for firms to change modes over time? In fact, studies have long shown that firms change their operation mode over time (Johanson & Vahlne, 1977; Johanson & Wiedersheim-Paul, 1975). Further, it is possible to switch not only from one mode to another, but changes can also be made within an existing mode like export (Benito, Pedersen, & Petersen, 2005), establishing the dynamic nature of internationalization.

However, while it is an accepted fact that internationalizing firms change modes over time as a part of their foreign market strategy; can firms use more than one mode at a given point in time? Much of the extant research on entry mode choice and internationalization studies are unitary in their approach as they consider foreign operation mode as a singular entity (Benito, Petersen, & Welch, 2009). They have focused on the analysis of alternative entry mode choices. For example, export or contractual agreements and production units have been compared as alternative ways of organizing international operations or different ways of doing export have been compared (Petersen & Welch, 2002). It means the choice is either this or that.

In contrast to the prevailing view, few researchers have remarkably noted that firms do not only change their mode of operation over time but also use modes in combination in a given market (Benito et al., 2009; Kedron & Bagchi-Sen, 2011, 2012; Petersen, Benito, Welch, & Asmussen, 2008; Petersen & Welch, 2002). They claim that **firms can enter a foreign market with more than one mode and new modes can be added to existing one to create "mode combinations" or "mode package"**. They cite multiple examples like the operations of Kone in Japan (Benito et al., 2009) and Ranbaxy and Dr. Reddy's in the US and Europe (Kedron & Bagchi-Sen, 2011, 2012) to support their claim that use of mode packages and subsequent changes within and between mode packages is not uncommon. Thus, foreign operations of internationalizing firms indicate a more complex reality where multiple and constantly

changing mode packages are utilized. In such complex and sophisticated governance forms, mode packages are attached to a broad range of business activities undertaken by the entrant in the host country.

At this point, it is essential to consider how operation modes are different in conceptualization as compared to entry modes. An entry mode signifies the mode used to enter a foreign market but not beyond that point. On the other hand, Benito et al. (2009) define foreign operation modes as **"the organizational arrangements that a company uses to conduct international business activities"**. Operation modes thus represent not a single mode but rather a package of modes that firms use in the host country to organize international business (Benito et al., 2009). Further, these modes can either have little connection and they might be directed to achieve different goals, or they might be tightly connected under the overall strategy to penetrate the market (Benito et al., 2009).

It is with this conceptualization of operation modes as proposed by Benito et al. (2009) this thesis will explore the operational strategies of Indian pharmaceutical firms in Sub-Saharan Africa.

1.2. Internationalization of Indian Pharmaceutical Firms: A Review of Literature

However, the extant literature on internationalization is practically silent regarding the functioning of Indian firms in the African[2] market. To explore this issue comprehensively we undertook a review of the internationalization strategies of Indian pharmaceutical firms. The review aimed to identify the current state of knowledge regarding motivations of Indian pharmaceutical firms to internationalize, choice of entry modes and geographical coverage. This review served two purposes. First, it allowed summarizing the current knowledge about internationalization behavior of Indian pharmaceutical firms globally, and second, it allowed us to identify the gaps in the current research on the market entry and operation strategies of Indian pharmaceutical firms in Sub-Saharan Africa. Fink's (2014) guideline for conducting research literature reviews was consulted for guidance to present a comprehensive picture of the foreign expansion by Indian firms. It involved searching online databases and article

[2] Unless otherwise stated the use of "African market" refers to the pharmaceutical market in Sub-Saharan Africa".

reference lists to identify the articles on internationalization of Indian pharmaceutical firms between 1991 and 2016. It seemed reasonable to select 1991 as the starting point for inclusion because it marked the beginning of the economic liberalization of India that led to several policies and reforms, like easing FDI norms, aimed at reducing inward and outward trade barriers (see chapter 2). Economic liberalization helped both – foreign firms to enter India and Indian firms to venture outside the home country. Further, India signed the multilateral agreement on the Trade Related Aspects of Intellectual Property Rights (TRIPS) in 1994 that led to a series of intellectual property reforms. These changes created a global concern and interest in the future strategies of Indian pharmaceutical firms. Further, a fixed time frame permits to select a reasonable number of articles to summarize the current understanding of the subject and identify gaps.

"Scopus" – one of the largest databases of peer-reviewed research – was the main source of information to identify eligible studies for inclusion in this review. The search was supplemented by "EBSCO" and "Google Scholar" databases to have a wider coverage of social science domains – economics, international business, international marketing, and entrepreneurship – in which articles on the topic of interest have been published. The keywords used for database search included, "market entry", "entry mode", "internationalization or internationalisation", in combination with "Indian pharmaceutical industry", and "Indian pharmaceutical firms" (to name a few). The reference lists of the articles identified through the database search were also checked to have comprehensive coverage. Further, studies citing the identified articles were also scrutenized using "Google Scholar".

To be eligible for the review a study had to fulfil the following three criteria: its focus had to be on Indian pharmaceutical firms, it must concentrate on the choice of foreign market entry modes and international business strategies of Indian pharmaceutical firms, and it had to be an empirical (qualitative or quantitative) study published between 1991 and 2016. Therefore, this review excluded papers that focused primarily on general trends in Indian pharmaceutical industry, comparative advantage, technological leapfrogging or effect of institutional changes on organizational reforms (Athreye & Godley, 2009; Chittoor et al., 2009; Fei-fei & Ying-ming, 2010; Kothari, Kotabe, & Murphy, 2013; Mahajan, Nauriyal, & Singh, 2015; Pradhan, 2006). Table 1.1 provides a comprehensive summary of the identified studies in terms of journals, theoretical framework, geographical region or country and firms in focus. It also outlines their core research questions and main findings.

1.2.1. Results of the Review and Development of Research Agenda for Thesis

1.2.1.1. Theoretical Frameworks Identified in the Review

Five theoretical frameworks – Ownership-Location-Internalization (OLI) model or eclectic paradigm, institutional theory, stage model and Linkage-Leverage-Learning – have been employed by the studies in this review including a new model proposed by Dixit and Yadav (2015), to analyze the internationalization of Indian pharmaceutical firms. The OLI or eclectic paradigm was proposed and by John Dunning in a series of publications (Dunning, 1980, 1988, 1995). He argued that foreign business operations of a firm are determined by three factors which include its ownership (O), location (L) and internalization (I) specific advantages. A firm will internationalize to exploit its existing ownership-specific advantages such as production technique, trademark, entrepreneurial skills, and intellectual property among others. Further, the choice of foreign location is motivated by the advantages it offers in terms of raw materials, labor, taxes and tariffs. Lastly, the choice of market entry mode is determined by comparing the advantages between own production, producing through a partnership or not producing in the foreign country at all (e.g. using exports) (Dunning, 1980, 1995).

Stage theory, also known as '*process view*, *Uppsala model*, or *chain of establishment approach*, was proposed by Johanson and Wiedersheim-Paul (1975) and Johanson and Vahlne (1977) through their works on Swedish firms. They asserted that the establishment of international operations of firms is a time-dependent and incremental process. Firms first develop in the domestic market and then gradually extend their international operations. This is because firms operate in uncertain environments and lack market knowledge. The perceived risk is higher and consequently the market commitment is low.

In the stage model, the internationalization of a firm has four distinct and successive establishment of operations:

i. No export, i.e., no international activity
ii. Export via independent representatives or agents
iii. Establishment of sales subsidiary
iv. Local manufacturing/production plant (Johanson & Vahlne, 1977; Johanson & Wiedersheim-Paul, 1975)

To reduce uncertainty, firms start their international activity through indirect export to countries where the perceived *psychic distance* is small. That is, they select countries which

are comparatively well known and similar regarding business practices, education, industrial development, and other factors (Johanson & Vahlne, 1977; Johanson & Wiedersheim-Paul, 1975).

Linkage-Leverage-Learning (LLL) emphasizes the role of networks and argues that it is easier for firms from emerging economies to build new capabilities through learning within established networks rather than using a sequential process of Uppsala model (Mathews, 2006). In other words, firms enter international business to develop new resources and capabilities by using external linkages. Finally, institutional theory suggests that it is the institutional environment of the countries that affect the behavior of the firm by putting the *rules of the game* place (North, 1990) (more on institutional theory in section 1.5).

Dunning's OLI framework is used by four studies in the present review. However, all of them have either used OLI framework with extensions or in combination with other theories. Kedron & Bagchi-Sen (2011, 2012) used an extended OLI framework that allows accounting for asset augmenting motivations of firms. Yeoh (2011) reported that mainstream theories like OLI and stage model could explain the early stages of internationalization while new theories like LLL developed particularly in the context of emerging economy firms are more useful in the later stages of internationalization. Similarly, Mowla et al. (2014), find support for OLI framework and partial evidence for the stage model.

Three studies (Chittoor & Ray, 2007; Kale, 2010a; Pradhan & Alakshendra, 2006) have used institutional theory to explain the internationalization strategies of Indian pharmaceutical firms. However, even though other authors (Dixit & Yadav, 2015; Kedron & Bagchi-Sen, 2011, 2012; Sweet, 2010; Yeoh, 2011) have used different frameworks, they explicitly mention the effect of government policies and regulations on the options available to firms and choices made by them. The institutional theory argues that firm behavior is shaped by its external (and internal) institutional environment.

The external environment can be both based at home or belong to the host country and create *push and pull* factors respectively that favors internationalization (One should also keep in mind that home country institutions can also deter international expansion while host country policies can create barriers to entry).

It is accepted that the protectionist institutional environment during 1970-1989 created the modern Indian pharmaceutical industry through a plethora of reforms directed towards

achieving self-sufficiency in medicines (see chapter 2). This period is famously marked by the Patents Act of 1970 that eliminated product patents and recognized only process patents. The industry also got support due to policies regulating foreign exchanges and drug prices. This era of process patent regime spurred technological innovation in local firms through reverse engineering, adaptation and process development. This domestic capacity building was also supported by government investment in scientific, skill and physical infrastructures like research institutions and laboratories, centers of higher and technical education, and banking sector (Pradhan & Alakshendra, 2006). Further, articles in this review also agree that institutional transitions in India in the 1990s – primarily economic liberalization and signing of TRIPS – gave thrust to the international expansion of Indian firms. First, liberalization reduced limits on FDI and access to international capital became easily accessible. Second, TRIPS resulted in the gradual strengthening of patent laws in India. These changes resulted in an increased domestic competition at home while opened doors to new markets (Chittoor & Ray, 2007; Pradhan & Alakshendra, 2006; Yeoh, 2011).

It is also noteworthy that regulatory changes in foreign countries also guided internationalization strategies of Indian firms. Introduction of Hatch-Waxman Act (1984)[3] and generic substitution measure to decrease cost in many European countries like the United Kingdom, Germany and France opened generic markets in these countries to Indian firms (Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012). In contrast, Indian firms took a cautious approach towards Japanese market until 2005 because it was perceived closed, lacking transparency and dominated by Japanese firms (Dixit & Yadav, 2015; Yeoh, 2011). The role of host country regulations is also evident from the following observation by Sweet (2010):

"The most important catalyst for Indian investment and activity in Brazil, however, was the establishment of a generics category in 1999. In the year before the law was passed, no Indian firm had local activities in the region. In the year following the generics law, five Indian companies established subsidiaries in Brazil, all pursuing market seeking strategies" (italics added).

[3] See section 2.4.1.1 for details.

Table 1.1 Review of internationalization strategies of Indian pharmaceutical firms

Study	Journal	Theoretical Framework (Used or Tested)	Geographical Region/ Host Country	Firms in Focus	Research Question/Major Research Focus	Major Finding
(Bartlett & Ghoshal, 2000)	HBR	-	Not specified/ general	Ranbaxy, Other firms from various industries and different countries	What is the business strategy of successful emerging country multinationals? How do these firms overcome the liability of origin? How do they exploit late mover advantage and capture and leverage learning in global markets?	- Strong commitment of the top management to global entrepreneurialism and their openness to new ideas - Overcoming the psychological burden to compete with developed country firms. - Hiring capable and qualified managers even from foreign countries - Supported the program directed to foreign operations and R&D efforts to develop either new drugs or new drug delivery system
(Bowonder & Mastakar, 2005)	IJTM	-	Multiple	Ranbaxy	Examination of the rapid international growth of Ranbaxy	- Ranbaxy used a three-pronged strategy: - Innovation: R&D, new business divisions catering different geographical regions - Alliances: R&D, clinical, marketing, manufacturing - Globalization: Global subsidiaries and joint ventures
(Pradhan & Alakshendra, 2006)	ISIDWP	IT*	Focus on developed countries	Ranbaxy	Comparison of acquisition and greenfield investment as suitable modes of internationalization for Indian firms	- Acquisition is a better mode of international expansion of Indian firms because it provides all the benefit of the former and also brings additional competitive advantages like distribution and market networks
(Chittoor & Ray, 2007)	JIM	IT*	Focus on developed countries	Sample of 40 firms for strategic group analysis (Also specific cases of Ranbaxy, Dishman, Dr. Reddy's, & Neuland Labs)	Do emerging economy firms coming from same geographical, economic and industry context follow a common or different competitive strategy to internationalize and compete successfully in global markets? If the strategies are different, then what are its performance implications?	- Most firms in the sample use exploitation of their existing advantages - Some firms supplement exploitation strategy with exploration along the direction of new products and markets (overseas acquisitions, import of know-how, equipment and so on) - Such differences in strategy originate from the top management leadership
(Kale, 2010a)	PB	IT	Europe/US	Ranbaxy, Dr. Reddy's, Wockhardt; Nicholas Piramal, & Sun Pharma	Analysis of motivation and internationalization strategies of Indian pharmaceutical firms	- Indian firms are using both subsidiaries and acquisitions to internationalize with the aim to access resources, move up the value chain and enter new markets.
(Sweet, 2010)	IJEM	-	Brazil	Multiple	Examination of the entry of y of Indian firms in the Latin American pharmaceutical market	- Operating in a weak institutional environment does not confer specific market advantages - Indian firms simultaneously cooperate and compete with local firms

(Kedron & Bagchi-Sen, 2011)	AG	OLI with extensions	US	Ranbaxy & Dr. Reddy's	Examination of foreign market entry strategies of Indian pharmaceutical firms in the United States	- Indian firms use multiple strategies simultaneously to pursue multiple goals - These strategies are evolving in nature and adjustable according to changing internal and external environment
(Yeoh, 2011)	IMR	Different theoretical frameworks to explain different stages of internationalization (OLI, Stage Model, LLL)	Multiple	Ranbaxy & Wockhardt	Study of internationalization strategies of two established Indian pharmaceutical companies	- Overseas acquisitions are more advantageous to Indian firms as compared to greenfield investment - Early and late internationalizers very in their approach to internationalization. Early internationalizers followed a more path dependent stage model of international expansion but late internationalizers like Wockhardt look both at developed and developing country markets simultaneously
(Kedron & Bagchi-Sen, 2012)	JEG	OLI with extensions	Europe	Ranbaxy & Dr. Reddy's	Examination of foreign market entry strategies of Indian pharmaceutical firms in Europe	- Indian pharmaceutical firms succeed in European markets by simultaneously pursuing multiple foreign operations motivated by asset augmenting and asset exploiting goals
(Mowla, Hoque, Mamun, & Uddin, 2014)	ASS	OLI & Stage Model	Multiple	Ranbaxy	How are Indian emerging multinationals taking decisions in case of entry mode selection and location choice?	- Ranbaxy has primarily used acquisition in Europe and USA to build dynamic capabilities and to overcome made-in-India image
(Dixit & Yadav, 2015)	JGM	Dixit-Yadav Model	Multiple	Undisclosed	What motivates Indian pharmaceutical firms to internationalize their operations? What is the internationalization process regarding markets entered, entry strategy, the sequence of market entry, and products offered?	- Motive: higher margins, market seeking, survival, following others, government benefit to exporters - Firms follow a sequential expansion from less-regulated to highly regulated markets. - Early-internationalizers differ from later-internationalizers in their sequence - Entry strategy: Marketing subsidiary, joint venture, exports, etc.

Journal: HBR = Harvard Business Review, IJTM = International Journal of Technology Management, ISIDWP = Indian Institute of Industrial Development, JIM = Journal of International Management, PB = Pharmabuzz, IJEM = International Journal of Emerging Markets, AG = Applied Geography, IMR = International Marketing Review, JEG = Journal of Economic Geography, ASS = Asian Social Science, JGM = Journal of Global Marketing. OLI = Ownership-Location-Internalization (or Eclectic paradigm), IT = institutional Theory, SM = Stage Model (Uppsala Model), LLL = Linkage-Leverage-Learning.

"" = Not explicitly mentioned by the authors but apparent from the use of institutional factors.*

1.2.1.2. Types of Internationalizing Firms

Chittoor & Ray (2007) classify internationalizing Indian pharmaceutical firms into five strategic groups: *exploiters, explorers, outsourcees, emerging global firms, and global firm.* Exploiters concentrate on exploiting their existing skills. They mainly deal in the international market for active pharmaceutical ingredients (APIs) and are at the lower end of the value chain. They leverage on the country-specific competitive advantage of skills in chemical synthesis and process research together with low manufacturing cost. Explorers are firms that have made some advancements in the formulations market of developed countries evident from their Abbreviated New Drug Application (ANDA) filings which is required by the United States Food & Drug Administration (USFDA) for the review and approval of a generic drug product (Here the focus is on developed markets because criteria for selection is ANDA filings). They also have one or two new chemical entity (NCE) under development. These firms take serious endeavor to acquire new capabilities and venture into new markets. Outsourcees are a special group of internationalizing firms who primarily rely on contract research and manufacturing (CRAM) for their international expansion. They rely on the traditional competencies of Indian pharmaceutical industry like exploiters. Emerging global firms are characterized by their relentless effort to acquire multifaceted capabilities to emerge as true international players. They are much ahead in the process of internationalization with very high number of ANDA filings and number of NCEs under development. Finally, a global firm (Ranbaxy, the only firm identified by the authors) is the one that has manufacturing and marketing operations in multiple countries and generates over 70 percent of its revenue in foreign markets.

1.2.1.3. Phases of Internationalization

Pradhan & Alakshendra (2006) have categorized the international expansion of Indian pharmaceutical firms in four time specific phases. Distinctive characteristics of these phases are summarized below:

- Phase 1 (1947-1969):
    - Domination by foreign MNCs
    - Lack of technical capabilities to support local production
    - Emphasis on education, skills, infrastructure
    - Import dependency and minimal export

- Phase 2 (1970-1989):
    - Enactment of the Patent Act of 1970 and creation of firm-specific advantage of local firms
    - Additional supporting regulations: Such as Foreign Exchange Regulation Act (FERA), and New Drug Polic.
    - Emergence of strong domestic industry, reduction in trade deficit of pharmaceuticals, foreign market entry mainly through exports and limited joint ventures and subsidiaries (only one during the period) in developing countries

- Phase 3 (1990-1999)
    - Industry dominated by domestic firms, rise in exports leading to trade surplus,
    - Apart from greenfield investments, acquisition emerged as a major mode of internationalization
    - Emergence of pharmaceutical contract manufacturing as a new growth strategy

- Phase 4 (2000-onwards)
    - Growing export and trade surplus
    - Increase in greenfield investments and acquisitions
    - Outsourcing and strategic alliances

1.2.1.4. Motivations to Internationalize

So, Indian pharmaceutical industry has come a long way from having almost no international activity to registering a globalized presence. What has been the motives for internationalization by Indian firms? Dixit & Yadav (2015), identify higher margins on exports and opportunity to grow in new markets as the primary motivation for internationalization. Other critical motives of Indian firms are to seek assets and gain efficiency. This is corroborated by Kale (2010), and Yeoh (2011). Indian firms mainly have market seeking motivation in developing countries but in developed countries market seeking motivation is supplemented by asset and efficiency seeking motivations (Sweet, 2010; Yeoh, 2011). By acquiring R&D capabilities, regulatory knowledge, new technologies, marketing and distribution channels and brands in developed countries, Indian firms are aspiring to move up the value chain and sustain global competitiveness (Kale, 2010a). Thus, foreign market entry is motivated by both asset

exploitation and asset augmentation goals (Kedron & Bagchi-Sen, 2011, 2012). Additionally, developing a presence in markets like the US, France, Germany and the UK grants legitimacy in high technology industries like pharmaceuticals. It also allows Indian firms to get rid of their liability of foreignness and overcome the negative made-in-India image from the perspective of foreign consumers (Mowla et al., 2014; Yeoh, 2011). Finally, concerns for survival in the new era of globalization, following the success of other Indian firms in international markets and advantages offered by the government of India for exports also drives firms to engage in the foreign market entry (Dixit & Yadav, 2015). Thus, contrary to the conventional wisdom that developing country firms learn from foreign MNCs located in the home country and technology transfer through FDI in local firms, Indian firms have taken a high-risk approach of locating themselves in developed countries to acquire knowledge and build capabilities.

1.2.1.5. Sequence of Internationalization and Market Entry Strategies

Indian firms have entered into numerous countries using a variety of market entry strategies at different times. Yeoh (2011) groups these countries into three categories based on the degree of stringency of the regulatory environment. Unregulated markets that include Africa and South-East Asia are characterized by the ease of pharmaceutical regulation and similarity to India. Regulated markets, made up of developed countries such as the US, the European Union, and Japan have stringent requirements for the marketing and registration of products. So, the barriers to enter the market in terms of intellectual property, product quality, regulatory knowledge, distribution channels are high but the same time the competition is low and profit margins are higher. Semi-regulated markets consist of Latin American Countries like Brazil and Mexico and South Africa which are not as liberal as unregulated markets but not as stringent as regulated ones. Studies by the researchers in this review point out that Indian firms – exploiting their low-cost and robust manufacturing capabilities – started their foreign expansion by entering into less-regulated countries of Africa and Southeast Asia where regulatory requirements were similar to home. Having taken lessons in internationalization by operating in less-regulated countries, Indian firms moved to semi- and highly regulated markets of developed countries. However, there is a marked difference in the sequence of Internationalization between the firms. Dixit and Yadav (2015) differentiate these firms as early and later internationalizers. The former ventured into internationalization very early and

prepared for each subsequent expansion sequentially as proposed by the stage model. However, the latter group entered into internationalization late but followed an accelerated pace by looking at multiple markets simultaneously and not following a strict sequential path. For example, one firm (coded XBR) in their study moved straight from a less-regulated market to a highly regulated market (US) and only then entered a semi-regulated market (Brazil). Similarly, Yeoh (2011) noted that While Ranbaxy followed a sequential path, Wockhardt followed an accelerated pace of internationalization (Russia-Africa-Europe-Latin America and South Africa/Japan-US). These firms taking an accelerated pace used industry experience of other firms to their advantage and set up practices according to international regulatory requirements.

Concerning the choice of entry mode, export remains the primary strategy of Indian firms, but it is increasingly supplemented by greenfield investments, acquisitions, joint ventures, strategic alliances and licensing. In the early years of the industry, firms mainly used joint ventures to enter into other developing countries. However, since 2000, acquisition has become the prominent mode of international expansion in the US and Europe. Researchers (Kale, 2010a; Pradhan & Alakshendra, 2006; Yeoh, 2011) agree in suggesting that acquisition is more advantageous than greenfield investments for Indian firms when expanding in developed countries. Acquisition targeted to foreign companies provide synergies between cheap production and process capabilities of Indian firms and marketing and distribution channels, regulatory knowledge, and high-end technologies of the acquired firms. Further, acquisition allows taking a 'learning leap' in building knowledge and technological capabilities at an accelerated pace. Indian firms also face the 'liability of foreignness' due to problems of legitimacy and credibility. Acquiring foreign firms permit to overcome these problems as a guarantor of their product quality and safety and frees them from the 'made-in-India' image.

In developing country setting of Latin America, Sweet (2010) observed that Indian firms have extensively favored greenfield projects than outright acquisitions. She explains that this can be attributed to lack of significant trade history to establish potential partners. This is combined with the geographical distance which increases the complexity of principal-agent problems. Additionally, choice of entry mode also depends on experience as found by Dixit and Yadav (2015). Firms with experience and resources have a preference to operate through their own marketing sales force and take higher risk mode like an acquisition. On the other hand, firms

with less experience and limited resources prefer export through a distributor or supplying to government agencies.

Only two scholars (Kedron & Bagchi-Sen, 2011, 2012) explicitly talk about the conception of entry mode as a mode packages in their study of entry mode choices of Indian firms in the US and Europe. Here they follow Benito et al. (2009) in their conceptualization of foreign market entry and operation that allows for:

i. Simultaneous use of multiple strategies
ii. Non-incremental adjustment of ongoing strategies
iii. Interaction between strategies, and
iv. Analysis of operation and strategies over time

Other researchers in this review have also taken the dynamic nature of internationalization into account as they follow the course of foreign expansion of selected firms. However, they have treated market entry as a onetime activity and have not addressed subsequent changes in strategy as a part of the package. Kedron & Bagchi-Sen (2011) show that how both Ranbaxy and Dr. Reddy's used their previous experience with the US market, when their Indian facilities were approved by the USFDA for exports, to acquire local firms. Over time these firms used multiple market entry strategies (export of generics, acquisition, and subsidiary) targeted to multiple goals to sustain in the US market. Also, they found that both Indian firms competed and cooperated with local MNCs a part of their strategy. Ranbaxy entered into an infringement lawsuit against GlaxoSmithKline over *Ceftin* but it does not stop them to continue their R&D partnership which was towards the development of NCEs, and both companies kept it separate from generic business. Simultaneous competing and cooperating behavior with local firms in Latin America was also reported by Sweet (2010).

1.3. Setting up the Scene

1.3.1. Gaps in the Literature and Rationale for Research

It is clear that from this review that the current entry mode research literature on Indian pharmaceutical firms does not focus on the African pharmaceutical market. Researchers have certainly augmented our understanding of the international expansion by Indian pharmaceutical

firms. However, their aim has been to analyze the market entry strategies of emerging country multinationals into developed country markets of North America, Europe, and Japan. Only one researcher (Sweet, 2010) in this review has investigated the entry strategies of Indian firms in a developing country context by focusing on Brazil.

Entry into African market is taken for granted, and post-entry operations of Indian firms within Africa have not received much attention in the internationalization literature. In fact, in line with the stage model of internationalization, entry to the African market is treated as part of the natural process where firms first enter countries that are culturally and geographically proximate, share a history of trade, and where the regulatory environment is similar to the home country. These factors reduce the psychic distance and increase the proclivity to internationalize and gradually as firms get the experience they make their way to more developed economies with highly regulated markets (Erramilli, 1991; Johanson & Vahlne, 1977; Johanson & Wiedersheim-Paul, 1975). While this argument holds true for many Indian firms (Dixit & Yadav, 2015; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Yeoh, 2011), nevertheless it is very simplistic and unitary in its approach for various reasons.

First, it does not look into post-entry operational modes. Markets are social constructs and dynamic in nature (Coriat & Weinstein, 2005; Fligstein, 1996; Fligstein & Calder, 2015; Spillman, 1999; Storr, 2010). They are under constant evolution due to change in the host and home country regulations, new technology in production, entry of large buyers, the arrival of a new therapeutic class for the treatment of a disease, changes in disease epidemiology and so on. As a response, firms continuously need to examine their strategies to be in the game. Also, firms keep on learning from previous experiences in the same market or by entering new markets. In fact, most of the big Indian firms like Ranbaxy had entered the African market decades ago (Bowonder & Mastakar, 2005), and during this time they have acquired new capabilities and know-how from their operations in developed countries. This indicates that even if a firm has used one particular mode like exports to enter the African medicines market in the past, it ought to evolve over time and firms can even use a combination of strategies together (Benito et al., 2009).

Second, the pharmaceutical market in Africa can broadly be divided into public and private markets. The public market includes procurement of medicine using funds either from national governments or international donors. On the other hand, private market can be either formal –

with a well-defined regulation or the unregulated informal market. **Each of these market segments operates under different sets of regulations and the behavior and interest of actors in each segment is often not the same.** Firm characteristics might be different in different segments, and the same firm can target different segments with diverse strategies altogether.

Third, African pharmaceutical market is also different due to the arrival of the new governance structure of donor-funded markets led by international organizations. These players act as "market makers" and work in a variety of ways to improve access to medicines. They recommend (and proscribe) drugs, shape national policies, assure drug quality, provide funding and technical assistance, manage supply chain, negotiate prices with manufacturers, decide who can compete and influence the behavior of competitors. The action of these organizations may also impact firm behavior and strategy towards the African market.

Fourth, extant literature has distinctively studied the internationalization paths and motivations of a few well established Indian firms like Ranbaxy, Dr. Reddy's, Sun Pharma, Wockhardt, and Nicholas Piramal who have successfully penetrated developed countries (Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Mowla et al., 2014; Yeoh, 2011). These firms indeed offer an intriguing case to research the rise of emerging country multinational firms in a high knowledge and technology-intensive industry such as pharmaceuticals. In fact, Ranbaxy had been a subject of analysis in 10 out of 11 articles in our systematic review (Dixit & Yadav did not disclose the name of the firms).

The focus on a handful of and globally successful companies also raises the question that does it represent all of the Indian pharmaceutical industry? Firms like Ranbaxy and Dr. Reddy's have the financial and technological capability to take the risk to enter into highly regulated markets in developed countries. In fact, most of the recent acquisitions in the US and Europe were carried out by only a minority of Indian firms and even among them it was highly concentrated between the top few players (D. Nayyar, 2008). Such treatment clearly ignores a large number of small and medium-sized Indian firms which make a substantial part of their revenues abroad, mostly in semi-regulated markets in Asia and Africa. These firms lack technological capabilities for product development and are too small to have financial ability to establish a foreign subsidiary or perform overseas acquisition (Chaudhuri, 2015a; Sampath, 2005). Most of these firms do not have a WHO prequalification (or other quality certifications

like USFDA and MHRA.) due to underlying investment and choose to operate in the private medicines market through exports and contractual agreements (Chaudhuri, Mackintosh, & Mujinja, 2010). This distinguishes Africa from developed country markets where only a few leading Indian firms, capable of conforming to the stringent regulatory environment, are successfully operating.

Finally, over the last two decades, a new breed of private, not-for-profit organizations have emerged that primarily engage in the development new drugs for diseases that disproportionately affect the developing world, particularly Sub-Saharan Africa, using public-private partnership model (Chataway, Brusoni, Cacciatori, Hanlin, & Orsenigo, 2007; Grace, 2010; Muñoz, Visentin, Foray, & Gaulé, 2014). These so-called Product Development Partnerships (PDPs) do not have their own infrastructure to carry out all the research and development in-house. Instead, they act as virtual pharmaceutical companies and outsource all the R&D work to a network of institutions (J. F. Li & Garnsey, 2014; Munos, 2006). Some of them such as the Drugs for Neglected Diseases Initiative (DNDi) and the Medicines for Malaria Venture (MMV) have successfully brought several new medicines to market in partnership with pharmaceutical companies (Abdulla & Sagara, 2009; Bompart, Kiechel, Sebbag, & Pecoul, 2011; J. P. Cohen, Sturgeon, & Cohen, 2014; DNDi, 2005). It is noteworthy that they are not only partnering with MNCs from developed countries but also providing opportunities to firms from developing countries like Indian and China. In fact, DNDi, partnered with Cipla, an Indian company, to launch a new formulation of an antimalarial medicine, "artesunate-mefloquine" (DNDi, 2012; S. Wells, Diap, & Kiechel, 2013). This opens a new avenue to examine the alliance of Indian firms with non-profit international organizations active in the field of drug development as a strategy to enter the African pharmaceutical market.

1.3.2. The Principal and Associated Research Questions

In line with the discussion in the previous section and following an empirical approach, the principal question that this thesis intends to answer is: **What are the market entry and operation strategies of Indian pharmaceutical firms in Sub-Saharan Africa?** It requires opening the black-box of pharmaceutical trade between India and Sub-Saharan countries and shedding light on various aspects of the supply chain – from production to procurement – and look at firm strategies. As such, it cannot be answered in isolation and necessitates the need to

examine and understand the institutional and historical context under which Indian pharmaceutical firms have developed their competencies and expanded internationally. In fact, Indian pharmaceutical industry has grown up to be one of the most competitive and affordable suppliers of generic medicines globally, and it could not have been possible without the home country *push factors*.

Similarly, it is equally important to understand the institutional environment that act as the *pull factors* for a firm to expand internationally. Notably, it entails identifying the institutional changes that led to increasing the demand for generic medicines in African countries. This is because developing countries have institutions that are significantly different from developed economies and have been recognized to be essential determinants of firm behavior (Dunning & Lundan, 2008; Peng, Wang, & Jiang, 2008). In the context of pharmaceutical markets, the institutional environment supporting the development of new medicinal products which are affordable and adapted to local populations in developing countries is also influenced and shaped by international organizations.

Thus, the thesis intends to answer the following questions as a means to respond to the core problematic:

1. What were the institutional changes that allowed Indian firms to develop their capabilities and expand abroad?
2. What were the changes in the institutional environment of host countries that acted as pull levers for Indian firms?
3. What is the role of the new international governance of donor-funded markets towards the expansion of Indian firms in the African market?
4. How is the African pharmaceutical market itself organized?
5. How PDPs and the regulatory framework put in place by international organizations can shape the strategy of a firm?

Through answering these questions, this thesis not only digs into the historic legal and political changes governing Indian pharmaceutical industry and explains the organization of the pharmaceutical market in Africa by focusing on market segmentation but also shows the role of international organizations in shaping the market and the growing role of Indian firms. Only

after answering these questions one can establish the context to study the entry and operation strategies of Indian firms.

1.3.3. Objectives and Methodological Outline[4]

Objective 1: To understand and highlight the political and regulatory environment in India that allowed Indian pharmaceutical firms to develop robust capabilities in the production of generic medicines and those that were conducive towards pushing them on the path of Internationalization.

Objective 2: To identify and explain the institutional factors outside India that pulled Indian firms towards foreign expansion.

To achieve the first two objectives a historical case analysis was conducted through an in-depth examination of scholarly articles and reports and policy documents from government and international organizations. A wide range of other sources such as government circulars, notifications, news articles, and press releases were also consulted.

The focus of the analysis was the capability building and growth of Indian pharmaceutical industry, regulatory changes in India supporting the internationalization process, generic medicine supporting policies in developed and developing countries, and the emergence and governance structure of the donor-funded markets with a specific focus on HIV and malaria medicines. To support the arguments we analyzed primary and secondary data regarding the capability building and growth of Indian pharmaceutical industry. Further, to show the importance of donor-funded market as a pull factor for internationalization, we also analyzed the procurement data of artemisinin-based combination therapies (ACTs) from the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

Objective 3: To analyze the organization of the pharmaceutical market in Francophone West Africa with a focus on Mali and examine the market entry and operation strategies of Indian firms within this context.

[4] Detailed methodologies are described within concerning chapters.

Our initial goal was to look into market entry and operation strategies of Indian firms at the broader scale of Sub-Saharan Africa. However, it would have required examining multiple case countries to account for institutional and regulatory differences which can influence firm behavior. Such a task was not possible within the constraints posed by funding and time. Therefore, **we limited our study to within the context of Francophone West African countries where Indian firms have registered a significant growth over the last two decades** (*source: International Trade Centre*). Even if the combined market-size of these countries is smaller compared to Anglophone countries, there is still a significant potential for expansion for Indian firms.

Moreover, selection of Mali as the case of examination was especially influenced by the ease of identification and access to key informants for data collection and availability on-site resources. This was particularly possible due to the initial technical insights provided by professor Hubert Balique (an expert on Malian healthcare system) to identify key stakeholders within the Malian pharmaceutical supply chain and the administrative and networking support gained by collaborating with The French Research Institute for Development (Institut de recherche pour le développement or IRD) in Mali. Such an approach in not unprecedented and has been identified by researchers as an important factor in selecting cases for analysis (Crowe et al., 2011; Rowley, 2002). Further, while beyond doubt, there are country-specific differences across the region with respect to the laws regulating the supply and distribution of medicines, it is also not difficult to find some fundamental similarities regarding the organization of the pharmaceutical market which can be helpful in the generalization of findings. The public and private markets in Francophone West African Countries can be broadly divided into four specific market segments: government-funded public market, donor-funded public market, formal private market and the informal market (Baxerres & Le Hesran, 2011; McCabe et al., 2011; Yadav, 2015). Thus, **examining the Malian system can give a general idea of the Francophone West African Countries**. Second, Mali was also the first country in Sub-Saharan Africa to start organizing its healthcare and pharmaceutical delivery system based on the principle of the Bamako Initiative. The Bamako Initiative was a formal statement that was supported by the WHO and the UNICEF and adopted by the African Ministers of Health in September 1987 in Bamako, Mali. **The initiative strongly promoted the use of generic drugs in African countries through user fees and community level management of primary healthcare service** (Govindaraj & Herbst, 2010; Semdé et al., 2012).

To achieve objective 3, a combination of multiple data sources methodologies were employed. First, we conducted two sets of semi-structured interviews following the data collection guidelines proposed by Barriball and While (1994) and Harrell and Bradley (2009). The first set of consisted of 34 interviews of diverse actors in the Malian pharmaceutical supply chain. The second set consisting of 11 semi-structured interviews of professionals working in Indian pharmaceutical industry was conducted in two specific phases. The first phase involved a fieldwork in India between September to December 2016 and the second phase was carried out between July and August 2017 using online tools.

Second, Malian market authorization list (version: December 2014) for pharmaceutical products was analyzed to provide additional evidence concerning the strategic choices made by Indian firms. Third, we also extracted trade data between 2001 and 2016 from International Trade Centre website to analyze the growth of Indian pharmaceutical firms in Francophone West African countries. Lastly, supplementary data on firms were collected from websites, annual reports, business reports, news articles and balance sheet of selected companies.

Objective 4: To provide an explorative account of the development of Synriam with the aim to understand the opportunities offered by Product Development Partnerships (PDP) and analyze the strategy employed by Ranbaxy to launch this product in India and other African countries.

Synriam is a fixed-dose combination (FDC) antimalarial that combines two parasiticidal drugs with independent modes of action – faster-acting arterolane maleate (also known as OZ277 or RBx-11160) and longer acting piperaquine phosphate (piperaquine). It was first approved by the Drug Controller General of India (DCGI) in 2011 for treating acute, uncomplicated *P. falciparum* malaria in patients from 12 to 65 years of age. Synriam offers a "three days-three tablets" treatment regimen where each tablet consists of 150 mg of arterolane and 750 mg of piperaquine (Patil, Katare, Baig, & Doifode, 2014; Valecha et al., 2012; T. N. C. Wells, van Huijsduijnen, & Van Voorhis, 2015). The drug is also unique in the way it was developed. One of its components, arterolane, is the outcome of PDP-funded research by Medicines for Malaria Venture (MMV) (Vennerstrom et al., 2004). For the further development of the molecule, MMV partnered with a Southern firm (Ranbaxy) from India. However, unsatisfied with the results of the early clinical trial, MMV left the partnership but not before giving Ranbaxy exclusive intellectual property rights (IPR) to continue further product development. After

MMV left, another partnership was formed between the government of India and Ranbaxy to complete the clinical phase.

The results of the trials were positive (Valecha et al., 2012) and it got approval from the Drug Controller General of India in 2011 (Patil et al., 2014). Synriam was launched in India in April 2012, and Ranbaxy became the first Indian company to launch a new chemical entity (Chemistry World, 2012). In 2014, Ranbaxy got regulatory approval to launch the drug in seven African countries - Nigeria, Uganda, Senegal, Cameroon, Guinea, Kenya and Ivory Coast (Business Standard, 2014).

The study is informed by a literature review and 5 in-depth interviews with the employees of erstwhile Ranbaxy (3), MMV (1) and the Indian Council of Malaria Research (1) who worked on the development of Synriam. It helped in two ways. First, it provided an opportunity to investigate and understand the new PDP R&D model and the opportunities that it can offer to Indian firms. Second, it also allowed understanding the market-entry strategies used by an Indian firm (erstwhile Ranbaxy) to launch a new antimalarial product in India multiple African countries. This in the face of the current situation where ACTs are already the gold standard for treating *falciparum* malaria.

1.4. Neo-Institutional Theory as the Theoretical Framework

It is widely accepted that institutions influence economic outcomes by providing fundamental political, social and legal rules for production, distribution, and exchange (North, 1990; Scott, 1995). The primary function of institutions is to reduce uncertainty (North, 1990) which they achieve by putting constraints on some behaviors while enabling others (Hodgson, 2006). The prevailing institutional structure can even incentivize specific actions, for example, tax holidays for investments in certain businesses. Proscription and prescription to limit and guide individual behavior are inherently liked to institutions. The institutional environment impacts how a firm does business, gains knowledge, manages human resources, connects with customers, and interacts with the government and other organizations (Kostova & Zaheer, 1999; Scott, 1995). (He & Bouthers, 2013)

Institutional theory is concerned with how various institutional actors like firms secure their legitimacy by conforming to the rules and norms of the institutional environment in which they

operate (Bruton, Ahlstrom, & Li, 2010). The importance of institutional theory to explain the international expansion of firms originates from its ability to incorporate contextual influences like laws, regulations, culture, values, norms, and politics into theoretical reasoning. Institutions matter because no firm can be "immune" from the institutional framework in which it is embedded (Peng, 2002). The institutional theory takes into account the dynamic interaction between institutions and organizations and considers strategic choices as an outcome of such interactions (Peng, 2003).

According to North "institutions are the rules of the game in a society or, more formally, are the humanly devised constraints that shape human interaction". They are "systems of established and prevalent social rules that structure social interactions" (Hodgson, 2006). Institutions include both formal (laws, regulations, rules) and informal (norms, cultures, ethics) constraints. Scott summarizes institutions into three categories of forces which he calls institutional pillars – regulatory, normative and cognitive – that are part of any institutional environment (Scott, 1995; Kostova & Roth, 2002).

Regulative pillar refers to the existing rules and laws that provide stability and order by proscribing certain types of actions and promoting others (Kostova, 1997; Kostova & Zaheer, 1999). Regulatory institutions deal with rule setting, monitoring and sanctioning when those rules are broken (Scott, 1995, p. 35). These rules primarily stem from government legislation but also from industrial agreements and court rulings. Firms need to comply with explicitly stated rules of each institutional environment where they operate: home country, host country and often other international organizations. Normative pillar represents norms, values, beliefs, and assumptions concerning socially appropriate or expected behavior (Bruton et al., 2010; Kostova, 1997). Normative institutions consist of values (*what is proper*?) and norms (*how things are to be done consistent with those values*) (Bruton et al., 2010) that are consciously shared by institutional actors, thus creating a social obligation to comply. Cognitive, institutional pillar refers to cognitive structures and social knowledge shared by the individuals in a given country (Kostova, 1997). They are internalized, taken-for-granted values and beliefs that guide individual behavior (Peng, 2014).

Researchers have noted that the extant literature under the influence of "Transaction Cost Theory (TCT)" and "Resource-Based View (RBV)" had until recently mostly ignored the role of institutions in studying the international expansion of firms (Meyer, Estrin, Bhaumik, &

Peng, 2009; Peng, 2002; Peng et al., 2008; Ramamurti, 2004). Such contextual underpinnings of the market exchange process, arising out of formal and informal institutions have been central to the institutional framework (Dimaggio & Powell, 1983; Granovetter, 2005)

Mainstream or traditional theories like TCT, OLI or RBV originated in mature market economies. They were primarily adapted to explain the international expansion of developed country MNEs, mainly American and to a lesser extent European, to other developed economies (Meyer & Peng, 2005; Peng et al., 2008; Ramamurti, 2009). In developed economies, it is reasonable to assume a relatively well developed, stable and efficient market supporting institutions (Peng et al., 2008). So, it is not a surprise that mainstream theories model firms and markets independent of their environment and assume institutions only as background conditions. Such an assumption takes the social embeddedness of firms and markets for granted (Coriat & Weinstein, 2005; Fligstein, 1996; Granovetter, 2005). However, if all the research is based in western countries then all the firms and markets are embedded in the similar institutional environment, and consequently, there is minimal variation which makes it difficult if not impossible to distinguish the impact of institutions on firm behavior (Peng, 2002).

The limitation of mainstream theories to include institutional factors came to light when emerging countries, most notably from Asia, started to take the world stage in the advent of globalization and countries from Central and Eastern Europe (CEE) started opening their markets. Though internationalization by emerging country firms is not a new phenomenon, their rate has increased since the 1990s (Rienda, Claver, & Quer, 2013). Two types of movements were noticed by the researchers. First, Western firms in their quest to grow and capture new markets started to expand their business operations to these countries (Bianchi & Arnold, 2004; Brouthers, Brouthers, & Nakos, 1998; Meyer & Peng, 2005). Second, and pertinent to the theme of this study, firms from emerging countries started internationalizing at a rapid rate to both developing and developed countries (Aulakh, 2007; Gill, 2012; Luo & Tung, 2007; Mathews, 2006; Ramamurti, 2012). This international expansion is characterized not only through export but rather active acquisitions through direct FDI. This is a curious case because traditional theories would expect developing countries like India, China, and Brazil to have an extended period of inward FDI to acquire a competitive advantage and produce globally competitive firms (Ramamurti, 2012).

One striking feature of these emerging economies is that their institutional framework is significantly different than to those in developed economies (Khanna & Palepu, 2000, 2012; Peng et al., 2008). Emerging countries are typically characterized by the presence of "institutional voids", i.e., the absence or poor functioning of intermediary institutions that pose constraints on the business activity of firms. Such institutional voids include underdeveloped financial markets, lack of information system, opaque judiciary, poor infrastructure, inadequate enforcement of property rights, lack of specialized human resources and so on (Khanna & Palepu, 2000, 2006; Stucchi, Pedersen, & Kumar, 2015).

Emerging economies like India, China, Brazil, and Russia do not have a homogeneous institutional environment (Hoskisson, Wright, Filatotchev, & Peng, 2013). These countries have undergone significant institutional transitions in the recent past, and their institutional framework is still evolving (Peng et al., 2008; Stucchi et al., 2015). For example, Russia, China, Poland and other CEE countries are moving from central planning to market competition; India has made many economic and regulatory reforms post 1991 liberalization of the economy. Such legal, political or societal changes have created new interactions between firms and their environment. On the one hand, these institutional developments have raised challenges, on the other, they have offered new opportunities to both domestic and foreign firms. These developments have led researchers to a general acceptance that institutions are not just background factors, but they play an active role in determining firm strategies to organize business operations (Dunning & Lundan, 2010). However, because mainstream theories were not developed to consider institutional contexts, researchers found difficulties in applying them to developing countries. This problem called for new theoretical tools to capture the complex and dynamic relationship between organizations and their environment in emerging economies.

Two paths have emerged out of this search. The first includes those studies that have tried to incorporate contextual variables in existing theories like TCT and RBV to improve their explanatory power. This is a complementary perspective of the institutional view (Meyer & Peng, 2005; Peng et al., 2008). For example, Dunning & Lundan (2008) included institutional origins of ownership advantages of firms in the OLI or eclectic paradigm. For them, institution-based advantages originate both from firm-specific norms, values and enforcement mechanisms, i.e., corporate culture and also from the human environment in which firms are embedded and operate (Dunning & Lundan, 2008). Some scholars have integrated resource-

based view and institutional perspective to explain export channel selection and performance (He, Brouthers, & Filatotchev, 2013), competitive advantage (Ahn & York, 2011) and entry strategies (Estrin, Baghdasaryan, & Meyer, 2009; Meyer et al., 2009; Peng et al., 2008). Similarly, economists have used institutional and cultural influences in association with transaction costs to explain entry mode choice and firm performance (Brouthers, 2002; Brouthers & Brouthers, 2000).

The second path has expanded institutional framework to investigate a broad range of international business and strategy issues.[5] Researchers have examined the impact of culture on the emergence and evolution of business practices (Kogut & Singh, 1988; Leung, Bhagat, Buchan, Erez, & Gibson, 2005) and entry mode choice (Brouthers et al., 1998). They have looked at the effect of institutional changes in emerging economies and how it shapes the behavior of domestic and foreign firms (Hoskisson et al., 2013; Peng, 2002; Stucchi et al., 2015; Wright, Filatotchev, Hoskisson, & Peng, 2005). Some economists have also focused on how firms deal with the liability of foreignness and gain organizational legitimacy while operating within the context of values and institutions of the host country (Bianchi & Arnold, 2004; Kostova & Zaheer, 1999). Another stream of research focuses on the role of firm's internal and external institutional environment in shaping its behavior through isomorphic pressure (Davis, Desai, & Francis, 2000; Lu, 2002).[6] Scholars have also examined the role of business groups in filling institutional voids (Khanna & Palepu, 2000, 2012), role of host country corruption in obtaining organizational legitimacy and strategic decision making (Rodriguez, Uhlenbruck, Eden, & Rodriguez, 2016), and even role of nongovernmental organizations (NGOs) in altering international business practices (Dahan, Doh, & Teegen, 2010; Teegen, Doh, & Vachani, 2004).

The discussion so far makes the point that firm behavior is shaped by its formal and informal contextual environment, and the effect of institutions becomes particularly conspicuous in developing country context due to the presence of various institutional voids. A firm is subjected to its external political, legal and social environments that set the *rules of the game*

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[5] For a detailed explanation please see Kostova, Roth, & Dacin (2008).

[6] Isomorphism refers to the "constraining process that forces one unit in a population to resemble other units that face the same set of environmental conditions" (Dimaggio & Powell, 1983).

under which it has to operate. These rules are exerted and influenced not only by the institutional environment of the home country but also by institutional environment of the host country. Here the institutional environment of a country refers to **"the set of all relevant institutions that have been established over time, operate in that country, and get transmitted into organizations through individuals"** (Kostova, 1997). Further, these rules are increasingly influenced by international organizations and NGOs (Dahan et al., 2010). This is particularly relevant in the field of pharmaceuticals, where they can exert structural power over both governments and firms. Thus, when, why and how firms decide to expand internationally, depends on multiple institutional environments populated by numerous actors.

The focus of this thesis on the operation of Indian pharmaceutical firms in Sub-Saharan Africa can be seen as an investigation of the strategies of developing country firms in other developing countries. Other researchers have also used an institutional approach when studying the entry strategies of Indian pharmaceutical firms by taking contextual factors of home (economic liberalization and TRIPS among others.) and host countries (for ex. Hatch-Waxman Act in the US) (Chittoor & Ray, 2007; Kale, 2010a; Yeoh, 2011). Taking an institutional approach will allow this to bring out the nuances of the interactions and interdependencies between firms, markets, and their environment.

1.5. Organization of the Thesis

Chapter 2 starts the investigation by exploring the institutional foundation that led to the development of a competent pharmaceutical sector in India. It discusses a number of pre-liberalization government policies and reforms like the Indian Patents Act, 1970 and the Foreign Exchange Regulation Act (FERA), 1973 among others and the establishment of specialized facilities for pharmaceutical research that were crucial for building indigenous capability in pharmaceutical production. It then discusses post-liberalization reforms and arrival of the international agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) that created push factors for the foreign expansion of Indian firms. More importantly, the chapter also explains the pull factors generated due to institutional changes in developing countries and the rise of the new governance of donor-funded markets in the context fight against the three major pandemics – HIV/AIDS, Tuberculosis, and malaria – in the southern countries. It further shows how this new donor-funded market is governed by international

organizations by elucidating the creation of the market of artemisinin-based combination therapies (ACTs) for malaria. It finally demonstrates the increasing role played by Indian firms in the donor-funded ACT market by analyzing a database of antimalarials medicines procured through the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

Chapter 3 sheds light on the institutional layout of the African pharmaceutical market by focusing on Francophone West Africa. It does so by analyzing the pharmaceutical supply system in Mali. It examines the organization and the regulatory framework governing the functioning of four different market segments:

i. Public market funded by the national governments
ii. Public market funded by international donors
iii. Formal private market
iv. Informal private market

Such classification is necessary because the "rules of the game" in each of these segments are different. Thus, internationalizing firms need to decide which markets to target and the strategy may change with the market segment owing to differences in regulations. The chapter then analyzes the entry and operation strategies of Indian pharmaceutical firms by concentrating on the nuances of supply chain in the three[7] market segments.

Finally, **Chapter 4** explores the PDP model of pharmaceutical R&D through a case study of Synriam to identify the opportunities such initiatives can offer to Indian firms and analyze the strategies used by Ranbaxy to bring this product to market when faced with the regulatory constraints put in place by international organizations within the broader framework of donor-funded markets.

[7] The thesis does not focus on informal market to explain the entry and operation strategies.

2. From National Capability Building to the New International Governance of Health: Institutional Underpinnings of the Foreign Expansion of Indian Pharmaceutical Firms

2.1. Introduction

Indian pharmaceutical industry is a success story of achieving self-reliance in pharmaceutical technology, drug production and providing affordable and good quality medicines not only to Indians but patients around the world. It has come a long way from the dark-age of no international activity by domestic firms to the present era of becoming a generic powerhouse. Currently, India accounts for 10% of the global pharmaceutical production by volume and supplies 20% of the world's generics. In fact, Indian firms supply 30% of all HIV/AIDS medicine (Department of Pharmaceuticals, 2015).

Indian players have not only made their presence in other developing countries, but they have managed to penetrate the highly regulated markets of North America, Europe, Japan and Australia (Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Löfgren, 2009; Pradhan & Alakshendra, 2006). Some of the Indian pharmaceutical firms have emerged as important performers in the global market and have been successfully competing with traditional multinational companies (MNCs) from developed economies (Chittoor & Ray, 2007; Kedron & Bagchi-Sen, 2011, 2012).

Internationalization by Indian firms is not a new phenomenon (Lall, 1982) but it was only after 1990 that there was a surge in their outward foreign direct investment (FDI) (Kale, 2010a; D. Nayyar, 2008; Pradhan & Alakshendra, 2006). This wave of internationalization was a strategic response to institutional changes of two types. The first set corresponds to changes that took place in India. It includes the adoption of a stringent product patent regime, liberalization of government policies, relaxation in regulations, the opening of global financial channels, and growing competitive pressure in the domestic market that *pushed* Indian firms to expand

internationally (Chittoor, Ray, Aulakh, & Sarkar, 2008; Kale, 2010b; Pradhan & Alakshendra, 2006). The second set of institutional transformations happened outside India. These changes such as growing business opportunities in developed markets due to patent expiration, generic substitution policies and decreasing international trade and investment barriers due to globalization acted to *pull* Indian firms towards internationalization (Pradhan & Alakshendra, 2006). The period also observed a renewed outward pull from developing countries, especially in Africa. First, there was a widespread adoption of National List of Essential Medicines based on WHO model formulary which promoted the inclusion of generics. Second, the Central Medical Stores (CMS) in many countries also underwent structural reforms and promoted the procurement of non-proprietary generics over branded originator products. For example, this was particularly the case in Francophone West Africa (Govindaraj & Herbst, 2010). Third and the most important, the early 2000s witnessed the emergence of a new international governance of donor-funded markets to counter global scourges like HIV/AIDS, tuberculosis (TB) and malaria. This fight has historically relied on the supply of low-cost generic medicines to solve the problem of affordability and increase the access to treatment to millions of people in the global south. Indian firms would rise to take a central stage in this new market.

However, it is worth noting that the international expansion of Indian pharmaceutical firms would not have been possible without building chemical and reverse engineering capabilities that allowed them to compete internationally. These attributes were acquired over an extended period due to favorable domestic policies such as the abolition of the product patent regime, the creation of public enterprises and research units and restrictions imposed on foreign firms.

Thus, Indian pharmaceutical industry offers a successful case of sector-wide adaptation and transformation in the face of institutional reforms. These institutional changes are embedded both in the measures taken by the government of India as well as the policies and initiatives taken by foreign governments and international organizations. To understand the international expansion of Indian firms, one must look into the historical institutional context that has allowed Indian firms to become one of the most aggressive foreign investors. In this regard, the purpose of this chapter is also to provide some insights into institutional transformations in both pre- and post-liberalized India as well as changes outside its national boundaries that thrust the internationalization of Indian pharmaceutical firms. The chapter relies on an in-depth examination of scholarly articles and reports and policy documents from government and international organizations. A wide range of other sources such as government circulars,

notifications, news articles, and press releases were also consulted. The focus of the analysis was the capability building and growth of Indian pharmaceutical industry, regulatory changes in India supporting the internationalization process, generic medicine supporting policies in developed and developing countries, and the emergence and governance structure of the donor-funded markets with a specific focus on HIV and malaria medicines. To support the arguments we analyzed primary and secondary data regarding the capability building and growth of Indian pharmaceutical industry. Further, to show the importance of donor-funded market as a pull factor for internationalization, we also analyzed the procurement data of artemisinin-based combination therapies (ACTs) from the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

The rest of the chapter is organized as follows. Section 2.1 discusses the institutional changes that were critical to the development of indigenous capability of the pharmaceutical industry. These changes were particularly directed to build indigenous capabilities and substitute imports with domestic production. Section 2.3 is dedicated to explain the institutional changes that were influential in pushing Indian firms on the course of internationalization. These *Push factors* mainly arose due to liberalization of the Indian economy and India's signing of the international agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). Section 2.4 discusses the *Pull factors* which are institutional changes not in India itself but rather in host country markets that paved the way for Indian generic products. Here institutional factors are discussed both from the perspective of developed and developing countries.

Section 2.5 draws attention to the new governance of the donor-funded markets. The donor-funded market as a factor influencing outward expansion of firms has not received the attention of researchers studying the internationalization of Indian firms. Precisely because they have not looked at the African context, instead their focus has been the expansion of Indian firms in developed country markets. This section explains the contextual underpinnings of the creation donor-funded market and the role of international organizations as market makers with particular reference to the political economy of HIV/AIDS. Section 2.6 goes on further to provides an institutional analysis of the creation of the donor-funded market of artemisinin-based combination therapies (ACTs) that constitute the therapeutic backbone of malaria. It shows the key role played by the WHO as an international prescriber in the creation and designing of this new market. Here we shall also see how the absence of patents on molecules involved in these treatments has been instrumental in the WHO policy recommendation and even so, the ACT market was first established as a quasi-monopoly of the multinational firm

Novartis Pharma (Novartis). Section 2.7 sheds light on the growing role of Indian firms in Africa, within the context of the donor-funded segment, by providing a quantitative analysis of the evolution of the ACT market. We use the antimalarial procurement data of the Global Fund to Fight AIDS, Tuberculosis, and Malaria (The Global Fund) along with supplementary information from the WHO prequalification program and the Assured Artemisinin Supply System. Section 8 presents a brief conclusion.

2.2. Institutional Changes Pertaining to Capability Building

Capability building institutional changes primarily refer to those government policies and initiatives that were directed to stimulate the growth and development of indigenous pharmaceutical industry and achieve self-reliance in pharmaceutical production. The supportive institutional environment can be grouped into two distinct phases based on the nature of policy measures taken by the government: from 1947 (independence) to 1969 and from 1970 to 1995. In this section, we will explore several reforms that played a crucial role in strengthening the Indian pharmaceutical industry.

2.2.1. Phase I (1947-1969): Early Foundations

At the time of independence, sized at INR 100 million, the domestic pharmaceutical market in India was minuscule, and more than 90% of it was under the control of foreign firms (Pradhan & Alakshendra, 2006). The newly independent government regarded foreign knowledge and technology as instrumental for industrialization. Consequently, the Industrial Policy Resolution of 1948 recognized pharmaceuticals as one of the technically demanding industries and took a liberal approach towards the operations of foreign companies in India (Joseph, 2011; Mazumdar, 2013). The government implemented this strategy with the hope that production activities by the affiliates of foreign MNCs will result in a technological spillover that would benefit the indigenous industry. Indeed, this liberal environment attracted foreign capital and boosted market growth. By the end of 1952, the pharmaceutical market had grown to INR 350 million (Mazumdar, 2013). However, contrary to government expectations, there was no scope for domestic capability building through technological spillover. Foreign MNCs were either importing ready to sell products or at maximum importing bulk drugs which were then

processed to final products for selling in the Indian market. Even to process the bulk drugs most firms did not invest in establishing their units but instead contracted out to local firms. This strategy was more profitable to foreign firms, who acted as trading/marketing agents for their parent companies, rather than investing into costly plants and machinery and engage in vertical manufacturing of drugs in India.

To address this problem, the government through its Industrial Policy Resolution of 1956 took a series of corrective measures to build domestic competence in pharmaceutical production. First, the new policy placed pharmaceuticals into "Schedule B" industries where progressively state-owned public sector was to take the leadership position and private sector was expected to supplement the efforts of the state (Thakur, Gupta, & Singh, 2012). Second, pharmaceutical firms were obliged to get an industrial license to start a new unit or to expand existing units.

To help the public sector to be able to provide technological leadership, the government founded two state-owned pharmaceutical firms to produce drugs from the basic stage with the following three objectives (According to the 22nd report of the Committee on Public Undertakings, cited in The Hathi Committee Report, 1975, p. 55)

i. To bring down the prices by large-scale production of high-quality lifesaving drugs

ii. To provide medical relief to the people on a mass scale

iii. To achieve not only self-sufficiency but also produce an exportable surplus and earn foreign exchange

The first manufacturing firm – the Hindustan Antibiotics Limited (HAL) – was established with the help of the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) in 1954 at Pimpri, near Pune to produce antibiotics (Mazumdar, 2013). Later, Indian Drugs and Pharmaceutical Limited (IDPL) was established in 1961 with the financial and technical assistance of the Soviet Union (Joseph, 2011; Mazumdar, 2013). IDPL started with two manufacturing units, one in Hyderabad for the production of synthetic drugs and the other in Rishikesh, dedicated to the production of antibiotics (Pradhan, 2006).

The technologies provided by the sponsors were modified and adapted according to local conditions by the in-house R&D departments of the two firms (Joseph, 2011; Mazumdar,

2013). Production in HAL started in 1955 while IDPL became operational in 1968. The government also took steps to share the technological know-how between the two firms through the transfer of scientists from one to another. The private sector also benefitted from technological spillover due to movements of scientists and technicians to private firms. The importance of these public sector enterprises towards the development of indigenous pharmaceutical industry can be understood from the fact that **founders of one-third of the 200 Indian firms had at some point or other worked at the IDPL** (Felker, Chaudhuri, Gyorgy, & Goldman, 1997). The arrival of HAL and IDPL also stimulated the university system to train specialized human resources needed by the pharmaceutical industry (Joseph, 2011).

Further, public funded research units under the aegis of the Council of Scientific and Industrial Research (CSIR) also played a critical role to advance the technological capability of the domestic industry. Institutions like Central Drug Research Institute (CDRI), Indian Institute of Chemical Technology (IICT) and National Chemical Laboratory (NCL) have developed and transferred process technologies to many leading Indian firms like Lupin, Sun Pharmaceuticals, Cipla, Orchid and so on (Chaudhury, 1997).

By 1973, the industry had proliferated, and the total turnover of bulk drug and formulations were INR 750 million and NR 3.7 billion respectively (Figure 2.1). The industry had 116 units in the organized sector registered under the Industries Development and Regulation Act of 1951 and over 2500 units in the small sector. In all, 66 firms had either full or partial foreign ownership distributed between both organized (51) and small scale sector (15) (Table 2.1).

Table 2.1 Foreign MNCs in India in 1973

Foreign Equity (In %)	Number of Units
100	10
50-99	24
40-50	15
26-40	11
Below 26	6
Total	66

Source: The Hathi Committee Report, 1975

The constant pressure from the government and the advent of public sector enterprises gradually led some foreign MNCs to engage in the local production of bulk drugs, but they preferred low-volume and high-value items like corticosteroids. Foreign and foreign majority units contributed less than 12% of the total production of bulk drugs in the organized sector in terms of volume but generated nearly 27% of the revenue at the end of 1973. Further, instead of making bulk drugs from the basic stage they frequently used penultimate or near-penultimate intermediates, usually imported from their parent companies at higher costs. The dominance of foreign firms was much higher in the formulation segment where they controlled about 70% of the market share (The Hathi Committee Report, 1975).

Foreign firms also benefitted from the existing product patent law in India and started introducing newer drugs like Metronidazole, Chloramphenicol, Tolbutamide, and Oxytetracycline where they had a monopolistic advantage over Indian firms. The Hathi Committee (1975) noted that foreign firms actively asserted their patent rights and proceeded legally against Indian firms if they imported bulk drugs to make these lifesaving medicines. Finally, despite the progress and significant increase in production, only 20% of the population had access to modern pharmaceuticals, and drug prices in India were among the highest in the world (Guennif & Ramani, 2010; Lall, 1974; The Hathi Committee Report, 1975).

2.2.2. Phase II (1970-1995): Reforming the System

Until 1970, the structural weakness of the institutional environment stalled government's objective of building national capability through technology transfer. Foreign firms were making hefty profits by selling formulations while investing very little into basic manufacturing. Throughout the 1970s, the government introduced a series of legislation in a comprehensive attempt to reform the pharmaceutical industry. In this section we will discuss the following four vital regulatory measures that drastically changed the structure of the Indian pharmaceutical industry and embarked India into a new era of self-reliance into pharmaceutical production:

i. The Patents Act, 1970 (Implemented 1972)
ii. The Drugs Prices Control Order (DPCO), 1970
iii. Foreign Exchange Regulation Act (FERA), 1973
iv. The New Drug Policy, 1978

2.2.2.1. The Patents Act, 1970

India inherited the Patents and Designs Act of 1911 at the time of independence. This act allowed patents on pharmaceutical products and all known processes for 16 years. The term of protection could be extended for another 10 years if the patent had not been *efficiently remunerative* to the innovator. This prevailing product patent regime had protected foreign MNCs against reverse engineering and process development activities by Indian firms. Thus, it acted as an obvious hindrance to the evolution of domestic technological capability and achievement of self-reliance in drug production. The government took a conscious step to change the patent regime with the introduction of the Patents Bill to the Parliament which culminated in the Patents Act of 1970 (Act 39 of 1970) (Puranik, Sangamesh, & Golshan, 2010). The Act came into force on April 20, 1972 and played a detrimental role in breaking the monopoly of foreign MNCs.

The Patents Act of 1970 was radically different from the previous regime as it brought an end to the product patent for drugs and food. It had the following salient features:

- It granted only process patent for chemical substances including pharmaceuticals and reduced the duration of patents to 7 years from the date of filing or 5 years from the date of sealing, whichever was shorter (Article 53).

- The Act excluded all imported substances from the domain of patent protection. (Ray & Bhaduri, 2012). Thus, patents could only be granted for new substances manufactured in India. Further, MNCs could patent only one process (Mazumdar, 2013).

- The law also shifted the burden of proof on the plaintiff in case of an infringement lawsuit.

- Chapter XVI of the Act also provided the provisions of ‘compulsory licensing” and “license of right” to curtail patent abuse. Anyone could apply for a compulsory license after three years from sealing of a patent if either the patented article was unavailable in the country or unavailable to the public at a reasonable price or if the patentee had been unable to meet the demand. The license of right was an automatic mechanism attached to every patent after three years of sealing that allowed an interested party to

obtain a license from the patentee under mutually agreed terms to manufacture the product.

The Act was crucial to the development of necessary knowledge base in the Indian pharmaceutical industry. **The arrival of a weak patent environment fueled imitative learning whereby Indian firms could develop alternative processes using reverse engineering or merely copy the known process to manufacture a drug**. The provision of process patents and limitation of patent term to 7 years along with licensing mechanisms created growth possibilities for domestic companies. Sensing this opportunity, many researchers and managers working in public sector units, research labs, and other firms started their entrepreneurial ventures. Among the most notable people who came from public sector units was Dr. Kallam Anji Reddy, the founder of Dr. Reddy's Laboratories, one of India's most successful pharmaceutical firms. As the number of manufacturers rose, the domestic market became highly fragmented and fiercely price competitive in which there could be as much as 100 brands for a given molecule (Kale & Little, 2007; Vijayaraghavan & Raghuvanshi, 2007). So, the success of a firm became dependent on developing efficient and cheap processes. Further, the process of "duplicative imitation" needed constant innovation because the publicly available information in the patent files is not always sufficient to develop a reverse engineered product (Kale & Little, 2007). In fact, MNCs often did not even bother to file a patent in India under the new law (Vijayaraghavan & Raghuvanshi, 2007). Many Indian firms developed in-house process R&D units to build their technical capability and obtained the required tacit knowledge for process development through learning-by-doing on the shop floor. The impact was a rapid sector-wise assimilation of reverse engineering skills as well as the honing of the chemical industry. Contrary to countries like Germany where pharmaceutical industry developed out of the chemical industry, in India the latter developed to supply raw material to the former (Bhaduri & Brenner, 2012). The sophisticated reverse engineering capabilities of Indian firms is evident in the short time lag between the introduction of a drug in the global market and its launch in India (Table 2.2). Bhaduri and Brenner (2012), also reported the delay to be further shortened for the drugs launched in the global market after 1995 as domestic firms were aware of India's impending TRIPS obligations.

2.2.2.2. The Drug Prices Control Orders (DPCO)

The regulation of drug prices in India started in 1963 during emergency following the Indo-China War when drug prices were frozen under the Defense of India Act of 1915 (Guennif & Ramani, 2010; Sawhney, 2016). It was followed by Drugs Prices (Display & Control) Order, 1966, issued under the Essential Commodities Act of 1955, which allowed for a selective increase in prices with prior government approval. The law was amended in 1968 to allow firms to fix the prices of *new drugs* but with the prior approval of the government. However, the government did not issue any guidelines and firms fixed the prices of new products as if there were no price control (Chaudhuri, 2015b).

The real and concrete effort by the government to rationalize drug prices came with the enactment of the Drug Prices Control Order of 1970 that brought the pharmaceutical industry under price control. Government fixed the ceiling prices of 18 bulk drugs while prices of others could not be increased without government approval (Chaudhuri, 2015b).

The order also stated that the profit of manufacturers should not exceed more than 15% of the total sales turnover before tax. Thus, allowing firms to fix the prices of formulations as long as the total profit did not surpass the stipulated norm. Further, the 18 bulk drugs accounted for less than 9% of the total market (N. Kumar & Pradhan, 2003). In this regard, DPCO was a weak law whose primary purpose was to have direct control over the profitability of pharmaceutical companies while having only indirect control over drug prices. It only had a mild impact on the profitability of MNCs who dominated the pharmaceutical industry.

In 1979, the government issued the revised version of DPCO in line with the New Drug Policy of 1978 based on the recommendations of the Hathi Committee (1975). It significantly expanded the coverage of price control and stipulated the ceiling prices of bulk drugs and their formulations. The government also kept the profitability ceiling which in the case of bulk drugs was fixed at 14% of the return on net worth or 22% of the capital employed (Chaudhuri, 2015b). In case of formulations, retail prices of controlled drugs were calculated using the concept of *Maximum Allowable Post-Manufacturing Expenses (MAPE).* Under this system, first, the ex-factory cost of a drug is calculated based on the fixed prices of bulk drugs. Then a maximum MAPE (as a percent) is added as a markup to arrive at the final price of the product before taxes like excise and value-added tax (Chaudhuri, 2015b). The DPCO of 1979 brought 347 bulk drugs under direct price control (Joseph, 2016). Also, pharmaceutical formulations were

categorized into four groups with different MAPE percentages applicable to them. Most of the lifesaving drugs were put under category I with the smallest MAPE of 40% (Table 2.3).

Table 2.2 Time lag between global and Indian launch of selected drugs

Molecule	World Launch	Launch in India	Time Lag (years)
Ibuprofen	1967	1973	6
Salbutamol	1973	1977	4
Mebendazole	1974	1978	4
Rifampicin	1974	1980	6
Cimetidine	1976	1981	5
Bromhexin	1976	1982	6
Lorazepam	1977	1978	1
Naproxen	1978	1982	4
Ranitidine	1981	1985	4
Ketoconazole	1981	1988	7
Captopril	1981	1985	4
Norfloxacin	1984	1988	4
Famotidine	1984	1989	5
Enalapril Maleate	1984	1989	5
Ciprofloxacin	1985	1989	4
Acyclovix	1985	1988	3
Astemizole	1986	1988	2
Astemizole	1986	1988	2
Omeprazole	1989	1991	2

Source: Adapted from: Kumar & Pradhan, 2003; Kale & Little 2007

Furthermore, firms in the small sector were exempted from price control. Also, indigenously developed new bulk drugs enjoyed an exemption from control for five years. The last two provisions acted as a stimulus to the growth of domestic production (N. Kumar & Pradhan, 2003). The DPCO of 1979 brought 90% of the drugs under price regulation. This had a remarkable impact on drug prices and by 1990s the prices of drugs were among the cheapest in the world (Kapczynski, 2009; N. Kumar & Pradhan, 2003). Table 2.4 compares the prices of selected drugs in India and other countries, both developing and developed, in 2005.

Table 2.3 Categories of drugs and respective MAPE, DPCO 1970

Category	MAPE
Category I: Lifesaving	40%
Category II: Essential	55%
Category III: Less Essential	100%
Category IV: Non-essential	No price control

Source: Joseph, 2016

Table 2.4 Prices of selected drugs in India and elsewhere in 2005 (All prices in INR)

Drug	India	Pakistan	Indonesia	USA	UK
Ciprofloxacin (500 mg tabs)	29.00	423.86	393.00	2352.35	1186.70
Norfloxacin (400 mg tabs)	20.70	168.71	130.63	1843.56	804.78
Cefpodoxime Proxetil (200 mg tabs)	114.00	357.32	264.00	1576.58	773.21
Diclofenac Sodium (50 mg tabs)	3.50	84.71	59.75	674.77	60.96
Ranitidine (150 mg tabs)	6.02	74.09	178.35	863.59	247.16
Omeprazole (30 mg caps)	22.50	578.00	290.75	2047.50	870.91
Lansoprazole (30 mg caps)	39.00	684.90	226.15	1909.64	708.08

Source: Pronab Sen Committee Report (2005)

2.2.2.3. Foreign Exchange Regulation Act (FERA), 1973

The government introduced the Foreign Exchange Regulation Act, 1973 with the aim to regulate foreign capital in India. The section 29 of the Act stipulated that all foreign companies need to register with the Reserve Bank of India (RBI) and put a 40% ceiling on the foreign equity share in the domestic industries. A relaxation was given to industrial companies to hold up to 74% foreign equity if they were engaged in either high priority industries that required sophisticated technology or primarily export-oriented (minim export of 60% of the total turnover) (Chaudhuri, 1979). Because the pharmaceutical industry was specified as a high priority in the Industrial Policy of 1973, FERA companies could have more than 40% of foreign

equity if they manufactured high technology bulk drugs and formulation products (Mazumdar, 2013).

Additionally, FERA companies were also required supply 50% of their bulk drugs to non-associated formulators. The law also limited the ratio of value bulk drugs to the value of total formulation in their own production to 1:5 (1:10 for domestic manufacturers), thus restricting the practice of captive consumption (Mazumdar, 2013).

2.2.2.4. The New Drug Policy, 1978

The growth of the domestic sector gained further momentum with the launch of the New Drug Policy (NDP) in March 1978. It had three-fold objectives of self-reliance, self-sufficiency and easy and cheap availability of drugs (N. Kumar & Pradhan, 2003). The NDP specified three categories of drugs. The first category consisted of 17 essential drugs that could only be manufactured by public sector units. The second group included 27 drugs reserved for production by domestic firms. The last group had another 64 items that were open to domestic as well as foreign firms. It also abolished brand names for five drugs: Analgin, Aspirin, Chloromycine, Ferropsulphate, and Piperazine (Bhaduri, 2001, p. 85).

The law also stipulated that large foreign MNCs with annual sales turnover of INR 50 million to build R&D facilities in India. They were further required to extend their quality testing services to small-scale Indian firms on a no-profit-no-loss basis (Bhaduri, 2001). Foreign firms which were engaged in producing formulations from imported bulk drugs and raw materials were given a two-year window to use maximum local content (Pradhan & Alakshendra, 2006).

These regulatory changes created a positive and protected institutional environment that was conducive to the growth of Indian pharmaceutical industry. A large number of domestic firms equipped with reverse engineering capabilities took over the national stage, and the industry witnessed a dramatic evolution in the production of both bulk drugs and formulations. By the end of 1989-90, the total production of bulk drugs and formulations was an estimated INR 6.4 billion and INR 34.2 billion respectively (Figure 2.1). The market share of the foreign firms in the formulations market had reduced to 40% not because they were producing less but because Indian firms were producing more (Guennif & Ramani, 2010; Pradhan & Alakshendra, 2006).

Advancement in production capabilities also energized the internationalization of Indian firms leading to an increase in exports mainly directed to other developing countries in Africa and the Commonwealth of Independent States (CIS) countries (Pradhan & Alakshendra, 2006). The export of pharmaceutical products by Indian firms grew from a mere $11 million in 1970-71 to $510 million in 1989-90 (Figure 2.2). Further, since the late 1980s, the export performance of the industry has led to consistent positive balance in trade.

2.3. Push Factors of Internationalization

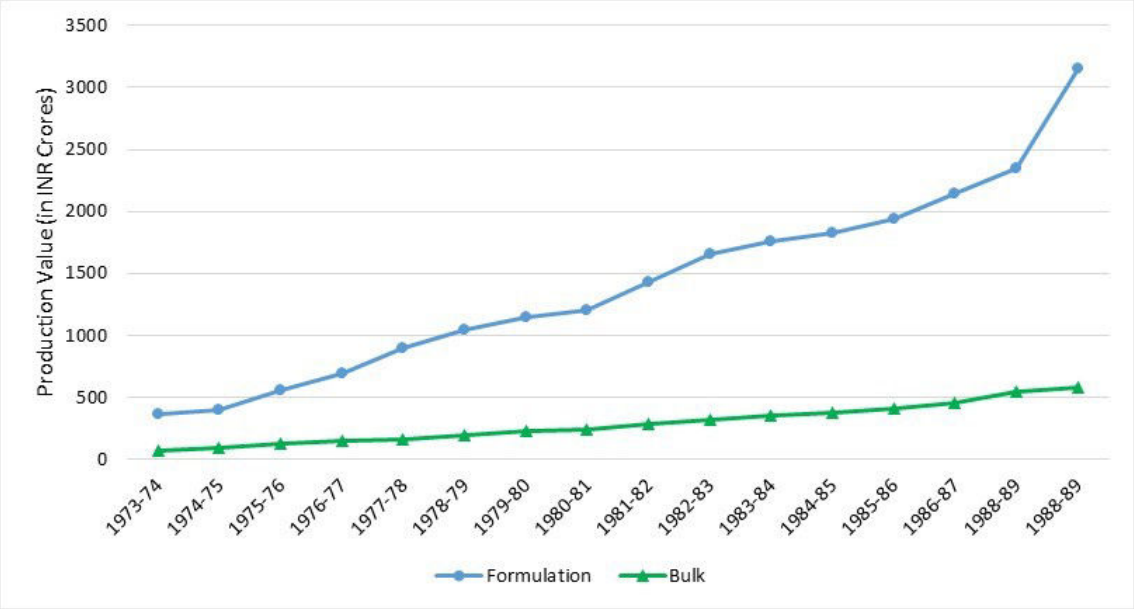
The regulatory reforms until the 1970s were directed towards strengthening domestic capabilities, achieving self-sufficiency and rationalizing drug prices. The government policies created an institutional environment which on the one hand was protectionist towards domestic firms and on the other discriminated foreign firms. As discussed in the previous section, these measures were phenomenally successful as evident from growth in pharmaceutical production and rise in the share of Indian firms. By the end of the 1980s, Indian firms were already gaining recognition as a supplier of cheap and quality generic in developing countries. In 1988, Ranbaxy became the first Indian company to get its Active Pharmaceutical Ingredient (API or bulk drugs) plant in Toansa approved by the USFDA for supplying the US market (Kedron & Bagchi-Sen, 2011). Few firms had also started investing overseas joint-ventures (JVs) in developing countries of Asia and Africa in collaboration with local partners with the motivation to exploit their ownership advantage of reverse engineering and price competitive drugs. In fact, 15 JVs were started by Indian firms, most notably Ranbaxy (4/15) between 1976 and 1988 (Pradhan & Alakshendra, 2006)[8]. However, the outward FDI framework of the Indian government was restrictive and only allowed minority JVs. Each such proposal had to get approval from an inter-ministerial committee on JVs. The government did not permit cash remittances as a means of financing foreign ventures. Instead, firms could export capital goods, know-how, technology or machinery towards their outwards equity contribution. Further, firms were required to repatriate 50% of the declared dividends to India (D. Nayyar, 2008).

[8] Of these 15 JVs, 6 were in Nigeria, 3 in Malaysia and 2 in Thailand. Indonesia, Tanzania, UAE and Nepal received 1 JV each. For details see, Pradhan & Alakshendra (2006).

However, the real thrust to the foreign expansion of Indian pharmaceutical firms came during the 1990s due to a series of institutional reforms triggered by India's economic liberalization and accession to the Trade Related Aspects of Intellectual Property Rights (TRIPS). These exogenous shocks threatened the very source of competitive advantages of Indian pharmaceutical firms which lied in imitating drugs that were patented elsewhere while enjoying a market with minimum competition from foreign firms due to the discriminatory policy regime against the latter (Chittoor et al., 2009). Nevertheless, these institutional reforms in trade policies and intellectual property laws also created opportunities for Indian firms by filling the institutional voids, for example, in the financial market. Thus, changes in the home country environment resulted in *push factors* which on the one hand made the home country more competitive but at the same time opened the doors for overseas expansion. Here we refer to all **the regulatory reforms that find their origin in India and that motivated and supported the internationalization of Indian pharmaceutical firms as *push factors.*** The outcome was an industry-wide adaptation through organizational and strategic innovation. Indian firms chose active internationalization as a strategic response to institutional changes brought about by liberalization and TRIPS (Chittoor et al., 2008). This internationalization was not only directed to find new markets for their products but also to acquire capabilities that would be necessary to adapt and survive in the new institutional environment (Kale, 2010).

This section will throw light on selected institutional changes that pushed Indian firms towards internationalization.

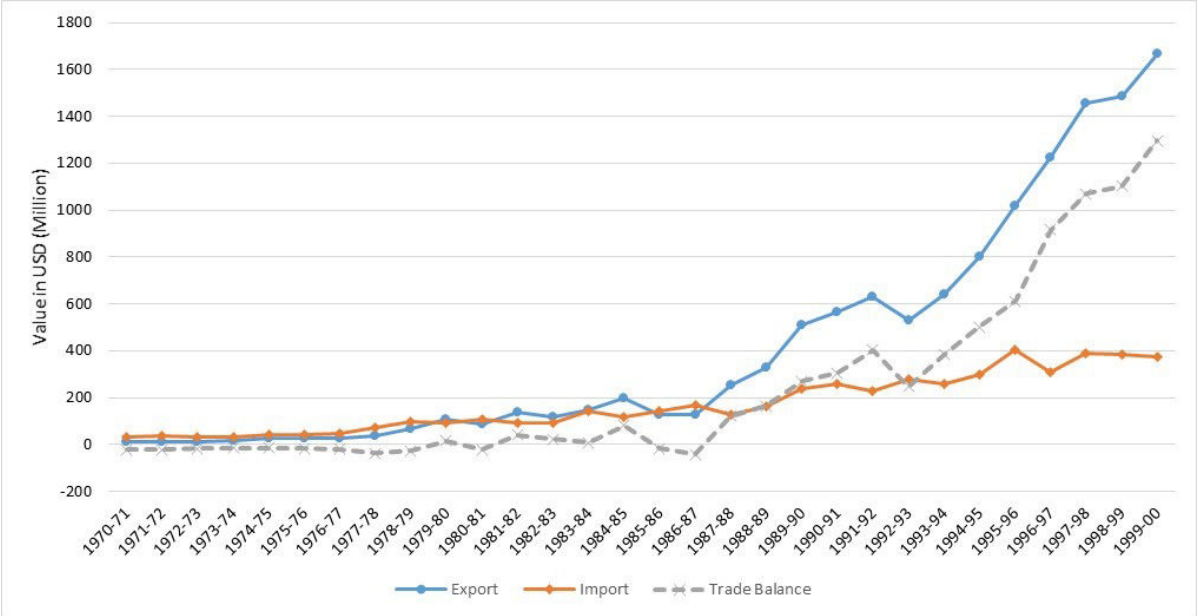
Figure 2.1: Trend in the production of bulk drugs and formulations in India between 1970s and 1990



Sources: (Bhaduri, 2001; Bhagat, 1992; Pradhan & Alakshendra, 2006)

Note: 1 crore = 10 million

Figure 2.2: India's trade in pharmaceutical products between 1970 and 2000



Source: Handbook of Statistics on Indian Economy, RBI (2001, 2002)[9]

[9] Handbook of Statistics on Indian Economy can be accessed at: https://rbi.org.in/Scripts/publications.aspx

2.3.1. Push due to Changes in Competitive Landscape

A series of structural reforms across Indian economy was initiated in 1991 after a severe balance of payment crisis. The Industrial Policy of 1991 was the first post-crisis step to attract foreign investment with the aim to achieve economic growth and integrate with the global economy. The government gradually lifted inward FDI restrictions, eased industrial licensing requirements, and reduced import tariffs to link Indian economy with the global market. Pharmaceutical sector was gradually opened to the private sector for all classes of drugs and control on medicine prices was also steadily reduced. The impact of these post-liberalization changes was an influx in the operation of foreign pharmaceutical firms in India thus increasing local competition. Some policies that stimulated the entry of foreign firms in India are explained below:

- The Industrial Policy of 1991 allowed 51% FDI through the *automatic route* to high priority industries which included pharmaceuticals. The limit was further raised to 74% in March 2000[10] and to 100% in June 2003[11]. The government also created a Foreign Investment Promotion Board (FIPB) consisting of senior officials to consider FDI proposals that did not qualify for automatic approval.

- In 1994, the government substantially changed the drug policy of 1986 to implement liberalization measures into the pharmaceutical industry. The modified drug policy abolished industrial licensing for all bulk drugs, their intermediaries, and formulations except for those produced by the use of recombinant DNA technology, those requiring in-vivo use of nucleic acids, and specific cell/tissue targeted formulations (Bhaduri, 2001). Moreover, licensing was also required for five bulk drugs – vitamin B1, vitamin B2, tetracycline, oxytetracycline and folic acid – that were exclusively reserved for the public sector. However, reservation for the public sector came to an end in 1999, thus opening these five drugs to the private sector[12].

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[10] RBI Notification No. FEMA 20 /2000-RB dated 3rd May 2000

[11] RBI Notification No. FEMA. 94 /2003-RB 18th June 2003

[12] DIPP Press Note No.3 (1999 SERIES) 26th February,1999: De-licensing of five bulk drugs: http://dipp.nic.in/sites/default/files/pn13_0.pdf

- Automatic approval for Foreign Technology Agreements was initiated for all bulk drugs, their intermediaries, and formulations except for those produced by the use of recombinant DNA technology.

- The ratio constraint of linking the value bulk drugs to the value of total formulation in own production was abolished. Also, the mandatory rule of supplying a certain proportion of bulk drugs to non-associated formulators was also removed (Joseph, 2016). The policy also scrapped the restrictions on the use of imported bulk drugs for producing formulations in India and progressively eliminated or reduced import tariffs on pharmaceutical ingredient from 85% in 1993 to a maximum of 30% in 2004 (Chittoor et al., 2008).

- Dilution of control over drug prices had already started with the DPCO of 1987 that reduced the number of bulk drugs under price control to 142 (Joseph, 2016). These drugs were grouped into two categories with MAPE of 75% and 100% (Bhaduri, 2001). Following liberalization and the drug policy of 1994, the government announced the new DPCO in 1995. It further reduced the number of bulk drugs under the ambit of price control to 74 which accounted for 40% of the total market based on the criteria of market competition and annual turnover. Also, all the drugs were put in a single category with a MAPE of 100%. The DPCO of 1995 also allowed an exemption period of 10 years for drugs produced through indigenous R&D. Following the DPCO of 1995, a National Pharmaceutical Pricing Authority (NPPA) was established in 1997 to regulate the prices of drugs in India (N. Kumar & Pradhan, 2003). In December 2012, the New Pharmaceutical Pricing Policy was launched under which the future prices would be regulated only for formulations based on the criteria of essentiality and through a market-based pricing. The government announced the following DPCO in 2013 that controlled all the formulations listed in the National Essential Medicines List (NEML), 2011 by setting up ceiling prices (Chaudhuri, 2015b). The ceiling price for a formulation is calculated by dividing, the sum of prices of all the brands having a market share of 1% or above of the total market turnover of the medicine by the total number of manufacturers of such brands of medicine (Chaudhuri, 2015b).

2.3.2. Push due to Changes in the Intellectual Property Regime

In April 1994, India became one of the founding members of the World Trade Organization (WTO) and acceded to the TRIPS agreement. This obliged India to make changes in its existing patent laws to become TRIPS compliant within a transition period of 10 years, starting from January 1, 1995. However, the arrival of TRIPS to India was not without controversy as researchers and activists questioned the impending impact of the new regime on the access and affordability of medicines in developing countries (Bhaduri, 2006; Chaudhuri, 2005; Gupta, 2003; Kapczynski, 2009; Orsi et al., 2007; Watal, 2000). The Indian government took due caution in revising the law. While it adhered to the minimum harmonization standards as required by the TRIPS, it also took advantages of incorporating TRIPS flexibilities to minimize the impact of patents on medicines. Further, India utilized the complete ten years of transition to avoid a sudden change. It implemented TRIPS through three successive amendments to the Patents Act of 1970.

The Patents (Amendment) Act, 1999 introduced a mail-box system with retrospective effect from 1 January 1995 to review new patent applications. Its purpose was to hold an application in the field of pharmaceuticals until the end of 2004, after which it was to be examined for the grant of a patent. However, the applicant could receive Exclusive Marketing Rights (EMR) for five years if the patent had been granted in some other WTO member country (Chaudhuri, 2005). The second set of changes were made through the Patents (Amendment) Act, 2002 that became effective on May 20, 2003. It extended the patent term to 20 years to all patents, introduced the definition of "inventive step," provision for compulsory licensing, exception to exclusive rights, reversed the burden of proof in process infringement and so on (Chaudhuri, 2005; Kapczynski, 2009; Nair, 2008). Finally, the third set of changes like introduction of compulsory licensing measures for export purposes and discontinuation of the EMR provisions were made through the Patents (Amendment) Act of 2005 which came into effect on January 1, 2005, making India a TRIPS-compliant country.

2.3.3. Push Factors Facilitating Internationalization

While these institutional measures made it easier for foreign MNCs to invest in India, they also supported Indian firms by relaxing the norms on outward FDI on the one hand and by providing access to capital from international financial markets on the other. Consequently, making it

easier for Indian pharmaceutical firms to adopt acquisition as a tool of foreign expansion. These acquisitions were primarily targeted to advanced markets like the US and Europe not only as a market penetration strategy but also to acquire new capabilities. Some of the regulatory changes that facilitated the internationalization are listed below:

- In 1992, the government created an "automatic route" for foreign investments by Indian firms and for the first time included the provision for cash remittance. Indian firms could invest up to $2 million in overseas ventures of which the cash remittance could be a maximum of $0.5 million (D. Nayyar, 2008).

- In 1995, the overseas investment came under the domain of the RBI, and the investment limit was raised to $4 million, but the cash remittance was still fixed at $0.5 million. For investment more than $4 million, the proposal had to be approved by a select committee comprising of the members of the RBI and the ministries of external affairs, finance, and commerce.

- FERA was repealed in 1998, and it was replaced by the Foreign Exchange Management Act (FEMA) which came into force in June 2000. FEMA significantly raised the scope of outward FDI to $50 million in a block of three financial years[13]. Also, the government permitted Indian firms to access foreign capital market to raise equity for FDI by issuing American Depository Receipts (ADR)/Global Depository Receipt (GDR). The limit to invest in overseas joint-ventures and wholly owned subsidiaries was extended to $100 million in 2002[14]. By 2004, firms could finance foreign expansion by an amount not exceeding100% of their net worth. The limit was gradually raised to 200% of the net worth in 2005[15] and then to the present limit of 400% of net worth in 2007[16]. Further, a firm can invest without any ceiling if the investment is made through

[13] RBI Notification No. FEMA 19/RB -2000 dated 3rd May 2000

[14] RBI Circular: A.P.(DIR Series) Circular No.27 (March 2 , 2002)
[15] RBI Notification No.FEMA.139/2005-RB
[16] RBI Notification No. FEMA. 173 / 2007-RB

the balances held in the Exchange Earner's Foreign Currency Account (EEFC) or out of funds raised in a foreign country through ADR/GDR.[17]

2.3.4. The Effect of Push Factors on Internationalization

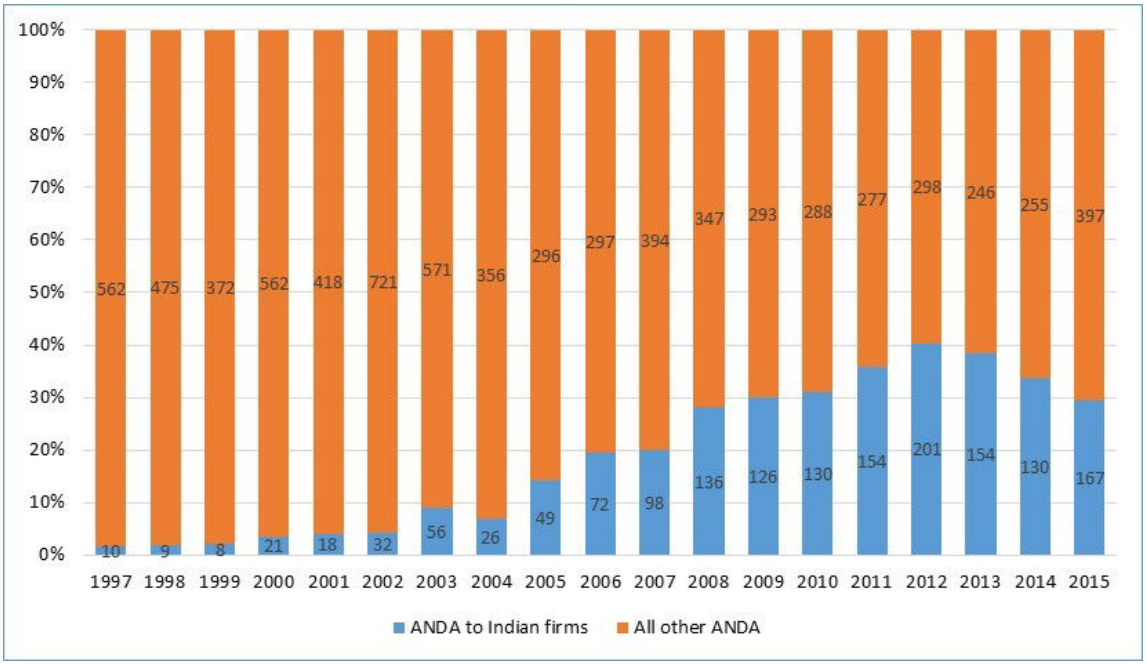
The push factors that emerged out of the dual impacts of liberalization and TRIPS resulted in an industry-wide restructuring and adaptation to the new institutional environment. Growth opportunities in the domestic market were weak under the new TRIPS-compliant product patent regime as new molecules could not be copied (Kale & Little, 2007). Liberalization further increased local competition due to the entry of foreign firm who could enjoy patent protection and had access to the same resource base as Indian firms (Kale, 2010a). However, liberalization also made it easier for Indian firms to venture into foreign markets that were more lucrative. A new wave of Internationalization, mainly targeting advanced markets, emerged as a strategic response to the changing environment (Chittoor et al., 2008, 2009; Kale, 2010a; Pradhan & Alakshendra, 2006). Some Indian firms like Ranbaxy, Dr. Reddy's, Wockhardt and Sun Pharmaceuticals, adopted an aggressive outward FDI to acquire foreign firms. Between 1990 and 1999, Indian firms invested in 142 foreign ventures of which 50 targeted to Europe and North America (Pradhan & Alakshendra, 2006). During the next decade (2000-2009), Indian firms carried out 139 foreign acquisition directed to 21 developed and 12 developing countries. The total worth of these acquisitions was over $3.4 billion of which advanced markets accounted for 92.6% (Pradhan, 2010). A large number of acquisitions targeted to developed countries was not only meant to find new markets for products but also to build new regulatory and marketing competencies that could sustain their survival (Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Pradhan & Alakshendra, 2006).

The change in the competitive landscape also required Indian firms to reconfigure their resources and capabilities and acquire new capabilities to survive. The long experience of learning by doing helped Indian firms to quickly adapt **from duplicative to creative imitation** to launch their product in the advanced markets once the patent was expired (D'Mello, 2002). In fact, since 2008, Indian firms have on an average persistently secured over 30% of all

[17] RBI Notification No. FEMA 120/ RB-2004 dated 7th July 2004

Abbreviated New Drug Applications (ANDAs) granted by the USFDA (Figure 2.3). Also, they started taking advantage of the new intellectual property regime to substantiate their value in the market by getting patents. The post-liberalization period saw an increase in the R&D intensity of the industry (Joseph, 2011; Pradhan, 2003). The government also supported R&D activities by introducing several tax relief measure on research expenditure (Ray, 2004). Indian firms started investing in R&D for creative imitation to develop non-infringing process, Novel Drug Delivery System (NDDS) and drug discovery, particularly, new chemical entities (NCE) to move-up the pharmaceutical value chain. The outcome was an increase in the number of patents filed by India firms post-1995 (Kamble, Ghorpade, Kshirsagar, & Kuchekar, 2012). Indian firms also started to invest in upgrading their production facilities and adopted the Good Manufacturing Practices (GMP) according to international requirements. This is evident from the current number of manufacturing sites in India that has been approved by international agencies such as the USFDA, the WHO and the UK MHRA among others (Table 2.5). Thus, the institutional environment in post-liberalized India paved the way and catalyzed the internationalization activity of Indian firms.

Figure 2.3: Trend in ANDAs granted to Indian firms



Source: (CRISIL, 2013; Kale & Little, 2007)

Table 2.5: Foreign certifications granted to Indian firms

Certification	Total Number
Units registered with the USFDA (April, 2015)	605
Formulation companies with the USFDA approvals	53
CEPs received (February, 2016)	1354
Manufacturers with CEPs	220
Units with EU GMP compliance (February, 2016)	631
Market authorizations granted by the UK MHRA (March, 2015)	1559
WHO GMP certified plants	1400

Source: 12th Annual report Pharmexcil

Note: CEP = Certificate of suitability of Monographs of the European Pharmacopoeia; MHRA = Medicines Healthcare Regulatory Agency; USFDA = United States Food and Drug Administration

2.4. Pull Factors of Internationalization

Pull factors refer to the institutional changes in pharmaceutical markets that happened outside India and created opportunities for Indian firms to expand internationally. The primary target of these institutional changes was to facilitate the inclusion and promotion of generic drugs. While stronger patent protection in the home market brought an end to the old business model of copying, it also opened new avenues advanced markets of North America, Europe, and Japan where the generic market was growing due to patent expiration, easing of generic registration requirements and generic substitution policies. Also, there were new shifts to promote generics in developing countries through the adoption of National Essential Medicines List (NEML) and changes in government procurement policies. Further, the launch of innovative mechanisms for fighting pandemics resulted in the creation of a donor-funded market that relied on the supply of generic drugs. We will discuss these changes in the following sections.

2.4.1. Pull Factors: 'Yes' to Generics in Advanced Markets

While the Indian pharmaceutical industry was experiencing changes from liberalization and TRIPS, generic use in advanced markets was gaining momentum due to rising pharmaceutical expenditure (Ess, Schneeweiss, & Szucs, 2003; Mossialos & Oliver, 2005; Wouters, Kanavos,

& McKee, 2017). The entry of generic drugs in the developed market was facilitated by a large number of blockbuster drugs (e.g., Prozac, Zantac, Zovirax) going off patent (Mullins, Palumbo, & Stuart, 2000) and thus open to being copied by non-originators.

The US was among the first countries to have a generic policy, but it was not without opposition from the originator pharmaceutical industry. Wouters et al. (2017) report that the first instances of generic drug substitution in the US were reported in the late 1940s. However, pharmaceutical trade associations like the National Pharmaceutical Council (NPC), the Pharmaceutical Manufacturers Association (PMA) in alliance with the American Medical Association (AMA) and the American Pharmacists Association (APhA) aggressively lobbied against such policies. They cited reasons ranging from scientific uncertainty about the effectiveness of generic drugs to the diminished role of physicians and violations of ethical and professional standards of the pharmacists. Consequently, by 1959, 44 states had legislated against generic drug substitution policies.

Nevertheless, during the 1960s and 1970s, the rising healthcare expenditure necessitated authorities to look for measures to cut the spending. Also, there was a growing support among pharmacists for substituting branded medicines with generics. In 1972, Kentucky became the first state to abolish ant-substitution law, and by 1984 all 50 states had legalized generic substitution (Wouters et al., 2017). The new legal framework resulted in a rapid growth of generic medicines market. In 1984 generics accounted for 19% of the prescriptions in the US compared to 53% in 2002, while by 2015, 88% of the prescriptions were filled generically (Thayer, 2014).

During the 1990s, several European countries as well had started to undertake active policy measures to promote the diffusion of generics – a movement which gradually spread across all of Europe in response to rising drug expenditures (Ess et al., 2003). These measures included generic prescription, substitution, use of reference pricing and incentivizing the use of generics (Magazzini, Pammolli, & Riccaboni, 2004; Wouters et al., 2017). Germany, Denmark, The Netherlands, Switzerland and the UK were among the first countries in Europe to allow pharmacists to implement generic substitution for originator drugs (Ess et al., 2003). These policy measures boosted the demand for generics and consequently a rise in market share throughout Europe. For example, by 2014, generic medicines accounted for 84%, 81%, and

71% of the pharmaceutical market in terms of volume in the UK, Germany, and the Netherlands respectively (OECD, 2016).

2.4.1.1. Simplifying the Entry of Generics in the US: The Hatch-Waxman Act

Further, the entry process of generic drugs in the US market was structured and streamlined after the enactment of The Drug Price Competition and Patent Term Restoration Act or the Hatch-Watchman Act of 1984. Under this Act, an applicant can file for an Abbreviated New Drug Application (ANDA) with the United States Food and Drug Authority (USFDA) to launch its generic product in the US market. These applications are called 'abbreviated' because the law relaxed the requirement for generic firms to generate safety and efficacy data through lengthy and expensive clinical trials. Generic firms were only required to show that their product is bioequivalent to the innovator product, i.e., it has the same active ingredients, strength, dosage form, route of administration and rate and extent of availability at the site of drug action compared to the innovator product.

A firm has four options to apply for an ANDA certification against the patents listed in the Orange Book:

i. There are no patents listed
ii. Listed patents have expired
iii. The product will not be launched before the expiry of the listed patents, and
iv. The patent is invalid or unenforceable, or the product does not infringe the patent listed in the Orange Book.

These are referred to as, Para I, II, III and IV filings respectively (Chittoor & Ray, 2007; Vijayaraghavan & Raghuvanshi, 2007). The para IV certification is particularly important because if a firm files an ANDA using para IV, then it is automatically considered an act of infringement. The applicant is required to notify the innovator company of the filing and provide the legal and factual basis for its claim. The innovator has the right to initiate a legal action against the applicant. However, the Hatch-Waxman Act also provides a 180-day market exclusivity to the first ANDA applicant with a para IV certification if the applicant is not sued or wins the case against the innovator (Vijayaraghavan & Raghuvanshi, 2007). Large Indian

companies like Ranbaxy and Dr. Reddy's have actively pursued para III and para IV filings to increase their share in the US market (Kale & Little, 2007).

The law also provided generic firms with a *research exemption* or Hatch-Waxman exemption under which protected them against legal action for patent infringement because of manufacturing drugs for getting regulatory approval. This exemption, also known as *Bolar Provision* or *Bolar Exemption* has been gradually incorporated in patent laws of various countries like Canada ((Section 55.2(1) of the Canadian Patent Act), Brazil (Law No. 9.279/96), China, Japan, Europe (Directive 2004/27/EC) among others (Tridico, Jacobstein, & Wall, 2014).

2.4.2. Pull from Developing (African) Countries

Indian firms had already started their international expansion to developing countries of Asia, Africa and the CIS in pre-liberalization era mainly using exports and to a limited extent through JVs. However, throughout the 1990s and 2000s, the regulatory and political environment governing pharmaceuticals in developing countries and particularly in Sub-Saharan Africa witnessed rapid structural changes that would increase the demand for generic drugs. The most important of these changes were the adoption of a National Essential Medicines List (NEML) by most developing countries based on the WHO model formulary, the embracement of generic procurement policies by the Central Medical Stores (CMS) and the rise of a new global governance structure of the donor-funded markets The last point concerning the donor-funded markets is particularly revealing. These markets are characterized by the active involvement of a variety of international health agencies that influence the supply and demand of medicines for selected diseases in the global south. We shall discuss these changes in the subsequent sections.

2.4.2.1. Adoption of National Essential Medicines List

The period following World War II saw a rapid growth of the pharmaceutical industry catalyzed by the discovery of miracle medicines. In fact, drugs like penicillin, chloroquine, streptomycin, tetracycline, chloramphenicol, isoniazid, erythromycin and the development of oral contraceptives had stimulated the acceptance of modern medicine (Management Sciences

for Health, 2012, p. 30). By 1970, effective medicines existed for nearly every major illness, but these were mainly available to the population of the affluent countries. There was a glaring difference between the industrialized world and developing countries where entire populations had little access to modern medicines. For them, medicines were either unavailable or unaffordable and often obscure, outdated, ineffective and even dangerous (Management Sciences for Health, 2012, p. 31; Quick, Hogerzeil, Velasquez, & Rago, 2002).

Faced with these challenges, the 1975 World Health Assembly introduced the concepts of 'essential drugs' and 'national drugs policy' to fill the gap in access and cultivate a more reliable supply of medicines in developing countries (Quick et al., 2002). According to the WHO,

"Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford" (WHO, 2015c).

The underlying idea was that a limited list would allow a more cost-effective use of available health resources and better management of medicine (WHO, 2003). Countries could frame their purchasing, supply, and training of healthcare professionals on items that were most needed and affordable.

A salient feature of the EML is its focus on adopting international non-proprietary names (INN) for listing drugs. Each pharmaceutical product or active pharmaceutical ingredient is assigned a unique INN or generic name which resides in the public domain. The INN is different from the brand name of a drug which is the property of a pharmaceutical company. For example, Brufen and Advil are two brand name products both of which can be identified with the same INN, i.e., Ibuprofen. Generic companies can further sell the medicine only with INN without creating a brand name. Thus, adopting EML permits countries to establish a competitive procurement system. In fact, EML has become a vital component of the procurement strategy of most countries and international organizations like MSF and UNICEF among others (Laing, Waning, Gray, Ford, & Hoen, 2003; WHO, 2003)

In 1977, WHO published its first model list of essential drugs that identified 208 specific medicines which could provide safe and effective treatment for the majority of communicable and non-communicable diseases (WHO, 2016c). The list serves as a basis for individual countries to define a national list of medicines which would provide safe and effective treatment for infectious and chronic diseases to its population. In 1978, the World Health Assembly passed a resolution (WHA 31.32) urging member states to create national lists of essential medicines and adequate procurement systems. In the same year, the WHO and UNICEF led International Conference on Primary Health Care in Alma Ata, Kazakhstan identified essential medicines as one of the critical components of primary health care (Laing et al., 2003). At the time of the publication of the first EML, only a handful of countries like Papua New Guinea, Sri Lanka, Cuba, Peru, Tanzania, and Mozambique had national medicine policy based on essential drugs. Gradually, most countries have adopted a NELM. By 2002, nearly 156 WHO member states had adopted essential medicines list, and some even have provincial and regional lists. (Laing et al., 2003; Quick et al., 2002). The EML is currently in its 20th edition and includes a total of 433 drugs deemed indispensable for addressing the most basic public health needs (WHO, 2017d).

It can be argued that the adoption and promotion of generics on such a large scale created new space for the expansion of Indian firms. By this time Indian pharmaceutical industry had already developed superior reverse engineering capabilities and was producing generic version of originator medicines at a fraction of the original price. The pharmaceutical supply-system in other developing countries also benefited as they could obtain better prices by procuring the low-cost generic versions of common medicines.

2.4.2.2. Changes in the Functioning of the CMS: Example from Francophone West Africa

In most low-income countries, the Central Medical Stores (CMS) handles the typical public-sector supply of medicines. It is responsible for the procurement and distribution of drugs to public health facilities on behalf of the government (Yadav, 2015). Historically, the CMSs were used to be owned by the government as distinct departments often as a part of the ministry of health and financed from the government budget. These state-run services were characterized by inefficiency and poor performance due to limited autonomy and functioning.

They faced problems concerning procurement, financial and logistics management, security, and storage (Govindaraj & Herbst, 2010). In the1980s and 1990s many governments in Sub-Saharan Africa started to incorporate market mechanisms to reform the CMS by providing managerial and financial autonomy as a part of the broader public sector reforms that called for decentralization, privatization, and cost recovery under structural adjustment programs (Calamitsis, 1999; Govindaraj & Herbst, 2010).

Several Francophone countries like Burkina Faso, Cameroon, Mali, and Senegal provide early examples of introducing some form of autonomy in the CMS, well before other developing countries (Govindaraj & Herbst, 2010; Johnson, Faure, & Raney, 1999). Among the many problems, before the 1990s, the CMS in these countries were primarily procuring nonessential originator drugs which were several times more expensive than their generic equivalents. In the early 1990s, all four countries were undertaking systematic and comprehensive reforms as a part of the primary care strategy **based on the principles of the Bamako Initiative that accentuated decentralization and cost recovery.** The design and implementation of CMS reforms during this period received financial and technical assistance from the international donor community (e.g., the EU, WHO, and the World Bank) who helped in drawing the objectives, organizational structure, and rules governing the CMS. On the one hand, these reforms allowed the CMSs to exert more autonomy in strategic, financial, procurement and logistics management. On the other, changes in regulatory frameworks to reduce price and increase the access to medicines required the CMS to procure only generic drugs listed on the NEML usually through international competitive bidding (Govindaraj & Herbst, 2010; Johnson et al., 1999).

Focus on essential medicines list, and generic based procurement was also getting momentum in other countries in Sub-Saharan Africa. For example, Kenya was one of the first African countries to recognize the importance of essential medicines and developed its list in 1981. In 1992, the ministry of health further intensified the effort to rationalize the pharmaceutical sector by updating the NEML and making it the basis of pharmaceutical management in the public sector (Management Sciences for Health, 2012, p. 298)

Based on the previous discussion, it can be reasonably argued that the CMS reforms must have increased the demand for generic drugs in francophone African countries by opening the public market which was previously closed to generic firms. Further, because the local pharmaceutical

industry was (and is still) not developed, it created growth opportunities for Indian firm who were already familiar with the African market through prior export linkages.

Finally, because the regulatory requirement for quality and safety were not as stringent as in the North American and European markets, a greater number of Indian firms could seek opportunities in the African market.

2.5. Pull from the New Governance Structure of Donor-Funded Market

Donor-funded markets **are an institutional intervention where demand and supply for pharmaceutical products are mediated through the action of international actors.** In fact, International organizations like the WHO and the Global Fund have played a critical role in shaping this global governance architecture for health which in the view of Biermann et al. is an "overarching system of public and private organizations, regimes, principles, norms, regulations, and decision making procedures that are valid or active in a given issue area of world politics" (Biermann, Pattberg, Asselt, & Zelli, 2009). The pertinent issue, in this case, is the access to medicines in resource-constrained developing countries. International agencies have not only contributed towards making access to medicines a global health agenda, but they have also become active market participants who influence and, in many cases, set the rules of the game.

As discussed later in the chapter, these markets are the outcome of a long political process to tackle some the major health problems of the south which could not be dealt without addressing the lack of access to medicines. In fact, the donor-funded market segment has become a striking feature of the pharmaceutical sector in low- and middle-income countries (LMICs). These markets do not encompass all pharmaceuticals products but instead they are disease specific. They primarily focus on a specific set of global health challenges such as HIV/AIDS, TB, malaria, diarrhea, influenza, childhood immunization and reproductive health. The selection of these ailments is the product of a global normative consensus whose roots lie in various international resolutions that culminated in the United Nations Millennium Declaration of 2000 (United Nations, 2000). However, even though the scope of this market is limited, its impact on improving health conditions has been enormous which is evident from the increase in the

number of people receiving treatment for various diseases and reduction in disease prevalence and mortality (GAVI, 2017; Unaids, 2017; WHO, 2015a).

Consequently, the rise of the institutional market for medicines has led to the evolution of complex relationships and interdependencies between states, firms and transnational organizations. The power to strike bargains in such relationships often does not lie with states but with international organizations who shape the institutional framework for efficient market functioning through a range of interventions. Such "structural power" in the words of Strange, "confers the power to decide how things shall be done, the power to shape frameworks within which states relate to each other, relate to people, or relate to corporate enterprises (Strange, 1998).[18]"

One the one hand, they are actively working in domains such as the assurance of medicine quality and price negotiations that used to be under the sole responsibility of national governments (Montalban, Smith, & Gorry, 2012). On the other hand, they are creating incentives for pharmaceutical firms by ensuring stability in the market through demand certainty. For example, the WHO acts as the global prescriber by recommending disease-specific treatment guidelines that serve as the basis for national policies (Orsi & Zimmerman, 2015). The WHO also certifies the quality of selected pharmaceutical products for use in developing countries. This has become the minimum standard of quality for procurement by other international agencies. Thus, deciding which manufacturers can compete in the market (Hoen, Hogerzeil, Quick, & Sillo, 2014). Further, international organizations such as the Global Fund provide billions of dollars to countries for the procurement of medicines and at the same time negotiate prices with manufacturers to get the best value for money. Moreover, international organizations have also entered into the R&D pharmaceutical products targeting the needs of populations in developing countries (Chataway et al., 2007; Grace, 2010; Moon, 2008).

The arrival of the donor-funded market has created a multibillion-dollar growth opportunity for pharmaceutical firms by supplying medicines to developing countries financed by

[18] Aslo see, May, (1996)

international donors. What is noteworthy is that this market has historically relied on the supply of generic drugs and Indian firms have played a vital role since the very beginning.

However, donor-funded market segments have not received attention in the extant literature on the internationalization of Indian pharmaceutical firms. For this thesis, an examination of this specific segment will allow shedding light on a new type of pull factor that has catalyzed the growth of Indian firms in developing countries. The following sub-sections present the historical and contextual underpinnings within the broader framework of the political economy of HIV/AIDS that led to the establishment of institutional market of medicines. We will also see how the Indian generic suppliers have played a significant role in this market since the very beginning. Lastly, we shall also look at selected international organizations and market shaping strategies.

2.5.1. From TRIPS to Doha: A New Era in Access to Medicines for Developing Countries

TRIPS came into effect in January 1995 as a part of the World Trade Organization (WTO) agreement which laid down the minimum standards for the protection of intellectual property to be provided by each member country. It made it mandatory for member countries to grant patents in all field of technology including pharmaceutical products. It also harmonized the term of patents for at least 20 years. Before TRIPS, most developing countries and some developed countries had excluded medicines from being patented (Hoen, 2009).

The impact of TRIPS on public health became evident in the wake of AIDS crisis in developing countries, particularly in Sub-Saharan Africa which was home to nearly 71% of the estimated 34.3 million people living with HIV/AIDS in 1999 (UNAIDS, 2000). In theory, TRIPS had a provision of "compulsory licensing" which could be used by countries to override patents in public interest, but its implementation by developing countries was thwarted due to the substantial political pressure and the threat of trade sanctions from developed countries. Moreover, TRIPS had also made it illegal to import generic versions of medicines which were significantly cheaper than originator products (Moon, 2008).

South Africa took one of the first attempts to use TRIPS flexibilities. In 1997, South African Parliament passed the Medicines and Regulated Substances Control Amendment Act to increase the availability of medicines to combat the increasing HIV epidemic. The law provided a legal framework for generic substitution of off-patent medicines, parallel imports,

compulsory licensing and price transparency (Hoen, 2009; Marc, 2001). In February 1998, the Pharmaceutical Manufacturers' Association of South Africa and 40 multinational companies initiated a lawsuit against the South African government on the premise that the act violated the TRIPS agreement (CPTech, 2001; Hoen, 2009).

Civil societies and NGOs widely publicized the lawsuit as an evidence of the negative impact of the patent protection on global access to HIV medicines (Owen, 2014). It received widespread media coverage and placed HIV/AIDS as the global public health crisis that was hard to ignore any longer (Gellman, 2000b, 2000a; Owen, 2014). Initially, the US and the European Union pressured the South African government to repeal the Act using political force and threatening trade sanctions, but they would later change stance in the light of growing activism at home.

The series of events culminated at the WTO ministerial conference at Doha in November 2001 and led to the Doha Declaration on TRIPS and Public Health. The Declaration affirmed the rights of member states to protect public health as contained in paragraph 4 that TRIPS "should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all" (World Trade Organization, 2001). Further, paragraph 5 specified the conditions for the use of TRIPS flexibilities of compulsory licensing and parallel importation. Additionally, the Declaration also granted least developed countries an extension until 2016 to implement TRIPS. In 2015, the TRIPS council further extended the deadline to 2033 (Saez, 2015).

While there are unresolved issues with some of the conditions for using compulsory licensing[19], the Declaration was crucial for creating the legal ground for making generic-versions of patented drugs available in large quantities. In the aftermath of the Doha Declaration, the WHO published the first edition of HIV treatment guidelines for resource-limited settings in March 2002. In the following month, WHO added several patented ARVs in its 12th and revised essential medicines list (Laing et al., 2003; WHO, 2003).

The inclusion of ARVs on the EML reaffirmed that the availability of these medicines was a priority health care need of patients in developing countries and that cost was not a criterion

[19] For details of these the conditions of use of compulsory licensing see Hoen (2009).

for being essential. By 2011, over 60 developing countries had undertaken large-scale procurement of low-cost generic medicines using TRIPS flexibilities of compulsory licensing or parallel importing (Hoen, Berger, Calmy, & Moon, 2011).

2.5.2. Millennium Development Goals and Beyond

One of the most significant event at the turn of the century was the United Nations Millennium Declaration in September 2000 that would later acquire a concrete form as the Millennium Development Goals (MDGs) (United Nations, 2000)[20]. The MDGs were at the time the biggest commitment to solving some of the major challenges faced by developing countries through collective global action and improving health outcomes was high on MDG agenda. Three of the eight MDGs had a direct link with health outcomes which would become the focus area of the donor-funded market for medicines.

- Goal 4: To reduce child mortality
- Goal 5: To improve maternal health
- Goal 6: To combat HIV/AIDS, malaria, and other diseases

MDGs were remarkable in taking a comprehensive and systematic effort in addressing the problems. It did not consist of only normative consensus regarding what are the problems that need to be addressed but also laid down the plan for financing, implementing and monitoring the success of efforts to achieve the goals. However, the transformation from the Millennium Declaration to the MDGs did not happen overnight, but instead it was a long and challenging political process (Hulme, 2009; McArthur, 2014). McArthur (2014) notes that MDGs' operational building blocks took shape in three distinct phases. The first phase refers to September 2000 to September 2001 which lead to the translation of the Millennium Declaration into a series of goals and targets under the label of MDGs.

The second phase was from September 2001 to mid-2002. The main achievement of this period was securing a commitment from developed countries to finance the MDGs. An intergovernmental agreement around official development assistance (ODA) was signed by the

[20] There was no mention of the word "treatment" in the Millennium Declaration. It would appear as specific targets (Three instances) when the MDGs were formalized.

world leaders at the International Conference on Financing for Development in March 2002 at Monterrey, Mexico (Monterrey Consensus). The paragraph 42 of the Monterrey Consensus urged the developed countries to make efforts to reach the target of 0.7% of gross national product (GNP) as ODA directed to developing countries[21]. Indeed, Dieleman et al. (2016) reported that between 2000 and 2009 MDG-related development assistance for health increased by $290 million per year.

The final phase was from mid-2002 to September 2005 that was concerned with the debates around consolidating the technical framework needed for the implementation of MDGs. The UN Millennium Project was established as an independent advisory body under the directorship of Professor Jeffrey Sachs to recommend an action plan for the MDGs. The Millennium Project created ten task forces consisting of global experts to identify operational priorities, organizational means for implementation and financing structures needed to achieve the MDGs (Arrow, Panosian, & Gelband, 2004). The final project plan for MDG achievement was launched in January 2005 and culminated at the UN World Summit in September that year where member states resolved to align their national development strategies with the MDGs[22].

However, it is noteworthy that while it took until the 2005 World Summit to reach an agreement regarding MDG-consistent national strategies, many health-related goals were put into action long before. This mobilization of efforts was in part due to the active involvement of the private sector. In fact, a salient aspect of the Millennium Declaration was legitimizing the participation of private sector in the field of international development[23]. It was reflected in MDG, Goal 8: "To develop a global partnership for development". Target 8E went on to state, "In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries". Thus, further clarifying the extent of the role played by private sector to go beyond non-profits by including the pharmaceutical industry in the global development process. MDGs became a reference point for setting development priorities and cooperation by private stakeholders like civil societies, NGOs, philanthropies, pharmaceutical industry and newly formed Global Health Initiatives like the Global Fund and the GAVI Alliance.Following the

[21] For details see: http://www.un.org/esa/ffd/monterrey/MonterreyConsensus.pdf

[22] https://documents-dds-ny.un.org/doc/UNDOC/GEN/N05/487/60/PDF/N0548760.pdf?OpenElement

[23] Evident from paragraphs 20 and 30 of the Millennium Declaration document.

end of MDGs, in September 2015 the United Nations endorsed the 2030 agenda for sustainable development. It consists of 17 Sustainable Development Goals (SDG) with 169 specific targets among them to be achieved by 2030. SDG3 is specifically dedicated to good health and well-being and aims to *"Ensure healthy lives and promote well-being for all at all ages"*. It has 9 targets of which target 3.3 extends the MDGs beyond HIV, TB and malaria to end the epidemic of neglected tropical diseases (NTDs) as well (and to combat hepatitis, water-borne diseases and other communicable diseases). This commitment is further strengthened by target 3.8 that calls for a universal health coverage including *"...access to safe, effective, quality and affordable essential medicines and vaccines for all"* and target 3.B which states to,

"Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all."

The arrival of SDGs has reinforced that access to medicines is not only the problem of a given state but rather it's a shared responsibility and is essential for global economic growth and prosperity. By emphasizing the relevance of the Doha Declaration, it also points out the importance of legal mechanisms for the production and supply of low-cost generic medicines to developing countries. Moreover, it is noteworthy that SDG3 has not only brought the elimination of NTDs and access to medicines on the global development agenda but it also highlights the gap in pharmaceutical R&D for diseases that affect developing countries. This goal to support R&D for new medicines and vaccines for the needs of populations in developing countries is particularly relevant to the donor-funded market for medicines which is shaped and governed by international organizations.

2.5.3. Making a Case for Generics

In 1996, researchers at the 11th International AIDS conference in Vancouver reported that a cocktail of ARV drugs was more efficient at reducing the viral load in HIV/AIDS patients. It was a ray of hope for millions of HIV patients because a life-threatening disease has

transformed into a chronic condition (Reich & Bery, 2005; Schwartländer, Grubb, & Perriëns, 2006). The rapid uptake of antiretroviral treatment was extending the life of HIV patients in industrialized countries. However, the situation was stark in developing countries, which accounted for 95 percent of HIV disease burden. The cost of treatment per patient per year was over $10,000 and beyond the reach of most patients. Further, assuring access to all patients through public sector procurement was out of consideration because the cost was many times higher than the average health budget of most developing countries (Moon, 2008; Schwartländer et al., 2006).

2.5.3.1. Early UN Initiative to Increase Access to ARVs

In 1997, UNAIDS launched the Drugs Access Initiative (DAI) as an experimental pilot program to increase the treatment access for HIV/AIDS in developing countries (Brousselle & Champagne, 2004; Reich & Bery, 2005; Schwartländer et al., 2006). The rollout of the new strategy was implemented in four countries – Ivory Coast, Uganda, Vietnam, and Chile. It was the first instance of successful negotiation with pharmaceutical companies to obtain a differential pricing for ARVs supplied to developing countries based on their ability to pay (Brousselle & Champagne, 2004). DAI was a good starting point, but it was only a pilot and so, extremely limited in its coverage and scope. The price of the first-line ARV treatment at the onset was $7,200 per patient per year and each country employed a different financing mechanism which was detrimental to success. In Uganda, patients covered 100% of the treatment cost through out-of-pocket payments. In Ivory Coast, the government intended to cover most of the cost but was unable to sustain financially, resulting in substantial interruptions and delay in access. The situation was made even more complicated due to decisions regarding eligibility and levels of co-payment by patients (Schwartländer et al., 2006). The program was comparatively successful in Chile where the government was able to cover the total treatment cost (Brousselle & Champagne, 2004; Schwartländer et al., 2006)

A more streamlined process to increase the access to HIV treatment was launched in May 2000. The Accelerating Access Initiative (AAI) brought together five UN organizations: the UNFPA, UNICEF, WHO, World Bank and UNAIDS; and six pharmaceutical companies: Boehringer Ingelheim GmbH; Bristol-Myers Squibb, GlaxoSmithKline, Merck & Co., F. Hoffmann-La Roche Ltd. and Abbott Laboratories. The companies offered a preferential pricing for their

HIV medicines to developing countries (WHO & UNAIDS, 2002). However, AAI required each country to sign individual pricing agreements and conditions of access with pharmaceutical companies which among other things stated that,

"Continued investment in research and development by the pharmaceutical industry on innovative new treatments for HIV/AIDS is critical to expanding the global response to HIV/AIDS. Therefore, intellectual property rights should be protected, in compliance with international agreements, since society depends on them to stimulate innovation" (WHO & UNAIDS, 2002).

Thus, AAI was a political compromise between the UN agencies and pharmaceutical companies (Chung, 2003; Gellman, 2000a). It served as an alternative to the use of TRIPS exemptions such as compulsory licensing or parallel imports. While international agencies were looking for possible means to increase the access to treatment, pharmaceutical companies were facing extreme scrutiny and declining public image in the wake of South Africa lawsuit and political pressure from international agencies, activists, governments, and media (Chung, 2003; Hoen, 2009; Owen, 2014). It was an attempt by pharmaceutical companies to ameliorate their image by offering voluntary price discounts. They were keen to show that they were taking measures to cut down prices and it was the responsibility of governments and the international community to increase access and that TRIPS flexibilities were not needed. Though they were well aware that even if prices went down to $1,000 it would still be out of reach for millions of HIV patients in developing countries (Gellman, 2000a). Indeed, there was no commitment from pharmaceutical companies, who negotiated prices of their proprietary ARVs separately with individual countries, to disclose their offering to the public. Only Glaxo-Wellcome had made its price available a month after the agreement (Chung, 2003; Gellman, 2000a). As Chaudhuri (2005) notes, it was after Cipla offered to supply its tri-therapy (stavudine, lamivudine, and nevirapine) for $350 in September 2000 that prices by originator companies began to crash.

2.5.3.2. Generics Work: The Case of Brazil and Thailand

Meanwhile, at the same time, Brazil had shown significant progress in increasing the access to treatment and controlling the HIV epidemic. The Brazilian government had initiated providing HIV treatment as zidovudine monotherapy in 1991 (Ford, Wilson, Chaves, Lotrowska, &

Kijtiwatchakul, 2007). In 1996, Brazil became the first country to implement universal access to ARV treatment which owes much to the intense mobilization by the civil society groups which put effective pressure on the government. By 2001, AIDS-related mortality in Brazil had fallen by 50%, and over 100,000 people were receiving HIV treatment (Galvão, 2002; Reich & Bery, 2005). A critical factor that made this scale-up possible was Brazil's ability to locally manufacture generic versions of the drugs which were unpatented in the country and a judicious use of the threat of compulsory licensing to negotiate prices with originator companies (Galvão, 2002).

Similar to Brazil, the case of HIV treatment in Thailand is regarded as a huge success. It initiated monotherapy treatment in 1992 and switched to dual therapy in 1995 (Ford et al., 2007). The Thai Government Pharmaceutical Organization (GPO) had started producing a generic version of zidovudine in 1992 reducing the price of drug up to 82% by 1996 (Hoen, 2009). The country embraced triple therapy in 2000 but reliance on patented medicines prohibited scale-up which would only commence in 2003 once the GPO produced generic drugs became available (Ford et al., 2007).

Initiatives like DAI, AAI and successful implementation of HIV treatment in Brazil and Thailand established that ARVs could be safely delivered even the most in resource-poor settings. Further, Brazil and Thailand (to cite two examples) had also demonstrated that generic drugs were not only effective in the management of HIV but also allowed for cost containment. These developments permitted to change the discourse from the problem of implementation to that of affordability. It was now possible to argue that if prices are reduced, access can be extended to millions more. The question was of course how to lower prices. While the use of generic drugs had emerged as a significant tool, there was also a growing understanding that that price negotiations could be more efficient in the presence of generic competition (Hoen, 2009; Hoen et al., 2011). Further, reliance on generics made it possible to put a realistic price tag on the scale-up of treatment to achieve universal access to ARVs, i.e., a global collective action was possible (Kapstein & Busby, 2009). Several NGOs like the Consumer Project on Technology (CPTech), Oxfam, Health Access International (HAI) and MSF called for a widespread implementation of generic medicines. They also advocated taking advantage of TRIPS flexibilities about patents on pharmaceutical products and enforce the right of countries to safeguard public health (Hoen, 2009; Kapstein & Busby, 2009)

2.5.3.3. Cipla Takes the Charge

In September 2000, Leive Fransen, then the HIV/AIDS coordinator at the European Commission organized a high-level meeting to discuss and agree on a tiered pricing model for the treatments of HIV/AIDS, TB, and malaria. It has brought together NGOs like Act-up and MSF, CEOs of the seven largest pharmaceutical companies, generic manufacturers like Cipla from India and the leaders of WHO and UNAIDS. It was here that Cipla announced that it was possible to make antiretroviral cocktail available at $350 per patient per year (Schwartländer et al., 2006). In February 2001, Cipla officially agreed to supply MSF at the abovementioned price, the three-drug cocktail of stavudine, lamivudine, and nevirapine (McNeil, 2001; MSF, 2001).

In August that year, Cipla developed and launched the world's first WHO recommended first-line antiretroviral fixed-dose combination (FDC) (Triomune®) of stavudine, lamivudine, and Nevirapine. That is to say, that Cipla managed to put the three separate drugs in a single pill and consequently reduced the daily dose from six to two tablets (The Hindu, 2001). It is regarded by many as a "turning-point" towards the access to antiretroviral treatment (ART) in southern countries (Coriat, Orsi, & D'Almeida, 2006; Orsi et al., 2007). The patents on the three drugs were held by three different companies: the Bristol-Myers Squibb (stavudine, also known as Zerit or d4T), Glaxo-Wellcome (lamivudine, also known as Heptovir or 3TC) and Boehringer Ingelheim G.m.b.H (nevirapine, or Viramune). This feat by Cipla was only possible because India did not recognize product patents until 2005.

By 2003, other Indian generic companies, Cipla, Ranbaxy and Matrix Laboratories entered an agreement with the Clinton Foundation – a global health initiative established by the former US president Bill Clinton – to supply ARV treatment for $140 per person per year (Clinton Foundation, 2003). In fact, Indian firms were widely critiqued as "Pirates" by originator companies for supplying generic ARVs. However, it also acted in favor of the Indian pharmaceutical industry by providing it legitimacy through acceptance and recognition not only by countries in the south but also by international organizations, activists, and researchers (Owen, 2013, 2014). The WHO prequalification[24] program was a deciding factor in providing legitimacy to generic products (Hoen et al., 2014). The program invited generic manufacturers

[24] The WHO prequalification program is discussed separately in 6.2.

for quality assurance since the beginning and Cipla was among the first to get its products certified in March 2002. In December 2003, Cipla's FDC, Triomune also received a WHO prequalification.

Soon, a number of Indian firms such as Hetero, Strides, and Sun pharmaceuticals among others followed the lead of Cipla and received a WHO prequalification for more than one ARV.[25] For example, Waning et al. (2010) reported that by 2008 generic antiretroviral (ARV) medicines produced in India accounted for nearly 90% of the donor-funded purchase volumes in developing countries and the situation has remained unchanged (CHAI, 2016). Further, in a recent analysis of adult ARV procurement data in LMICs between 2003 and 2015, Sagaon-Teyssier et al. (2016) reported that the procurement of generic ARV treatments increased from 71% of total purchases in 2003 to 97% in 2009 and remained stable around 99% between 2010 and 2015. **Indian firms accounted for more than 94% of generic treatments procured in this period.** In fact, the market for generic ARVs for adults was controlled by eight Indian firms (i.e., Aurobindo, Cipla, Emcure, Hetero, Macleods, Matrix, Ranbaxy, and Strides) during the observed period. Further, since then Indian firms have not stayed confined to the ARV market but have also got WHO prequalification for products targeting other diseases such as malaria, tuberculosis, diarrhea, influenza and reproductive health (WHO, 2017c).

2.5.4. International Organizations as Market Participants and Their Role in Shaping Market Processes

The first decade of the new century also witnessed the reconfiguration of stakeholders in the global health system. Events such as TRIPS and AIDS crisis have undoubtedly transformed the roles of transnational actors such as the WHO and other UN-bodies active in the field of global health. For example, the 1996 World Health Assembly mandated the WHO to provide technical guidance to member states for implementing TRIPS in ways that could limit the negative impact of strict patent protection on medicine availability (Hoen, 2009). Additionally, in 2001, the WHO established the prequalification program in response to the need for quality assurance of generic medicines (Hoen et al., 2014). However, the massive scale of interventions

[25] Source: WHO prequalification website

needed to attain the targets set by the MDGs could not be undertaken by the WHO or other entities in the UN-system working in isolation due to resource constraints and bureaucratic intricacies. It called for an extensive collaboration between public and private sector players.

In fact, the post-MDG period has marked the coming of a new breed of organizations in global health. These so-called global health initiatives (GHIs) work on a specific disease or set of diseases by incorporating a broader strategy which is implemented across a range of countries (Hanefeld, 2014). They act as mechanisms for financing, resourcing, coordinating and implementing disease control interventions. GHIs can be either bilateral like the US President's Emergency Plan for AIDS Relief (PEPFAR) or multilateral like the Global Fund. These new actors in the global health landscape are playing a crucial role in the institutional market for medicines by employing a variety of market shaping strategies such as pooled procurement, price negotiation, and price transparency. They act as the **visible hand of the market** and influence both the supply and demand side factors to increase the access to treatment. Some of the GHIs and market shaping strategies are discussed subsequently.

2.5.4.1. The Global Fund to Fight AIDS, Tuberculosis, and Malaria

The Global Fund to Fight AIDS, Tuberculosis and Malaria is a multisectoral health partnership to combat three of the world's most debilitating diseases. Multisectoral means that the Global Fund is a public-private partnership that draws in participation from both the state and non-state actors like governments, civil societies, NGOs, philanthropies and pharmaceutical companies.

The foundations of the Global Fund were laid at the 2000 G8 summit in Okinawa, Japan. While HIV crisis was looming large in developing countries, they were also facing the scourge from the reemergence of TB and malaria (Aramburú Guarda, Ramal Asayag, & Witzig, 1999; Bates, 1995; Blower & Gerberding, 1998; J. M. Cohen et al., 2012; Kremer & Besra, 2002; Krogstad, 1996; Malakooti, Biomndo, & Shanks, 1998; Nchinda, 1998; Sawert, 1996). The leaders at the summit acknowledged the threat posed by these diseases and the need for greater resources and new mechanisms that reach beyond traditional approaches to tackle them (G8, 2000). In April 2001, at the African Summit on AIDS held in Abuja, Nigeria, then the UN Secretary-General Kofi Annan called for the creation of a global AIDS fund. In June of the same year, the UN General Assembly Special Session (UNGASS) on HIV/AIDS endorsed the establishment of a

"Global AIDS and Health Fund" (UN, 2001). In July, leaders at the G8 summit in Genova, Italy announced that $1.3 billion had been committed towards the creation of the Global Fund (G8, 2001). However, the management of the fund was a contentious issue and no less political. There was an implicit agreement that the new organization should be politically independent and be able to address the inefficiencies of existing top-down donor-driven approaches (Duran, Silverman, Fan, & Glassman, 2013). A Transitional Working Group was established to design the framework and governance structure of the new entity (Duran et al., 2013). The Global Fund became operational in January 2002 and approved the first round of grants in April 2002.

The Global Fund's operational model presents several innovations. First, it only acts as a financing mechanism. Project implementation is not a part of the Global Fund's mandate. Implementation is done by principal recipients (PR) at the country level. Second, PR does not need to be a government agency. It can be a local office of a multilateral organization, a civil society organization or universities. Third, funding is driven by recipients needs and is performance based. Fourth, funding is not requested by governments as such but through a country coordinating mechanism (CCM) which is a multisectoral instrument consisting of representatives from the government, local health experts, NGOs, and people living with the disease. Last but not the least, an independent Technical Review Panel made up of experts reviews the grant proposals sent by country CCMs and makes recommendations to the Global Fund Board.

Since its creation in 2002, the GFATM alone has disbursed $33.8 billion to fight HIV/AIDS, TB, and malaria (GFATM, 2017a). Nearly, 40% of the GFATM grants are directed towards the purchase of medicines and health products, primarily generics (GFATM, 2015a). Further, quality assurance is an important aspect of all medicines procured through the Global Fund Grants. The organizational procurement strategy specifies that grant recipients are obliged to procure pharmaceutical products that are either prequalified by the WHO and/or authorized for use by a stringent regulatory authority (GFATM, 2017b).

2.5.4.2. PEPFAR/PMI

The President's Emergency Plan for AIDS Relief (PEPFAR) is a bilateral assistance program of the United States government to support HIV treatment, prevention, and care activities, in developing countries, primarily in Sub-Saharan Africa. The initiative was announced by President Bush in 2003 at his State of the Union Address and later enacted by the US Leadership Against HIV/AIDS, Tuberculosis, and Malaria Act of 2003 (Public Law No: 108-25). It was further strengthened under the administration of President Obama. PEPFAR is the single largest Global Health Initiative for AIDS relief to be led by a single country and has played a crucial role in the scale-up of access to ARVs. Between 2003 and 2016 it has contributed $51.8 billion and $2.2 billion to bilateral HIV/AIDS and TB programs respectively and an additional $12 billion to the Global Fund (PEPFAR, 2017b). The Original authorization required PEPFAR to spend 55% of its fund on treatment for HIV. Since 2008, the PEPFAR Stewardship and Oversight Act requires at least 50% of the funding to be spent on treatment and care (Kaiser Family Foundation, 2017). As of September 2016, PEPFAR was supporting ARV treatment for 11.5 million people up from 1.5 million in 2007. Use of generics have been crucial to this scale-up. Indeed, the procurement of generic drugs compared to originator products by PEPFAR increased from 16% in 2005 to 98% in 2015 (PEPFAR, 2017a). Moreover, since 2004, the US Food and Drug Administration (USFDA) utilizes its existing product approval mechanism to assure the quality of ARVs for PEPFAR use through an expedited review process (USFDA, 2017). Only ARVs approved or tentatively approved by the USFDA are eligible for PEPFAR procurement (PEPFAR, 2017a). As of October 2017, the USFDA had granted 199 New Drug Applications (NDA) and Abbreviated New Drug Applications (ANDA) for ARVs (USFDA, 2017).[26]

Furthermore, in 2005, within the mandate of the Public Law No: 108-25 of 2003, the US launched the President's Malaria Initiative as an interagency program to provide funding for bilateral malaria efforts and the Global Fund. Currently, PMI supports malaria control and elimination programs in 27 countries including 24 in Sub-Saharan Africa. By 2016, PMI had contributed nearly $5 billion in bilateral funding to prevent, treat and control malaria.

[26] NDAs are submitted for new versions like new fixed dose combinations or formulations of approved drugs, and ANDAs are submitted for generic drugs (PEPFAR, 2017a).

2.5.4.3. Unitaid

Unitaid is an innovative financing mechanism that focuses on stimulating the market for greater access to new commodities targeting the prevention, diagnosis, and treatment of HIV, TB, and malaria in resource-poor countries. It was established in 2006 at the UN General Assembly by the governments of Brazil, Chile, France, Norway, and the UK as a tool to reach MDGs and by 2013 it was supported by 17 contributing members. The multilateral partnership is hosted by the WHO (UN, 2006; Unitaid, 2013a). Unitaid exemplifies a sustainable fundraising approach through a transnational solidarity levy on airline tickets initially implemented by France and later adopted by several other countries including Cameroon, Chile, Congo, Guinea, Madagascar, Mali, Mauritius, Niger, and the Republic of Korea (Unitaid, 2017). Since its creation in 2006, Unitaid has raised over $2.5 billons in contribution from donors (Unitaid, 2017). Airline ticket tax has consistently been the prime source of revenue for Unitaid (Unitaid, 2016). This novel approach highlights that the prosperity engendered by globalization can be an engine for dependable long-term financing for health tools where burden can be shared by individuals from around the globe (Fraundorfer, 2015). Additional grants come in the form of bilateral contributions from other countries like the UK, Brazil, and Norway among others and the Gates Foundation.

Unitaid finances a broad range of market shaping projects which are implemented by other international agencies already active on the ground such as the Clinton Health Access Initiative (CHAI), WHO, the Global Fund, UNICEF, Population Services International (PSI) and MSF among others (Unitaid, 2013a). These interventions are directed towards making the market for health products work better in southern countries through price reduction strategies, improvement in drug quality, generating market intelligence and the development and delivery of new innovative medical technologies which are not only affordable but also adapted to the needs of the population. Among its many achievements, Unitaid has created a pediatric market for ARVs through a market intervention implemented by the Clinton Health Access Initiative (CHAI) (Unitaid, 2013a). Negotiations with manufacturers have led to a price reduction of 80% between 2006 and 2013. It has also worked with the TB Alliance and Medicines for Malaria Venture (MMV) to develop and deliver child-friendly treatments for TB and malaria respectively (Unitaid, 2013a). Additionally, in 2010, Unitaid launched the Medicines Patent Pool (MPP) Initiative which for the collective management of intellectual property of medicines. The MPP negotiates with the patent holders of HIV, hepatitis C and TB medicines

for appropriate voluntary licensing terms. These licenses can be used by generic companies to manufacture and supply patented medicines in developing countries. Moreover, generic companies can also develop new medicines such as fixed-dose combination or child-friendly formulations under these licenses (Bermudez & Hoen, 2010). Currently, the MPP has licensing agreements for 18 drugs – HIV/AIDS (15), Hepatitis C (2) and TB (1) (MPP, 2017). Last but not the least, Unitaid is the most significant funder of the WHO prequalification program.

2.5.4.4. Selected Market Shaping Strategy of International Organizations

2.5.4.4.1. Pooled Procurement

Pooled procurement is a typical market shaping strategy of international agencies like the Global Fund, PEPFAR and Unitaid to get reduced prices for health commodities. It typically involves aggregating multiple small orders from different countries into a high volume purchase that increases the negotiating capacity of procurement entities to get competitive prices from manufacturers with quality assured products through international tenders.

Pooled procurement has several advantages. First, pooling results in the consolidation of demand volumes and strengthen the purchasing power of the buyers through collective representation (Huff-Rousselle, 2012). That is, it leads to a situation of oligopsony, where demanded medical technologies be procured in large quantities by a small set of institutional buyers. Second, while a consolidated market reduces the market power of suppliers, it provides them with the incentive of achieving economies of scale so that they can work on a high-volume, low-value business model (Waning, Kyle, et al., 2010). It also leads to increased competition between suppliers because if they do not participate, they will lose revenues from a high return generating market segment. Third, it also acts as a safeguard for guaranteeing the product quality because the tender is restricted to manufactures with assured quality (ideally products approved by the WHO prequalification program or a stringent regulatory authority) (GFATM, 2017d). Fourth, pooled procurement has the additional benefit of reduced transaction costs because multiple country-specific purchases are combined into one. Consequently, means that the operational and administrative expense to manage procurements is diminished (Huff-Rousselle, 2012).

The Global Fund encourages its PRs to use the Pooled Procurement Mechanism (PPM; earlier known as Voluntary Pooled Procurement) – a system created for the efficient management of the Global Fund grants. Recently, the Global Fund has linked its PPM to an e-platform, wambo.org, which acts as a global marketplace for a range of quality assured pharmaceutical products at competitive and transparent prices[27]. Further, the Global Fund strictly advises to its PRs that procurement of a healthcare product should not be done above the reference prices for such product (GFATM, 2017b). Reference prices are a catalog of negotiated prices for specific pharmaceutical products by the PPM and other international agencies like the MSF, CHAI, Stop TB Partnership's Global Drug Facility, and UNICEF among others (GFATM, 2017c). In 2016, alone PPM handled procurement orders worth $1.1 billion for recipients in 63 countries (GFATM, 2017d).

2.5.4.4.2. Ceiling and Reference Pricing

Price negotiation is yet another market shaping strategy undertaken by international organizations for promoting efficient procurement practices. The benchmark for it was set by the Clinton Health Access Initiative (CHAI) in 2003 (Clinton Foundation, 2006). CHAI negotiates price ceilings for drugs and diagnostics, primarily with generic manufacturers. Ceiling prices are the maximum amount participating supplier agrees to charge for a specific product and reflects the cost of production plus a sustainable margin (Clinton Foundation, 2006; Waning et al., 2009). These prices are accessible to all national governments that are members (currently 78) of the CHAI Procurement Consortium. Buyers can get further price reductions through direct negotiation with manufacturers. In return, Consortium members agree to pay promptly and share demand forecasts. On the other hand, manufacturers benefit from a stable and certain market. Clinton Foundation also provides manufacturers with technical assistance to some suppliers to lower down the costs and to expedite regulatory approvals (Clinton Foundation, 2008).

More recently, the Global Fund has signed framework agreements with the manufacturers of ARVs, ACTs, and Long Lasting Insecticidal Nets to get pre-negotiated reference prices for

[27] The website can be reached at: http://wambo.azurewebsites.net/home

procurements channeled through the Pooled Procurement Mechanism (Arney, Yadav, Miller, & Wilkerson, 2014; GFATM, 2016b).

2.5.4.4.3. Price Transparency

Manufacturers do not offer a single price for a specific product to all the buyers, and the same manufacturer can offer very different prices depending upon the country, program, procuring agency and other factors. The outcome is a series of prices unknown to all the buyers and competitors alike. In the absence of information regarding prevailing market prices, buyers cannot make meaningful comparisons to get the best value for money during procurements.

Member states raised this issue at the 2001 World Health Assembly which passed a resolution outlining the WHO medicines strategy. Among other things, the resolution mandated the WHO to take action to increase price transparency by working along with NGOs. Following the resolution, various price transparency mechanisms led by different international organizations have come into existence.

MSF was among the first to instate a market intelligence guide on ARV pricing through its "Untangling the Web" (UTW) series in 2001. Currently, in its 18th edition, UTW obtains pricing information directly from manufacturers and acts as a supplement to information obtained by other market intelligence initiatives (Hinsch, Kaddar, & Schmitt, 2014).

The Global Fund also started a web-based system called the Price and Quality Reporting (PQR) mechanism in 2004 (Huff-Rousselle, 2012). The system requires all principal recipients to enter consignment data upon the receipt of health products purchased through the Global Fund Grants. The PQR gathers data on six categories of products – LLIN and indoor residual spraying (IRS) products, condoms, diagnostic products, ARVs, antimalarial medicines, and Anti-TB medicines (GFATM, 2014a). It consists of among other fields the data on pricing, volume, manufacturer, manufacturing site, date of order and delivery, and means of transport. On the one hand, this information allows the Global Fund to ensure that procurement made by PRs meet the required standards and prices correspond to international reference prices. On the other hand, countries, PRs and other institutional buyers have access to market information to make more efficient procurement decisions.

In 2005, the WHO started a collaborative platform called the Global Price Reporting Mechanism (GPRM) to share and disseminate pricing information on international transactions concerning the purchase of HIV, TB and malaria commodities in LMICs. It receives information from the Global Fund PQR, PEPFAR, Unitaid and many procurement organizations such as the UNICEF, Crown Agents, Mission Pharma, Management Sciences for Health (MSH), and the Partnership for Supply Chain Management (PFSCMS) among others. This makes the GPRM the most comprehensive database on pharmaceutical products procured through donor funding.

To sum up, these initiatives make pricing information widely available to all the stakeholders. Purchasers can leverage information on comparative pricing to get better terms of negotiation with manufacturers. It also has a positive impact on competition as suppliers know each other's offering. Further, it also leads to improved procurement efficiency by reducing search and operational cost.

2.6. Understanding the New Governance Structure of Donor-Funded Markets: The Case of ACTs[28]

Our discussion from the previous section has made it clear that the market for medicines against diseases like HIV/AIDS would not have existed if left alone to market forces. Creation of these markets revolves around international organizations who act as *market makers.* They leverage their dominant position to stimulate all dimensions of the marketplace to develop and maintain a competitive and affordable supply of quality-assured medicines that meet organizational demand while assuring transparency.

However, while access to HIV medicines and the role of Indian firms in that market is much discussed in the literature, works have concerned to show the institutional underpinnings of the constitution of the antimalarial medicines. This section is dedicated to explaining the new governance of the donor-funded markets by explaining the creation and specificity of artemisinin-based combination therapies (ACTs) that constitute the therapeutic backbone of

[28] The section draws on Orsi & Zimmermann (2015) and Orsi, Singh & Teyssier (2018).

malaria control programs. This is important for our purpose, as we shall see in the subsequent section, Indian firms are playing an increasingly important role in this market.

2.6.1. Bringing ACTs to the Central Stage: WHO as the Prescriber

The WHO is an intergovernmental agency within the UN system that holds the constitutional authority to protect and promote health. It is the single largest global health entity that is built on the universal membership of all the sovereign member states of the UN. Thus, its mandate in setting the global health policy and governance remains decisive. WHO has played a pivotal in the construction of the ACT market. One of its many functions is to develop norms and standards for the treatment of specific diseases. This allows WHO to be an ex-officio prescriber to designate and define reference treatments for illnesses. It does so by publishing treatment guidelines principally intended for public authorities of southern countries. By issuing the evidence-based reference standard, WHO specifies the legitimate treatment for the disease that should be purchased by the national health authorities.

In the case of malaria, the first WHO recommendations came in the wake of a strong resurgence of malaria cases in the 1990s, especially in Sub-Saharan Africa due to increasing resistance to classic treatments like chloroquine and sulphadoxine-pyrimethamine (Wongsrichanalai, 2002). As such, there was an urgent need to propose alternative treatments. In 2001, the WHO for the first time recommended using ACTs in countries where *P. falciparum* had developed resistance against conventional antimalarials (WHO, 2001).

Artemisinin and its derivatives – artemether, artesunate, and dihydroartemisinin – were discovered by the Chinese in the 1970s in their efforts to find new antimalarial medicines. However, it was not until the 1990s that their effectiveness started to be appreciated by the rest of the world (Lin, Juliano, & Wongsrichanalai, 2010).

The program was launched by the Chinese government in 1967 at the request of their North Vietnamese allies during their war against the United States. Malaria was decimating their armed forces, and all the existing treatments proved to be ineffective. This program relied on the large-scale screening of medicinal plants used in traditional Chinese medicine. In 1971, sweet wormwood (*Artemisia annua*) was identified as a candidate with strong antimalarial potential. One year later, artemisinin was identified as the active ingredient, and an extraction

process was developed. Derivatives of artemisinin, including artesunate and artemether, were quickly synthesized. The first clinical trials were carried out in China in the 1970s (Miller & Su, 2011). The country soon contacted the WHO for technical assistance in the development of preclinical and clinical trials, while new research collaborations were established with the Special Program for Research and Training in Tropical Diseases (TDR).[29,30] Trials of several ACTs were carried out in Southeast Asia in the mid-1990s under the direction of the TDR, hosted at the WHO[31] and financed by the US Agency for International Development and the Wellcome Trust.

At the end of the 1990s, the WHO organized informal consultations and debates about the role and use of artemisinin and its derivatives, in an attempt to revise the guidelines of the UN organization concerning the fight against malaria (WHO, 1998). Several studies showed that artemisinin, until then used mainly in the countries of Southeast Asia, was an active ingredient that acted rapidly against *P. falciparum*, without serious side effects, and any observed clinical resistance. artemisinin-based monotherapies had already developed as a substitute for classic treatments in south-east Asia. For a time, artemisinin was one of the WHO's drugs of choice for the treatment of uncomplicated malaria but remained primarily recommended for cases of poly-resistance (WHO, 1998, p. 25).

Given the dramatic rise in cases of malaria and resistance to treatment, considerable international pressure was exerted on the WHO, in particular through the MSF's "ACT now" campaign, to recognize these drugs as first-line treatments in all malaria-endemic zones. In 2006, WHO launched the first malaria treatment guidelines recommending ACTs to be used as the first line of treatment against *falciparum* malaria in all countries (WHO, 2006). These recommendations were well received by the international community, and global efforts were directed to support the introduction, implementation, and scale-up of ACTs. The following years witnessed a rapid update of national policies for the management of malaria, and by 2011, 79 countries had adopted ACTs as the first-line treatment (WHO, 2012).

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[29] See in particular Li et al., (1994).

[30] Special programme of the UNDP, UNICEF, the World Bank and the WHO, created in 1975.

[31] For more on this programme, see: http://www.who.int/tdr/about/en/

ACTs typically combine artemisinin derivatives with another antimalarial drug from a different therapeutic class. Such combinations were recommended with the aim of slowing down the development of resistance since the principle of combining drugs with independent modes of action had proved to be effective in preventing the appearance of resistance.[32] From the WHO's point of view, the aim was not only to eliminate classic treatments like chloroquine but also to avoid the deployment of artemisinin-based monotherapies in malaria-endemic regions, to thwart the rapid development of resistance to this active ingredient. That is why discussions were held, from the outset, about the interest of promoting fixed-dose combination drugs (FDCs), where two active ingredients are combined in the same pill, but which require expensive pharmacokinetic and toxicological studies, or, to a lesser degree, the development of co-blisters, where two different drugs are presented separately but in the same pack, a less costly solution but which is thought to lead to lower patient compliance.

In 2006, the WHO also issued a strong recommendation to stop the use of oral artemisinin-based monotherapies. Pharmaceutical companies were asked to stop the production and take their products off the market. Several pharmaceutical companies including the firms like Cipla and Ipca were among the first to show their support to the WHO call. It also carried out several technical briefings with selected manufacturers who accepted the Code for Artemisinin Marketing Practice (CAMP). The code required the participants to manufacture and market medicines in line with the WHO guidelines for the treatment of malaria and observe WHO or Stringent Regulatory Authority (SRA) approved GMP practices. The WHO also provided technical assistance to manufacturers who were interested in the WHO prequalification program.

While on the one hand, the WHO was negotiating with manufacturers to produce ACTs and stop monotherapies, on the other, it worked with member countries to stop authorizing monotherapies. In 2007, the World Health Assembly[33] approved the resolution 60.18 on malaria. The resolution advised all WHO member states to deploy ACTs and to withdraw oral artemisinin-based monotherapies from the market progressively. This commitment was

[32] Antibacterial and antimalarial chemotherapies were the first try-outs of this principle of combining drugs with independent modes of action. The idea was then adopted for cancer chemotherapy, and then in the treatment of HIV/AIDS and leprosy (WHO, 1998).

[33] This resolution can be consulted at: http://www.who.int/gb/ebwha/pdf_files/WHA60/A60_R18-en.pdf

repeated in successive annual World Malaria Reports (WHO, 2009). By the time major funding and procurement agencies as well as international suppliers had already accepted the WHO recommendations to procure and fund ACTs over monotherapies.

Currently, there are five ACTs recommended by the WHO, namely, Artemether-Lumefantrine (AL), Artesunate-Amodiaquine (ASAQ), Artesunate-Mefloquine (ASMQ), Artesunate-Sulfadoxine-Pyrimethamine (ASSP), Dihydroartemisinin-Piperaquine (DHA-PPQ) (WHO, 2015b). ACTs are available either as co-blister (two separate drugs packed together) or fixed-dose combinations (FDCs, where both drugs are co-formulated in a single pill). Nevertheless, for reasons of patient compliance and resistance prevention, FDCs became the WHO gold standard in the fight against malaria. This orientation of the WHO was decisive in the construction of the market.

2.6.2. Assuring the Quality: WHO Prequalification Program

The quality of drugs is, of course, a significant concern for the different players involved in the fight against pandemics. The question of the quality control of pharmaceutical products is central, not only because of the risks of toxicity but also because of the urgent need for therapeutic effectiveness[34]. Traditionally, the quality control of drugs is entrusted to national or regional authorities, at the level where new drugs are subject to an application for marketing authorization. As these authorities are responsible for organizing the marketing authorization procedures (such as preclinical and clinical trials and toxicology studies), they play a decisive role in the construction and organization of markets for drugs (Montalban et al., 2012). Their function – to certify the non-toxicity and effectiveness of the drug – is, therefore, one of technical prescription in the sense of Hatchuel: “to intervene in the purchasing process by providing concepts initially unknown to the buyer” or to “remedy a more complex uncertainty extending as far as ignorance of possible practices” (Hatchuel, 1995, cited in Montalban et al., op. cit, our translation).

[34] A drug is effective if it works under non-ideal settings of real world. This is different than efficacy that is the ability of a drug to bring intended effects under ideal circumstances.

Given the difficulties faced by developing countries in achieving a satisfactory level of quality control of imported drugs, and in the framework of the global fight against the three great pandemics (AIDS, TB, and malaria), an "intermediary" for quality control was created between the drug producers and the marketing authorization agencies. This intermediary is the WHO prequalification program, set up in 2001. In this program, the producers of generic and brand-name drugs are invited to follow a procedure with two main stages. The first is an analysis of the quality, safety, and effectiveness of drugs, based on the data provided by the producers. If the results of this analysis are positive, the second stage involves an inspection of the concerned production sites to verify their conformity with international GMP standards (Lantenois & Coriat, 2014).[35]

With the establishment of this program, the WHO became an international technical prescriber whose role in drawing up the rules of trade became decisive. The WHO prequalification was to become one of the keystones in the organization of international trade when it became a precondition for all transactions carried out with the help of international funding. In particular, the Global Fund, the leading international funding agency, has adopted the principle that funds for the purchase of drugs and diagnostics by beneficiary countries can only be granted for products that have either obtained WHO prequalification or approved by an SRA (GFATM, 2017b).

What is interesting is the growing interest of Indian firms in this market which is evident from the number of products that have received a WHO prequalification. As of July 2017, a total of 540 medicines for eight therapeutic classes have been approved by the WHO. Of this 322 (60%) belong to Indian firms (Table 2.6). This does not include Mylan (57 prequalified medicines: 43 for HIV/AIDS; 3 for influenza; 2 for malaria; 8 for reproductive health and one for TB) which even though is American by origin, manufactures all its products in India.

[35] The WHO reserves the right to carry out random controls on prequalified drugs and production sites to verify that standards of effectiveness, safety and quality for drugs that have obtained their prequalification are respected over time. For a detailed analysis of the birth of the WHO prequalification programme, see Lantenois and Coriat (2014).

Table 2.6 Number of WHO prequalified medicines by disease and firm origin

Therapeutic Area	Northern Firms	Indian Firms	Other Southern Firms	Total
Diarrhea	1	2	-	3
HIV/AIDS	113	209	16	338
Hepatitis	2	-	-	2
Influenza	8	7	-	15
Malaria	12	21	13	46
NTD	1	1	1	3
Reproductive Health	25	11	4	40
Tuberculosis	18	71	4	93
Total	180	322	38	540

NTD = Neglected Tropical Disease

Source: WHO prequalification database for medicines[36]

2.6.3. WHO-Novartis Agreement: From the Initial Public Market and Beyond

The first ACT to gain global recognition was the fixed-dose combination of artemether and lumefantrine (AL). The combination was of Chinese origin and developed by the researchers at the Beijing Institute of Microbiology and Epidemiology of the Academy of Military Medical Sciences, with the support of the WHO. The combination was registered in China in 1992. With the consent of the national authorities, contact was made with the Swiss multinational company, Novartis (then Ciba-Geigy) to start a partnership with the academy in 1994 to launch the product in the international market (Spar & Delacey, 2008). The reason for such partnership is best explained in the words of Professor Zhou Yiqing, one of the inventors of this first FDC, "No Chinese pharmaceutical company was capable of introducing this medicine to the rest of the world".[37] Chinese researchers retained the patent for the FDC and Novartis received an exclusive worldwide licensing rights outside China. The partners conducted a series of clinical trials to develop the fixed-dose combination to be marketed under the name of Riamet® in the northern hemisphere and Coartem® in the south. Coartem got it first marketing approval in

[36] http://apps.who.int/prequal/query/ProductRegistry.aspx

[37] "Ancient Chinese anti-fever cure becomes panacea for malaria. An interview with Zhou Yiqing", Bulletin of the WHO: http://www.who.int/bulletin/volumes/87/10/09-051009/en/

Gabon in 1998.[38] Subsequently, Riamet was approved by the Swissmedic in 1999 (Hamed & Grueninger, 2012).

In 2001, WHO and Novartis signed a memorandum of understanding where Novartis agreed to supply Coartem at "cost-price" to national authorities in developing countries and the WHO which would provide twelve-months rolling quarterly forecasts for expected orders. Demand forecasts allowed the WHO to anticipate a new and unpredictable market while giving Novartis a four-month lead time to supply the orders (WHO, 2011a). Soon, Novartis extended the offer to other public-funded procurement agencies. In 2002, AL was included in the WHO essential medicines list and subsequently, in 2004 became the first ACT to get a WHO prequalification (WHO, 2011a).

The primary justification for selecting Novartis as a partner of choice was it being the only available firm supplying quality-assured ACT in a fixed-dose combination. Quality assured refers to those medicines which have been either approved by an SRA or have received a WHO prequalification. Quality assurance is an essential requirement for a product to be procured by using donor-funding. Until 2007, Novartis was the only firm with a WHO prequalification. Thus, there was no competition in the market.

These earlier events led to the development of a public market which was under quasi-monopoly of Novartis. This was contrary to what one would expect because there were no patents on the individual molecules of ACTs. Further, even though patents protected the AL-FDC, firms from countries like India that had still not implemented the TRIPS could have produced the medicine without trouble. However, it is important to note that in 2001, the ACT market was still in its infancy as it was not in prominent use in most endemic countries. The market for ACTs would only proliferate after the arrival of the 2006 WHO malaria treatment guidelines which acted to consolidate the demand as more and more countries accepted the guidelines. Also, Since 2004 the Global Fund had switched its financial support towards the procurement of ACTs replacing classic treatments like chloroquine to selected qualified countries (Kindermans, Pilloy, Olliaro, & Gomes, 2007). Thus, this created incentives for

[38] https://www.fda.gov/ohrms/dockets/ac/08/slides/2008-4388s1-02-Novartis.pdf

countries to switch to ACTs and for generic manufacturers to enter a low-cost, high volume market as demand started growing.

Further, there was already an existing market for artemisinin monotherapies, especially in Southeast Asia. These monotherapies were comparatively cheaper than the ACTs and effective at treating malaria (the main reason for using a combination was to delay the onset of resistance against artemisinin derivatives). Nevertheless, it is worth emphasizing that it was the absence of patents that allowed the WHO to advocate the use of FDC from the very beginning. It was also the reason that Indian and Chinese firms could enter the donor-funded market within few years. This situation of ACTs was very different from the case of ARVs where patents were held by different companies who were not ready to collaborate and WHO could not recommend an FDC from the very beginning of the epidemic.[39]

Post-WHO-Novartis agreement, the market not only formed as a quasi-monopoly but had several other shortcomings as well. The agreement resulted in a price that ranged from $0.9 - 2.40 depending on the age/weight of the patient. This was the presented by Novartis as the "cost-price" on which the company made neither profit nor loss[40]. Also, this was the ex-factory price that does not include the cost of freight and the markups by different intermediaries until the product arrives the final destination. Moreover, the price was valid only for the public-sector procurements, Novartis was free to set price in the private sector. This was crucial towards real access to ACTs because it is above all the private distribution networks that supply populations with antimalarial therapies (Bitran & Martorell, 2008; Laxminarayan & Gelband, 2009). It is equally important to point out that the certain ACTs were available in the form of co-blisters at much lower prices. The ASAQ combination was available for $1.30 per adult treatment and the ASSP combination for $1.20 (Snow, Eckert, & Teklehaimanot, 2003). However, ACTs were still nearly 20 times more expensive compared to conventional chloroquine, which ranged between $0.10 and $0.15 in 2001 (MSF, 2003). The Higher price of the only prequalified ACT (Coartem) also limited the number of treatments that could be delivered with donor-funding.

[39] For details see (Orsi & Zimmerman, 2015)

[40] For details on "cost-price", see Orsi & Zimmermann (2015) and Orsi, Singh & Teyssier (2018).

In 2005, the quasi-monopoly of Novartis was challenged by the agreements signed between the GFATM and Indian generic companies Ajanta Pharma (Ajanta) and Cipla Ltd. (Cipla) to produce AL-FDC. Novartis reacted with the first price-cut in 2006 (WHO, 2011a). This was also in response the prospective arrival of a fixed-dose combination of ASAQ due to a public-private partnership between institutional actors and Sanofi-Aventis (Sanofi). This leads us to another dimension of interventions undertaken by international organizations to shape the ACT market.

2.6.4. International Organizations Enter Research & Development

A crucial shortcoming of the ACT market in the early phase of scale-up was the lack of availability of FDCs adapted to specific populations. AL was the only ACT available in FDC and other ACTs like ASAQ, ASSP and ASMQ were only available as co-blisters. FDCs are better than coblister packs for treatment adherence by patients and for delaying parasitic resistance against the drug. Further, malaria incidence and mortality, among other factors, varies with age such that it disproportionately affects young children (Carneiro et al., 2010; Hay et al., 2010). In fact, the proportion of all malaria cases concentrated among children under five years of age can be as high as 60 percent in high transmission areas (Griffin, Ferguson, & Ghani, 2014). At the same time, nearly 80 percent of malaria-related mortality is observed in this age-group (Hay et al., 2010; WHO, 2013). ACTs were the outcome of the military research program and were adapted to the adult populations. Indeed, the lack of pediatric formulations was a critical shortcoming of the ACT market in the early years. In December 2007, the World Health Organization (WHO) launched *make medicines child size* initiative that aimed to accelerate the development and access to essential medicines tailored for children (WHO, 2007).

Few international organizations proactively worked to solve these problems by guiding research and development of new ACT formulations through public-private partnerships. Two

most notable organizations working in this field are Drug Neglected Diseases Initiative (DNDi) and Medicines for Malaria Venture (MMV)[41].

2.6.4.1. Development of ASAQ-FDC and Other Initiatives

Fixed-dose combination of artesunate-amodiaquine (ASAQ-FDC) was developed by the Fixed-Dose Artesunate Combination Therapies (FACT) partners and Sanofi under the aegis of DNDi following an agreement in December 2004 (Pécoul, Sevcsik, Amuasi, Diap, & Kiechel, 2008).

As studied by Anne Branciard (2012), Sanofi had a long-established presence on the African antimalarial drugs market, where it sold Flavoquine® (INN: amodiaquine). It, therefore, possessed experienced commercial networks in Africa. It also had a factory in Morocco. In 1996, it started marketing Arsumax (artesunate, for which the active ingredient was produced by the Chinese firm Guilin Pharmaceutical). In 2003 it launched Arsucam, an ASAQ co-blister, and applied for WHO prequalification. In 2002, it had launched a program to develop an FDC combining Arsumax® and amodiaquine. In 2004 it abandoned this project, which had shown little progress, to enter an industrial partnership with DNDi for the production of an FDC of ASAQ. According to the agreement, DNDi was responsible for preclinical, clinical and pharmaceutical development while Sanofi was in charge of the industrial scale-up, registration, and production of the drug. Pre-formulation of the ASAQ-FDC was developed by the Université Victor Segalen Bordeaux II (France). Another key challenge in the development was to create a bi-layer that could keep artesunate and amodiaquine components separate. This problem was tackled by Ellipse Pharmaceuticals. The resulting product, when packed in a double aluminum foil blister pack, had a shelf-life of three years and suitable for tropical conditions (Bompart et al., 2011). The drug was innovative that it reduced the number of pills from six to one or two, once a day, in a three-day regimen. Also, it was dispersible in water, making it easier to be administered to infants and young children.

[41] These organizations are popularly known as Product Development Partnerships and are discussed in detail in Chapter 4.

This FDC was produced in the Sanofi's Moroccan factory at Maphar (Casablanca), whose initial production capacity of 18 Mt/year was increased to 70 Mt/year thanks to an investment of €25M and the validation of GMP standards in 2008.The registration dossier for ASAQ Winthrop® was submitted in December 2005, and it obtained marketing authorization in Morocco in February 2007 and subsequently got a WHO prequalified status in October 2008. As the product was developed as a "non-exclusive, not patented, not-for-profit" public-good, Sanofi agreed to supply it "at cost plus a small margin" to public sector procuring agencies (DNDi, 2013). It was announced at a cost price of less than $1 per adult treatment and $0.5 per child treatment in the public sector.[42] Sanofi also agreed to pay a royalty of 3% to DNDi over its turnover in private sector for seven years (Branciard, 2012). By the end of 2010, Winthrop was already registered in 30 malaria endemic African countries. By the end of 2015, 500 million treatment of ASAQ-FDC were delivered worldwide by Sanofi and other generic companies (DNDi, 2015).

The development of ASAQ is widely regarded by many scholars as a milestone in the field of R&D for tropical diseases (Bompart et al., 2011; Branciard, 2012; Cassier, 2016). The success of the project was in part because of the absence of intellectual property on individual molecules (artesunate and amodiaquine) but also due to the collaborative model that brought together universities, biotech start-ups and a multinational pharmaceutical company (Sanofi) under the of leadership of DNDi for a humanitarian cause. The project was mainly funded through grants from public agencies and private philanthropies (Cassier, 2016) which made it possible to break ownership barriers and enable access in low-income malaria endemic countries. The development of ASAQ-FDC demonstrated that it is possible to invest and develop new medicines adapted to the need of patients in developing countries by aligning the incentives across partners, most notably pharmaceutical companies

Other new ACT formulations also came out due to the initiatives taken by international organizations. DNDi also partnered with the Brazilian government-owned pharmaceutical

[42] The drug was marketed under the brand name Coarsucam®, with free pricing in the private sector and at cost price in the network of private pharmacies involved in the Sanofi-Aventis programme (a commercial promotion tool).

company Farmanguinhos/Fiocruz to develop a fixed-combination of artesunate-mefloquine (ASMQ-FDC), and the product was first registered in Brazil in 2008 (S. Wells et al., 2013). DNDi facilitated an agreement between the Brazilian company and Cipla for a south-south technology transfer to scale-up ASMQ-FDC in Asian and African countries. The product was registered in India in 2011 and received a WHO prequalification in 2012 (DNDi, 2012).

Further, Medicines for Malaria Venture (MMV) joined hands with Novartis in 2003 to develop dispersible artemether/lumefantrine tablets suited to young children (Abdulla & Sagara, 2009; Hamed & Grueninger, 2012). The result of this partnership was Coartem Dispersible that was launched 2009. Since their launch in the market, procurement of these new formulations has significantly increased.

2.6.5. Assuring the Raw Material: Supply of Artemisinin

While the donor-driven market of ACTs was still taking its shape, international organizations were faced with yet another challenge of securing and stabilizing the supply of raw artemisinin which is extracted from the plant *Artemisia annua.* Since the announcement of the WHO recommendations to use ACT as the first line treatment, the cultivation of *Artemisia annua* was trapped in a cycle of boom and bust leading to an extremely volatile market for artemisinin. The increased demand after the WHO recommendations skyrocketed the price of artemisinin at $1100/kg in 2005 (Kindermans et al., 2007). This led to massive investment in the cultivation of *Artemisia annua* resulting in an oversupply and prices were down to less than $200/kg in 2007 (Orsi & Zimmerman, 2015). This forced many extractors out of the market and led farmers to plant alternative crops. This fluctuation of prices combined with the long cycle of 14 months from planting the crop to the finished ACT product necessitated advance planning and storage of stock (Shretta & Yadav, 2012). It was believed that market forces alone would not invest in the expansion of artemisinin supply needed to meet future demands.

In November 2008, the MMV and the WHO convened an Artemisinin Forum in Guilin, China to discuss the ways to scale-up the production of artemisinin and to ensure the supply in case of shortage (Unitaid, 2013b). It was decided to put in place a temporary non-market corrective intervention to create equilibrium between supply and demand and to generate market intelligence for better communication and organization of supply chain. The forum led to the creation of Assured Artemisinin Supply System (A2S2) in mid-2009 to address the forecasted

artemisinin shortages. The project was financed by the UNITAID and received guidance from the WHO, the Roll Back Malaria Partnership, and MSF among others. A2S2 had two central functions. First, it provided a pre-finance facility to artemisinin extractors selected by eligible ACT manufacturers, i.e., approved for procurement by GFATM, UNICEF, and WHO. Second, it collected and disseminated market intelligence on the actual artemisinin supply situation to increase market transparency and responsiveness.[43,44]

In March 2012, the UNITAID Executive Board decided to close down the A2S2. Nevertheless, despite challenges the project had a positive impact on artemisinin marketplace and provided valuable lessons for future work. Most importantly, the case of A2S2 shows the willingness of international organizations to stabilize the market.

2.7. Growth of Indian Firms in the Donor-Funded ACT Market

2.7.1. Methods and Dataset Configuration

For this study, we obtained transactional data about antimalarial medicines from the Price and Quality Reporting (PQR) platform of the Global Fund[45]. The PQR platform provides market intelligence information on donor-funded procurements made by using the Global Fund grants and is publically available. The dataset not only provides information about prices, quantities and drug-characteristics like pack-size, strength, and type of formulation but also enables to identify the countries of destination, manufacturers and procurement agents.

The raw dataset consisted of 2,438 observation and was systematically cleaned and harmonized for analysis. We restricted our analysis to solid dosage forms of ACTs supplied to Sub-Saharan countries between 2006 and 2012[46]. We harmonized purchase prices in US dollars in terms of

[43] For more details check the "Independent Final Review of the A2S2" at: https://unitaid.eu/assets/End-of-project-evaluation-Assured-artemisinin-supply-system.pdf

[44] A2S2 website can be consulted here: http://www.a2s2.org

[45] See website: http://www.theglobalfund.org/en/pqr/

[46] We restricted our analysis to 2012 due to the completeness of the dataset until that year. This is due to the lag in reporting to the PQR platform which can be of several months (verified by personal communication with the PQR administrator). Including years beyond 2012 might have resulted in a misinterpretation of the overall market picture.

Ex works, i.e., factory gate prices which means that the cost paid does not include freight or other related expenses.[47] We also removed any outliers with extremely high or low prices[48]. The final dataset consisted of 1098 transactions for the purchase of ACTs made by 41 countries. We calculated volumes in each transaction the number of treatments and prices for each treatment[49]. Details of the overall data cleaning process is shown in figure 2.4. All analyses were done in STATA 12.1 (StataCorp LP, Texas, USA).

2.7.2. Evolution of ACT Procurement

Procurement of ACTs in Sub-Saharan Africa has significantly increased since 2006 reaching nearly 100 million treatments in 2012 (Figure 2.5). Three main types of ACTs recommended by the WHO – Artemether-Lumefantrine (AL), Artesunate-Amodiaquine (ASAQ) and Artesunate-Sulfadoxine-Pyrimethamine (ASSP) – were procured by Sub-Saharan countries using the Global Fund grants between 2006 and 2012.

AL was the most procured antimalarial during the period accounting for 64 percent of all purchased treatments. It was followed by ASAQ which made 25 percent by volume of procured ACTs. Remarkably, the procurement of ASAQ-FDC showed an increasing trend, and it surpassed the procurement of co-blister combinations of ASAQ in 2009. ASSP was the least procured among the ACTs comprising only 4 percent of purchased treatments. AL was available only in fixed-dose combination and ASSP only in co-blister; ASAQ formulations were available both in fixed-dose and co-blister combinations. Over the period considered, a total of 89 percent of all purchased treatments were FDCs.

[47] This required information on incoterms (International Commercial Terms; e.g. Ex works) for each of the transactions. Though it is unavailable on the PQR platform the same was requested and received from the PQR administrator.

[48] See appendix 6.1 for harmonization in Ex works and outlier estimation.

[49] See appendix 6.2 for more details on calculation of treatment volumes and prices

Figure 2.4: Dataset cleaning

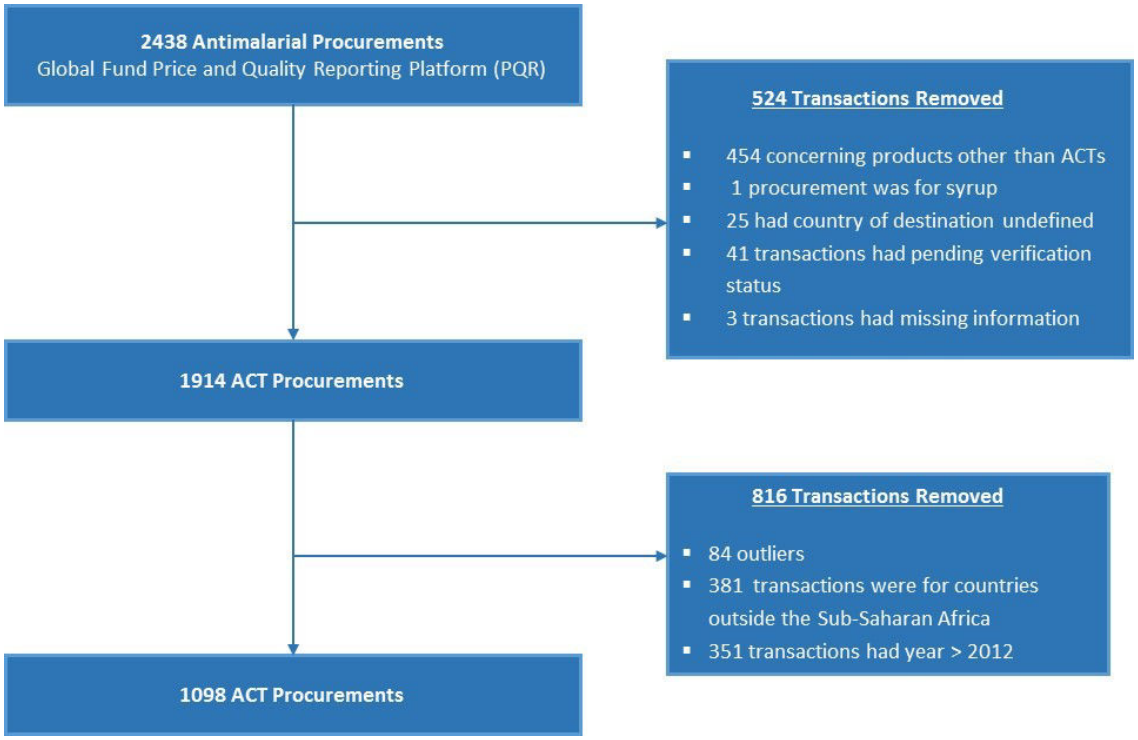
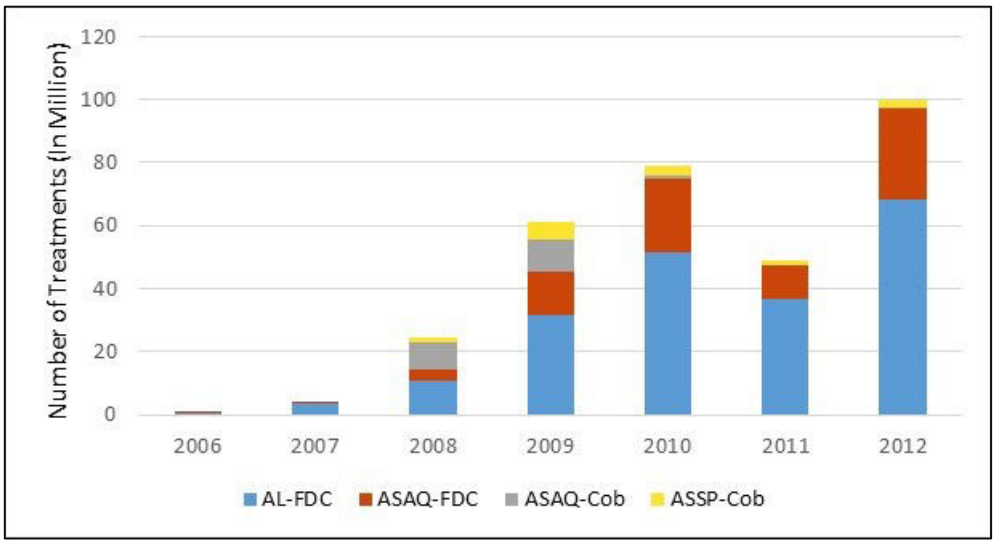


Figure 2.5: Evolution of ACT procurement using the Global Fund grants in Sub-Saharan Africa



2.7.3. Trend in ACT market share and purchase trends by firm origin

Our results assert the growing importance of Southern firms (Indian and Chinese) in the donor-funded ACTs market. The share of ACTs supplied to Sub-Saharan countries by Southern firms increased steadily from no activity in 2006 to account for 49 percent of purchase volumes in 2012 (Figure 2.6). The proportion of ACTs supplied by southern firms is even higher for certain ACT types. The share of Novartis has decreased considerably over the years. Our analysis confirms a market dominated by Novartis for AL in the early years after product registration (Figure 2.7).

Figure 2.6: Overall market share of ACTs by firm origin

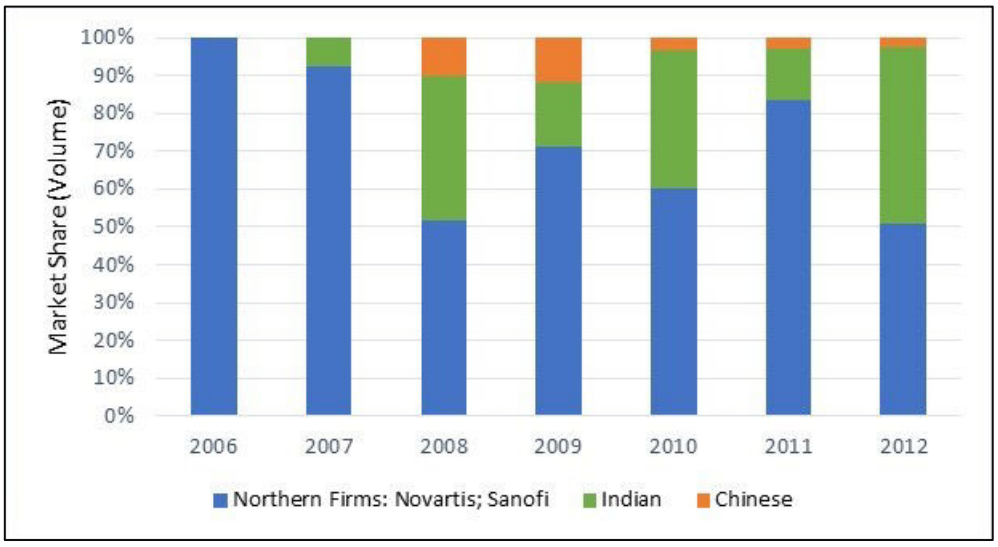
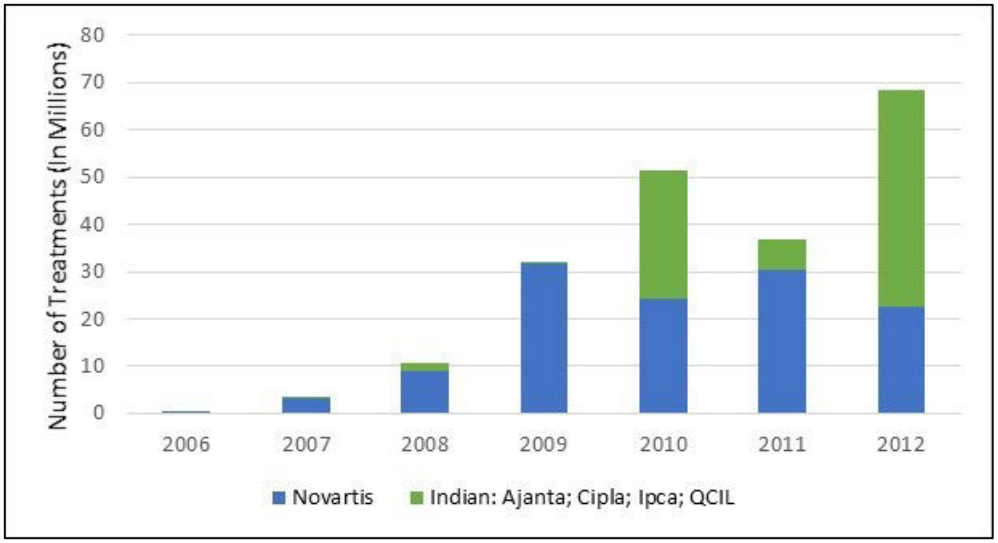


Figure 2.7: Market share of AL by firm origin



Until 2007, Novartis was the only manufacturer with a WHO prequalified product, and the agreement between the multinational and the WHO placed Novartis in a situation of quasi-monopoly. However, three Indian firms: Ajanta, Cipla and Ipca Laboratories Ltd. (Ipca) got a prequalification for AL between December 2008 and December 2009 and became eligible to supply in the donor-funded market. Their entry gradually ended the monopoly of Novartis. Cipla, Ajanta, and Ipca – accounted for 67 percent of AL treatment volume procured in 2012 (Figure 2.7).

Until 2012, Sanofi was the primary supplier of ASAQ-FDC treatments while two Indian firms namely, Cipla and Ipca supplied limited quantities in 2009 and 2012, respectively (Figure 2.8). On the other hand, the market of ASAQ-coblister combination was marked by the presence of various southern manufacturers: Cipla, Guilin, and Ipca (Figure 2.9).

Figure 2.8: Market share of ASAQ-FDC by firm origin

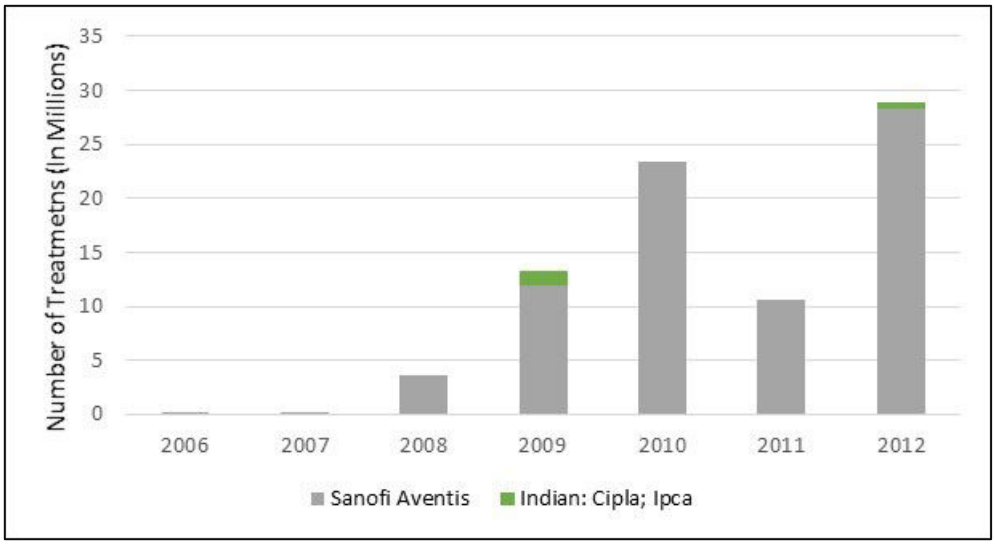
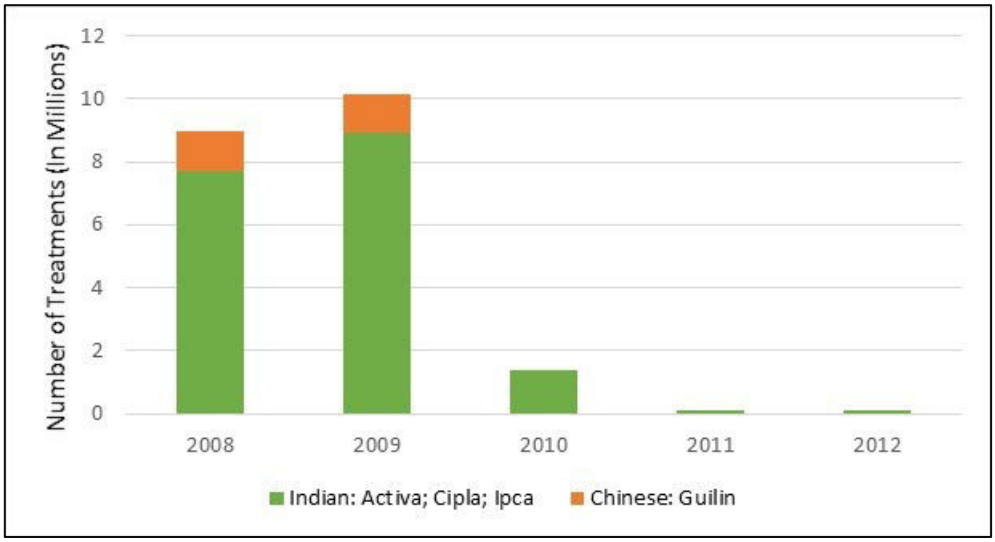


Figure 2.9: Market share of ASAQ-Coblister by firm origin



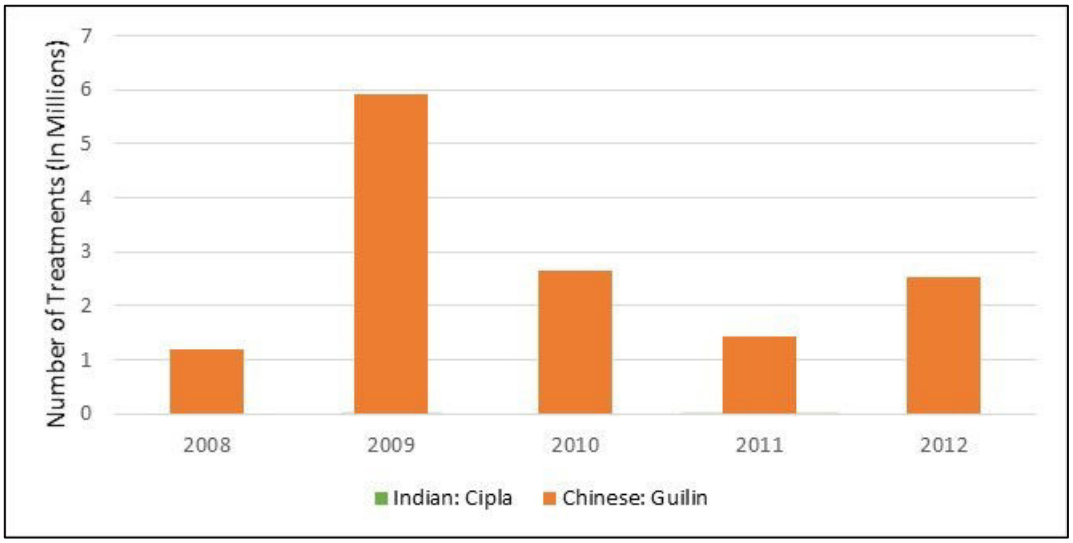
Also, it is interesting to note that these firms who were producing coblister combination of ASAQ switched to the production of ASAQ-FDC as the market of coblister formulations diminished following the WHO recommendation to phase out the use of co-blister combinations. In the advent of such intense competition from southern firms, we can argue that the dominance of Sanofi in the ASAQ-FDC market must have reduced after 2012. By the end of 2010, Sanofi's Winthrop® was already registered in 30 malaria-endemic African countries (Bompart et al., 2011). However, an analysis of the WHO prequalified products reveals that between 2012 and 2014, three Indian firms (Ipca –June 2012; Ajanta – July 2013; Cipla – April 2014) and one Chinese firm (Guilin – November 2012) received prequalification for ASAQ-FDC. Thereby raising the number of WHO prequalified manufacturers to five (including Sanofi) and products to fifteen[50].

For the market of ASSP, Chinese firm Guilin was the dominant supplier (Figure 2.10). Northern firms are absent from this market, and though Cipla marked presence through two transactions to Somalia in 2009 and 2011, respectively, the combined volume was less than 50,000 treatments. In fact, the market for ASSP is relatively much smaller compared to other ACT combinations like AL and ASAQ-FDC (Figure 2.5). This is unsurprising, given that only

[50] See the website http://apps.who.int/prequal/query/ProductRegistry.aspx

two Sub-Saharan countries – Somalia and Sudan – have included ASSP as the first-line treatment against *falciparum* malaria in their national guidelines. In fact, until 2017 Guilin is the only firms with a WHO prequalification for ASSP.

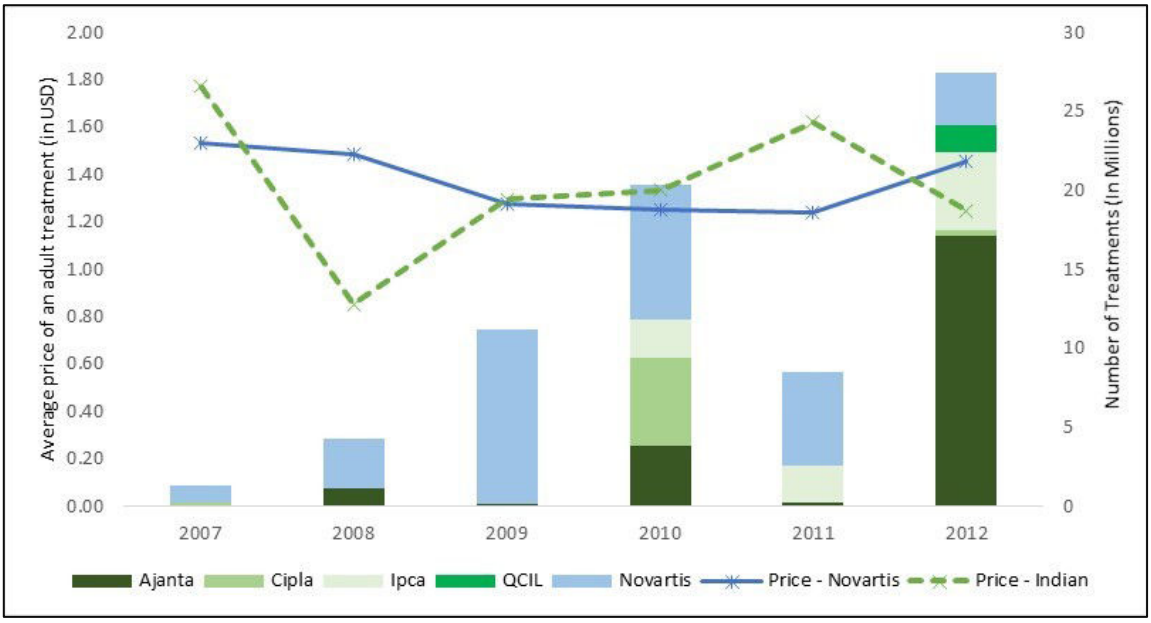
Figure 2.10: Market share of ASSP by firm origin



There were two additional Indian firms: Activa Pharmaceuticals (FZC) and Quality Chemical Industries Ltd. (QCIL) who supplied ASAQ-coblister and AL in 2008 and 2012 respectively. While Activa is a joint venture of Ipca, QCIL is a Uganda based subsidiary of Cipla.

We plotted average adult treatment prices and volume of AL (strength: 20 mg + 120 mg; pack-size 24) for both Novartis and Indian firms (Figure 2.11). Our results verify that the price offered by Novartis has decreased significantly from the first price of $2.40 in 2001. By 2012, Novartis charged on average $1.46 for a pack of 24 tablets. As discussed before, this can be attributed to both the entry of Indian manufacturers and launch of ASAQ-FDC by Sanofi (Figures 2.11 & 2.12). However, figure 2.11 also shows that prices offered by Indian manufacturers have varied considerably over the years.

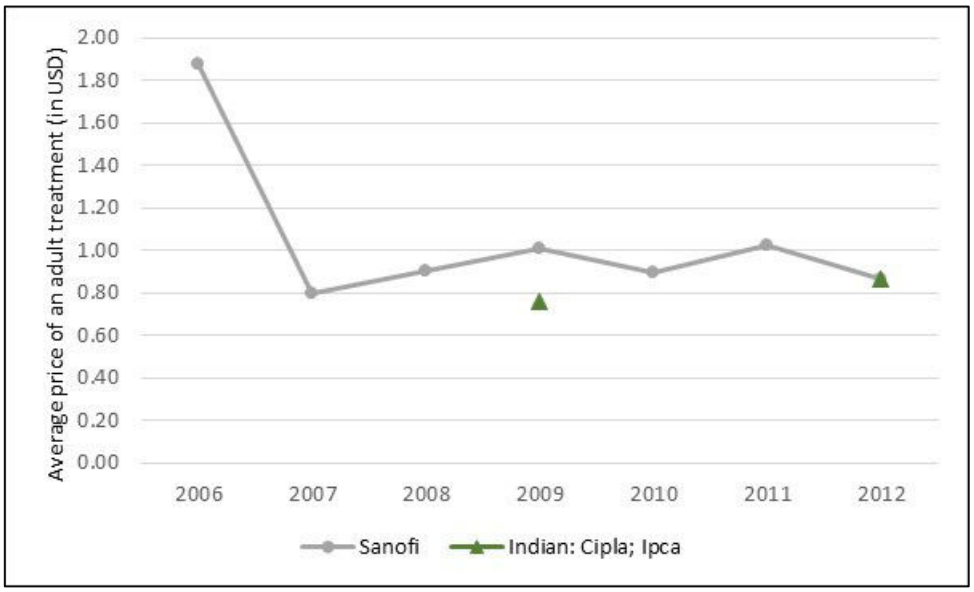
Figure 2.11: Average adult treatment prices of AL for Novartis and Indian firms



Note: 1. Prices are for AL: strength = 20 mg + 120 mg and pack-size = 24

2. We took 2007 as the first year as there were no transactions reported in the dataset for adult packs in 2006

Figure 2.12: Average adult treatment prices of ASAQ-FDC for Sanofi and Indian firms



Note: Prices are for ASAQ-FDC: strength = 100 mg + 270 mg and pack-size = 6

This could be due to various reasons. At the time of entering the market, Indian firms did not have the advantage of economies of scale in a market dominated by Novartis. This explains the high price charged by Cipla, the only Indian firm active in 2007. In 2008, Ajanta responded to international competitive bidding for supplying AL to Kenya at a price which was 40 percent lower than the market price (Tren, Hess, & Bate, 2009). This is equally confirmed by our results. Researchers have questioned the price offered by Ajanta, but it can be regarded more as a strategy to enter a new market. However, Ajanta seems to have raised its price in 2009 following the WHO prequalification for AL in December 2008. In 2010, all three Indian firms had prequalification for AL and a greater market access evident from both the increase in volume (Figure 2.10) and geographical coverage (Table 2.5). Novartis seems to have responded to this situation through a price cut. In fact, the lack of patents on individual molecules might have allowed Novartis to offer competitive prices as there was no investment for discovering new chemical entities for AL.

The trend for 2011 can be explained by the cancellation of round 11 grants of the Global Fund which might have an effect on reducing the demand, resulting in lower volumes and higher prices by Indian firms. However, these firms could offer a lower price as they reach the economies of scale as shown in 2012. Further, we report that Ajanta received approval for dispersible formulations of AL in December 2012. Additionally, two new Indian firms (Strides Shasun and Macleods Pharmaceuticals) also had a WHO prequalification in 2013. Moreover, the ASAQ-FDC was cheaper than AL and mostly remained close to one dollar as stated in the agreement between Sanofi and DNDi (Figure 2.15).

In terms of value, in 2012, Indian manufacturers accounted for 57 percent of the total (US$82 million) ACT purchases made through the Global Fund grant, while Novartis and Sanofi accounted for 41 percent of the market value and Guilin for 2 percent (Table 2.7).

Between 2006 and 2012, 36 countries procured ACTs from Novartis or Sanofi at least once. The number of countries purchasing ACTs of Indian origin gradually has also increased. 25 countries procured ACTs from Indian manufacturers at least once while 5 countries procured ACTs from the only Chinese manufacturer, Guilin, supplying ACTs during the same period (Table 2.7).

Table 2.7: Trends in ACT purchase by Sub-Saharan countries using the Global Fund grants

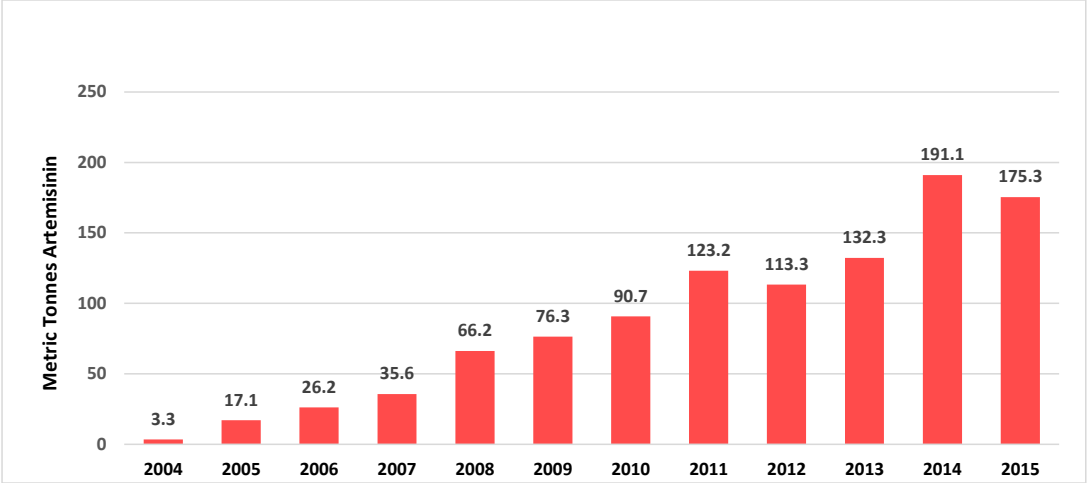
	2006	2007	2008	2009	2010	2011	2012	Total in Dataset
# Countries Reporting Any ACT Purchase	2	3	15	27	27	22	26	41
# Manufacturers	2	3	7	6	6	6	7	8
Value ($Millions)	0.69	3.55	15.80	43.10	59.90	33.50	82.10	238.64
Indian Generic ACTs								
# Manufacturer	-	1	4	3	3	3	4	5
# Purchases	-	3	32	22	93	53	106	309
# Purchasing Countries	-	1	8	5	10	10	12	25
Value ($Millions)	-	0.48	3.77	3.13	24.30	6.27	46.40	84.35
Chinese Generic ACTs								
# Manufacturer	-	-	1	1	1	1	1	1
# Purchases	-	-	9	12	4	5	9	39
# Purchasing Countries	-	-	2	2	1	2	2	5
Value ($Millions)	-	-	1.37	5.46	2.05	1.14	1.94	11.96
Originator ACTs								
# Manufacturer	2	2	2	2	2	2	2	2
# Purchases	5	15	42	144	211	135	198	750
# Purchasing Countries	2	2	7	22	22	17	20	36
Value ($Millions)	0.69	3.06	10.70	34.50	33.60	26.10	33.70	142.35

2.7.4. Limitations

This analysis is not without limitations. Our quantitative study only captured procurements made by using the Global Fund grants and does not include donor-funded procurements from other international organizations or purchases made by the governments in the public sector. Further, even though we systematically cleaned the data, we cannot be confident to identify all the reporting errors associated with publically available data. Also, our analysis does not account for the private market of ACTs in Sub-Saharan Africa. Finally, an obvious limitation of this quantitative analysis is the lack of data beyond 2012 due to the incompleteness of the dataset beyond that year.

However, an analysis of the WHO prequalified products reveals that until 2011 only 4 Indian ACT products were approved. Between 2012 and July 2017, additional 17 Indian products have received a WHO prequalification (6 AL; 9 ASAQ-FDC; 2 ASMQ-FDC). Thus, of the 38 ACT formulations approved by the WHO, 21 belong to five Indian firms – Ajanta (8 products: 5 AL; 3 ASAQ-FDC), Cipla (6 products: 1 AL; 3 ASAQ-FDC; 2 ASMQ-FDC), Ipca (4 products: 1 AL; 3 ASAQ-FDC), Mcleods (1product: AL) and Strides (2 products: 1 AL; 1 ASAQ-Coblister). This indicates the attractiveness of the donor-funded market to Indian firms. Further, the import of raw artemisinin (needed to synthesize active pharmaceutical ingredients such as artesunate and artemether used in ACTs) to India has also been rising. Figure 2.13 shows the evolution of artemisinin import to India between 2004 and 2015. The artemisinin import data is an explicit proxy for the growing role of Indian firms in the overall ACT market because if companies are importing more of the raw material, then they must be producing more of the ACTs. Moreover, because Sub-Saharan Africa accounts for 90% of the malaria cases (WHO, 2016d), it is the apparent market of choice.

Figure 2.13: Evolution of Import of artemisinin to India



Source: Data retrieved from the market intelligence platform of the Assured Artemisinin Supply System (A2S2[51])

2.8. Conclusion

The central objective of this chapter was to show the institutional aspects of internationalization that created conditions for the expansion of Indian firms. The findings substantiate the idea that internationalization of Indian firms is rooted in institutional changes both within and outside India. These changes did not take place overnight but rather were the outcome of dynamic and complex political processes and negotiations over the course of several decades.

The establishment of public manufacturing units and research labs not only developed the much-needed technological knowledge base for the industry but also provided a reservoir of future entrepreneurs. The weak patent regime and protective domestic environment helped Indian firms to build reverse engineering capabilities by copying patented molecules. This was useful for the industry when India implemented a stricter patent regime as firms already had the essential experience to move from duplicative to creative imitation which was a primary requirement to expand to foreign countries. Further, the concurrent arrival reforms due to liberalization and TRIPS created both competitive and supportive push factors for Indian firms to find new avenues of growth outside national boundaries.

[51] http://www.a2s2.org/market-data/artemisinin-imports-into-india.html

Indian firms were also pulled outside due to generic supporting policies in both developed and developing countries and the creation of new donor-funded markets. This new institutional structure helped Indian firms to exploit the skill of making and supplying generic drugs at a much lower price compared to their European counterparts. A novel contribution of this chapter has been in explaining the emergence of donor-funded markets for HIV and antimalarial medicines and the role played by international organizations in the functioning of these markets. The chapter also shows that the institutional contexts for the creation of ARV and ACT markets were different. Access to ARVs was intricately linked to intellectual property over these medicines which were held by originator firms. This was the reason why WHO could not recommend the use of FDCs from the beginning. Whereas, in the case of ACTs, the absence of patents on individual molecules used in the medicine permitted the invention of new formulations and in particular the development of FDCs and a rapid rise growth in competition led by Indian firms. Lastly, even though the institutional context of ARV and ACT markets have been different, they have acted as new avenue for internal expansion of Indian firms in developing countries, especially in Sub-Saharan Africa.

3. Organization of the Pharmaceutical Market, Market Entry and Operation Strategies of Indian Pharmaceutical Firms in Francophone West Africa

3.1. Introduction

Indian pharmaceutical firms present a successful case of internationalization by emerging country multinationals. From no international activity at the time of independence, Indian firms have evolved into a generic powerhouse and a major player in the global arena. They have successfully penetrated highly regulated markets of the US and Europe. This has drawn the interest of economists and business researchers to study the paths and motivations of internationalization of Indian firms (Bowonder & Mastakar, 2005; Dixit & Yadav, 2015; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Pradhan & Alakshendra, 2006; Sweet, 2010; Yeoh, 2011).[52] However, except for Sweet (2010), who has studied the growth of Indian firms in the Brazilian pharmaceutical market, no other researcher has specifically examined the complexities of foreign market entry and operation of Indian firms in developing country context. Particularly, entry into the African market has been taken for granted as an intermediary step in the broader process of internationalization events. In this simplistic understanding, Indian firms enter other developing countries where regulatory requirements are weak to gain experience and then gradually move to highly regulated markets of developed countries. Even though Africa has consistently been the second leading export destination after North America for Indian pharmaceutical products (Pharmexcil, 2015, 2016, 2017), the subtleties of the functioning of Indian firms within this market is mostly unexplored. Thus, the primary aim of this chapter is to limit this gap in the scientific literature by examining the

[52] Please refer to chapter 1 for a review of the internationalization of Indian pharmaceutical firms.

market entry and operation strategies of Indian pharmaceutical firms in Francophone West Africa by focusing on Mali.

However, **we cannot understand firm behavior without understanding the institutional context of the pharmaceutical market in the host country, in our case Mali**. A stream of studies has established that **strategy of firms is conditioned and determined by the features of the institutional environment in which they operate** (Dunning & Lundan, 2008; Meyer et al., 2009; Meyer & Peng, 2005). There is a dynamic interaction between institutions and firms and strategic choices by the latter are outcomes of such interactions (Fligstein, 1996; Fligstein & Calder, 2015; Peng et al., 2008). More specifically, Firms must adapt their operation in host country according to the prevailing set of rules and constraints posed by the institutional environment (Kostova & Zaheer, 1999; Tordjman, 1998). Indeed, the regulatory environment is a key driver for the functioning of the pharmaceutical market and consists of laws for pharmaceutical production, distribution and sales and the framework for surveillance, enforcement, and sanctions. It provides the structure for the drug registration or market authorization process, organization of supply chain and pre- and post-marketing surveillance among others.

Literature has provided evidence that there is not a single and all-encompassing pharmaceutical market in West African Francophone countries but instead four distinct market segments (Baxerres & Le Hesran, 2011; McCabe et al., 2011; Yadav, 2015). The public sector consists of the government-funded and the donor-funded market segments. On the other hand, the private sector consists of the formal private and the informal markets for medicines. In fact, donor-funded segment adds another layer of regulatory norms on the top of state laws and policies about the procurement and management of pharmaceutical products targets to specific diseases like HIV, tuberculosis (TB), and malaria.

Thus, **our goal was to understand the organization of pharmaceutical supply chain and isolate the regulatory framework governing the functioning these market segments in Mali and to analyze the market entry and operation strategies of Indian firms within the influence of this broader institutional environment**. This is because any Indian firm entering Mali must adjust its business strategies according to the market segment(s) in which it intends to operate.

The chapter uses a number of data sources and methodologies to support its findings. First, we conducted two sets of semi-structured interviews in India and Mali respectively. Semi-structured interviews, in the words of Barriball and While (1994), "are well suited for the exploration of the perceptions and opinions of respondents regarding com plex and sometimes sensitive issues and enable probing for more information and clarification of answers.". Furthermore, they allow to capture the background information through expert knowledge and rich description of processes (Harrell & Bradley, 2009). Data collection guidelines proposed by Barriball and While (1994) and Harrell and Bradley (2009) was consulted to organize the interviews. These guidelines not only provide techniques for designing, planning, collecting and handling qualitative data in a scientific and consistent manner but also explain the challenges and complexities of conducting a field-based research using semi-structured interviews. A description of the data collection procedure is described below.

The first set of 34 interviews was conducted between February and April 2016 in Bamako, Mali. The early phase of preparation we organized several discussion sessions with Professor Hubert Balique, who is an expert on the Malian healthcare system to identify and categorize potential interview participants. We relied on a judgement based sampling to include those actors whose knowledge and opinion would be important for research (Harrell & Bradley, 2009). The logic was to cover a broad set of informants who are involved in the regulation, importation, warehousing and distribution of medicines in Mali and might possess different information, views and experiences. It meant including participants from diverse organizations and domains of functioning (e.g. public, private, NGOs) which was also essential for improving the representativeness of the sample and strengthen the validity of the findings. Thus, we had an initial list of potential participants. The list was further updated during the course of the fieldwork. For example, few important wholesalers were identified through the literature on pharmaceutical markets in francophone West Africa (Mahamé & Baxerres, 2015; McCabe et al., 2011), others interesting players were known from interview participants.

After arriving in the field, the initial contact with the identified organizations was made through telephone to secure a meeting. Here the administrative support from the IRD was valuable in securing appointments because of its existing research linkages and legitimacy as an international research and development agency. In most cases the first face-to-face meeting was dedicated to explain and discuss the project and its objectives, answer any questions and arrange a convenient time for interview. In few cases, the first meeting resulted in the interview.

In light of the security risks because of terrorism, all the meetings and interviews were confined to the capital Bamako.

Our interview participants included officials from eleven public sector organizations (12 interviews) including the national pharmaceutical regulatory authority (Direction de la Pharmacie et du Médicament), national laboratory for quality control of medicines (Laboratoire National De La Santé), department of inspections for pharmaceuticals (Inspection de la Santé), central medical store (Pharmacie Populaire du Mali), national malaria control program (Programme national de lutte contre le paludisme), department of customs (Direction du renseignement et de enquêtes Douaniers), government-owned pharmaceutical company (Usine Malienne de Produits Pharmaceutiques), national order of pharmacists (Conseil National de l'Ordre des Pharmaciens du Mali), national health directorate (Direction National de la Santé), national association of community health centers (Fédération Nationale des Associations de Santé Communautaire du Mali) and the department of commerce (Direction Nationale du Commerce et de la Concurrence).

Nine private importers and wholesalers, one promotion agency and a local agent for a top Indian pharmaceutical company also agreed to participate in the study. Further, we interviewed managers from three international and one local NGO including Population Services International (PSI) and Catholic Relief Services who are the principal recipients of the Global Fund malaria and tuberculosis grants in Mali. We also managed to have detailed interactions with officials from three national hospitals (Point G, l'Hôpital du Mali, and Gabriel Touré) as well as a local pharmacist. Lastly, we used the "mystery shopper" approach to communicate with four informal shopkeepers in the market of "Dabanani" in Bamako. The diversity of the participants ensured a comprehensive understanding of the functioning of the pharmaceutical market in Mali.

Next, the second set of interviews were conducted with the owners and managers of Indian pharmaceutical firms in two specific phases. The first phase involved a fieldwork in India affiliated to the Centre for Studies in Science Policy (CSSP), Jawaharlal Nehru University between September to December 2016. The second phase was carried out between July and August 2017 from France using online tools.

The initial strategy was to target a sample of firms whose presence we had identified in Mali. However, India is a big country and not all firms are located in the same place. So, we decided

to focus on firms located in the state of Gujarat which is one of the leading hubs of pharmaceutical production in India and accounts for over 42% of India's pharma total turnover and 22% of India's exports (Dutta, 2013). Nevertheless, the task turned out to be complex and challenging due to unfamiliarity with the research site and the problem in getting access to the identified firms. Indeed, as Johl and Renganathan (2010) note that gaining access to individuals may take a long time depending upon the level of access required by the researchers and depends upon their reputation.

To overcome this challenge we switched to "opportunity sampling" which relies on making use of opportunities as they arise to interview individuals that the researcher had not planned to encounter (Harrell & Bradley, 2009). With this approach, eleven interviews were conducted. It included the owners of three pharmaceutical companies and one merchant exporter based out of Ahmedabad (Gujarat), an additional company owner and a director of Indian Drug Manufacturers' Association (IDMA) in Delhi and five managers of top tier Indian pharmaceutical firms who are working as the head of business development or marketing for African countries. Even though limited in number, these interactions were helpful in understanding the realities of the market and triangulating the findings obtained from Mali.

Separate interview guides (Appendixes 6.3 & 6.4) with specific set of questions were prepared for conducting interviews with the participants in Mali and India. The interview guides were broad in scope, so questions were adapted according to the knowledge and expertise of interview participants. They were asked only those questions that were relevant to their professional knowledge. Further, at the beginning of each interview participants were asked general questions about them, their organization and their role to establish a rapport. Interviews were audiotaped whenever possible and combined with concurrent notetaking.

The interview guide for Mali (Appendix 6.3) consisted of the following nine themes: (i.) regulatory framework, (ii.) process of marketing authorization, (iii.) cost recovery of malaria management, (iv.) pharmaceutical licensing and inspection, (v.) pharmacovigilance, (vi.) organization of pharmaceutical supply chain in the public sector, (vii.) organization of pharmaceutical supply chain in the private sector, (viii.) informal market of medicines, and (ix.) quality control of medicines.

The interview guide for Indian fieldwork (Appendix 6.4) dealt with the following themes: organization of business in the African market, reliance on local partners, market-specific challenges, understanding of market segmentation and local production.

The qualitative data collected from both sets of interviews were analyzed using explanation building approach as proposed by Yin (2003). It involves extracting the abstract concepts from each unit of analysis to explain a phenomenon of interest through analytical generalizations. The data is examined, categorized, tabulated, and recombined to make valuable conclusion. In the present case, we started by classifying the extracted information by attaching them to specific market segments. More precisely, the Malian data was examined to find the general architecture and regulatory features of the pharmaceutical market and the market entry and operation strategies of Indian firms by asking among others the following questions with respect to the four market segments (government-funded, donor-funded, formal private and informal sectors): who are the market participants? How are medicines imported into the country? What type of pharmaceutical products are imported? Who pays for importation? Which channels are used for distribution? What are the criteria for product quality? Who are the local partners importing and promoting Indian products? What are the conditions of such partnerships? This allowed to sketch a general regulatory outline for each of the market segments and the possible strategies used by firms.

Similarly, the responses from the second set of interviews were analyzed by looking for answers to the following set of questions: What is the general structure of the pharmaceutical market in Francophone West African Countries? What are the different possibilities for Indian firms to export medicines to these countries? What is the importance of local partners? Who are the possible partners in host countries and what is the basis of their selection and under which conditions? What are the barriers to entry? On the one hand, information from these interviews permitted to get a broader understanding of the pharmaceutical market and strategies used by Indian firms not only in Mali but other countries of West African Francophone Africa as well. For example, it allowed us to understand the strategy of Ajanta Pharma in Ivory Coast (the case is presented later). On the other, they allowed triangulating the information obtained from the fieldwork in Mali by checking if the two set of interviews are leading towards a common understanding.

Second, Malian market authorization list (version: December 2014) for pharmaceutical products was analyzed to provide additional evidence concerning the strategic choices made by Indian firms. The initial list allowed to know name of the product either as international non-proprietary name (INN) or brand, name of the manufacturer, and product characteristics such as pharmaceutical form (tablets, syrup, injection), pack-size and the name (only in the case of non-proprietary products) and strength of the active pharmaceutical ingredients. This information was employed to identify the geographical origin of manufacturers so that we could identify all Indian manufacturers present in Mali. Next, from the list of Indian manufacturers, we selected those firms who had on or more products prequalified by the WHO. A detailed product analysis of these firms was performed by looking at the type of medicines they are supplying. Brand name products had no information regarding active pharmaceutical ingredients. This information was found using company websites or other online sources that provide market data about pharmaceutical products by matching with the product information in the dataset.[53]

Details about product registration have already been employed, though in a limited way, by researchers to identify the presence of Indian firms in Tanzania (Chaudhuri et al., 2010). In fact, market authorization data does not only reveal firm characteristics, such as origin and size, and the type of medicines they are supplying, but it can also tell about their strategy towards market segments. For example, we matched the product details of selected Indian firms with WHO prequalification data to identify if these firms have registered WHO approved products in Mali. Major international donors like the Global Fund only allow purchasing of WHO prequalified products, and if a firm has not registered such products in the country, then it shows that it is not functional in the donor-funded segment.

Third, we also extracted trade data between 2001 and 2016 from International Trade Centre website (trademap) to analyze the growth of Indian pharmaceutical firms in Francophone West African countries. The website provides a detailed country wise information on global trade including pharmaceutical products. Lastly, we undertook a review of the literature including national legislation and reports by international organizations. Supplementary data on firms

[53] https://www.1mg.com; https://www.zaubacorp.com/; https://www.practo.com

were collected from websites, annual reports, business reports, news articles and balance sheet of selected companies.

Rest of the chapter unfolds as follows: section 3.2 offers a succinct presentation of the healthcare system in Mali. Section 3.3 explains the organization of the pharmaceutical supply chain in Mali with respect to the four market segments, i.e., government-funded market, donor-funded market, formal private market and informal market. Section 3.4 discusses the entry and operation strategies of Indian pharmaceutical firms concerning different market segments. Section 3.5 concludes the chapter.

3.2. Country Profile: Mali

3.2.1. Geography

Mali is a landlocked West African country covering an area of 1,241,238 square kilometers, and it shares a frontier of nearly 7,420 kilometers with seven neighboring countries: Mauritania, Algeria, Niger, Burkina Faso, Ivory Coast, Guinea, and Senegal (DPM, 2008). It is the eighth largest country in Africa and second in West Africa after Niger. Mali is divided into eight administrative regions, namely Kayes, K**o**ulikoro, Sikasso, Ségou, Mopti, Tombouctou, Gao, Kidal and the district of Bamako which has a special status as the country capital. The regions are divided into 49 *cercles* which form the second level of administrative units in Mali. These *cercles* along with the district of Bamako are further divided into 703 communes constituting the third level of administration. Of these communes 666 are rural and 37 urban including 6 communes of Bamako (IMF, 2013).[54]

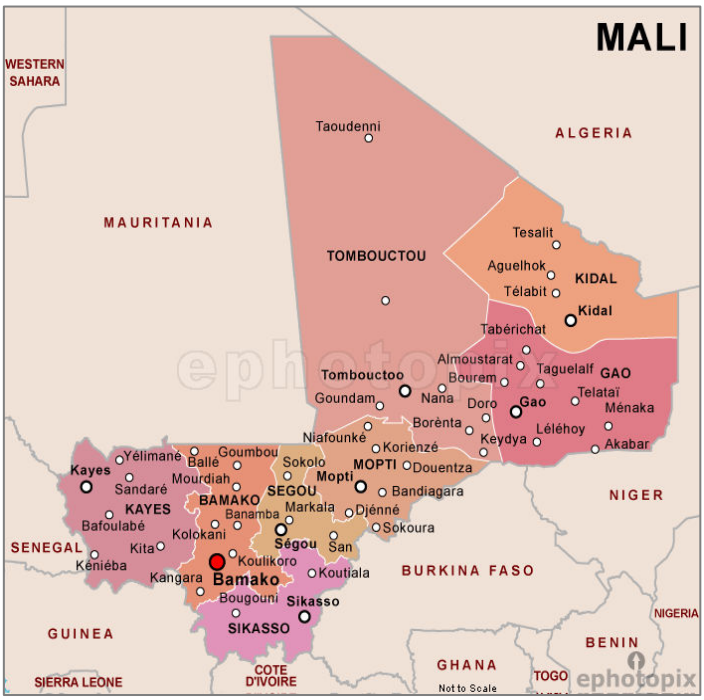
3.2.2. Demography

In 2015, Mali had an estimated population of 17.6 million (WHO, 2016a). Most of the country is however scarcely populated. The regions of Tombouctou, Gao, and Kidal together constitute

[54] Note: In 2012, two new regions of Taoudénit and Ménaka were created in the north of Mali out of Tombouctou and Gao respectively. Thus, making the total number of regions equal to ten. Nevertheless, detailed information regarding the two regions is not available.

two-thirds of Mali, but only 10% of the population lives in these regions (IMF, 2013). According to a WHO report, 30% of the country is inhabited by 91% of the population (African Health Observatory, 2016). Nearly 65% of the population of Mali is less than 25 years of age, and 70% of the population lives in rural areas (IMF, 2013).

Figure 3.1: Political map of Mali



Source: (Ephotopx.com, 2016)

3.2.3. Health indicators

Mali is classified as a low-income country with a total GDP of $12.04 billion in 2014 (World Bank, 2016). Health indicators of Mali have improved over the years, but the statistics remain alarming. Malaria is the leading cause of morbidity and mortality in Mali. In 2013, 2.3 million clinical cases of malaria were reported in the country and accounted for 42% of all outpatient visits (USAID, 2015). Life expectancy at birth in Mali for both sexes is 58 years which is much lower than the global average of 71.4 years. HIV prevalence among adults 15 to 49 is 1.4%. Antiretroviral coverage among people with HIV infection eligible for treatment according to 2010 guidelines was 52% in 2012 (Global Health Observatory, 2016).

3.2.4. Healthcare Delivery System

Mali adopted a multisectoral health policy in 2002 (Loi 02-049 AN-RM) which is based on the fundamental principles of equity, solidarity and the participation of the population and civil society and also takes into account the international commitments towards the Millennium Development Goals made by the country. The ten-year plan for sanitary and social development (Le Plan Décennal de Développement Sanitaire et Social; PDDSS) and five-year program for health and social development (Programme de Développement Sanitaire et Social; PRODESS) provide the framework for the implementation of this sectoral health policy (Lamiaux, Francois, & Woods, 2011; SDADME, 2010). PRODESS has become the reference document for coordination, monitoring, and evaluation of all the partners.

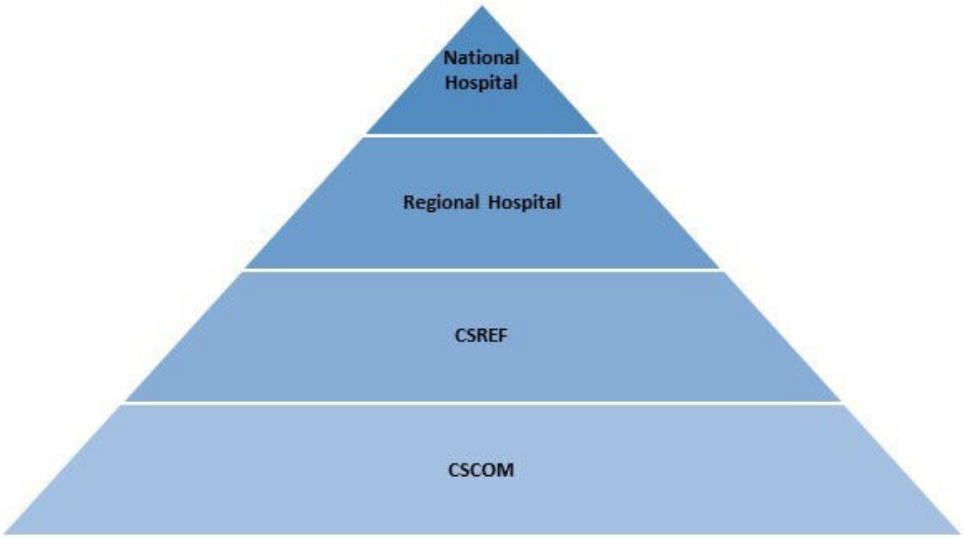
The health policy also emphasizes the strategy of decentralization and community participation towards increasing health coverage. The national territory is divided into multiple health districts each of which further consists of multiple health areas (aire de santé). The boundary of health districts is same as the *cercle*, however, depending upon the geographical and demographical requirement, a *cercle* can be comprised of two or three health districts. This division is revised every five years (République du Mali, 2002). Further, as depicted in figure 3.2 the healthcare delivery system in Mali has a pyramidal shape with four levels which is characterized by the presence of public, private and community-based entities (Lamiaux et al., 2011; PRODESS, 2014).

At the community level, there are community health centers (Centre de Santé Communautaire or CSCOM) which form the base of the health pyramid in Mali and the first point of contact with patients. CSCOMs are private not for profit civil societies that are managed by community health associations (Association de Santé Communautaire or ASACO) (USAID, 2013). Each CSCOM is obliged by the law to offer a minimum health package consisting of curative, preventive, social and promotional services to the community (Lamiaux et al., 2011). As of 2016, there were 1360 functioning CSCOMs in Mali *(source: personal communication)*. At the sub-regional level, each health district has a referral health center (Centre de Santé de Référence or CSREF) that has better facilities and more qualified personnel compared to the CSCOM. It takes charge of patients referred by CSCOMs falling under its catchment area thus forming the first referral level (Lamiaux et al., 2011). A CSREF serves as the link between CSCOMs and regional hospitals. Each CSREF has several CSCOMs reporting to it. The

"médecin chef" (Chief Doctor) of each CSREF has a supervisory role over the reporting CSCOMs. There are currently 64 CSREFs in Mali *(source: personal communication)*.

The regional level consists of seven hospitals of the second reference. These include the regional hospitals of Kayes, Sikasso, Ségou, Mopti, Tombouctou, Gao and the maternal and child hospital (l'Hôpital Mère Enfant le Luxembourg) in Bamako (PRODESS, 2014). Finally, at the central level, there are six national public hospitals of which four - Point G, l'Hôpital du Mali, Gabriel Touré and Kati – are for the general purpose. Remaining two - Centre National d'Odontologie – Stomatologie (CNOS) and Institut d'Ophtalmologie Tropicale d'Afrique (IOTA) offer specialized services. Together they comprise the third level of reference (PRODESS, 2014).

Figure 3.2: Healthcare pyramid in Mali



Source: Adapted from (USAID, 2013)

3.2.5. The Unique Nature of CSCOMs

The unique position of CSCOMs in the Malian healthcare system calls for particular attention. Implementing the principals of the Bamako Initiative (1987), Mali adopted a community-cantered approach to health care through decentralized health structures or CSCOMs (Balique, 2001). The ministerial decree N° 94-5092/MSSPA-MATS-MF delineates the conditions of creation and management of a CSCOM. The article 3 of the decree defines a CSCOM as a

health center of the first level that is created through the commitment of a defined population that organizes as an association (Association de Santé Communautaire or ASACO) to effectively and efficiently respond to health problems (Government of Mali, 1995). Thus, a CSCOM is a private not-for-profit health clinic that consists of a dispensary, a maternity ward, and a pharmaceutical depot and managed by beneficiaries themselves through ASACOs which are created under the private law as not-for-profit societies (Balique, Ouattara, & Ag Iknane, 2001; Lamiaux et al., 2011).

At the creation, each ASACO signs a convention with the state that describes precisely the mutual commitments of the state and the association and terms of its service to participate in the delivery of public healthcare services (Balique et al., 2001). CSCOMs benefit from certain advantages such as exemption from taxes and duties, participation in government training programs and obtaining grants while working under the administrative and technical supervision of the state (Balique et al., 2001). Thus, while they are private regarding their creation and management, CSCOMs are well integrated into the public healthcare system. Each CSCOM has a designated catchment area where it is tasked to deliver a minimum health package that includes curative, preventive, and promotional activities. They form the base of the health care pyramid and are essential vehicles for the government and NGOs to deliver primary health services to people. There are three sources of financing for CSCOMs:

- Cost recovery through consultations and sales of pharmaceuticals
- Contribution from the community
- Subsidies from the government and NGOs

According to a 2011 World Bank report, 87% of the population was located within 15 km radius of a CSCOM and 51% within 5 km (Lamiaux et al., 2011). Thus, CSCOMs are crucial to access to basic healthcare services including access to medicines. In fact, interviews suggest that CSCOMs are the primary buyers of medicines from the central medical store of Mali. At the time of fieldwork, there were 1360 functioning CSCOMs all over the country, up from 900 CSCOMs by mid-2009 *(source: interview with FANASCOM)*. However, CSCOMs suffer from several inefficiencies. The World Bank reports that the average CSCOM suffers from low personnel productivity and limited management capabilities of ASACOs. It is also worth noting that not all CSCOMs have a medical doctor. According to the strategic plan for health and social development, only 30% of CSCOMs were headed by a medical doctor in 2011

(PRODESS, 2014). The origins of CSCOMs as a "community driven" approach is also jeopardized in many instances. For example, Balique (2001) reported that in several instances the president of the association can capture the governance and functioning of CSCOM and take decisions without involving the management. Similarly, Boidin et al. (2012), in their analysis of CSCOMs in the Kayes region of Mali found that cash and material contributions from "migrants" outside the community not only results in financial inequality across CSCOMs but also leads to the involvement of outsiders in day-to-day functioning causing a slow and inefficient decision-making process. They also reported that most staff lack a permanent work contract and there are wide disparities in their financial remuneration which often does not correspond to the educational diploma. Further, the exercise roles and responsibilities between government officials and ASACO remains ambiguous and national texts are often not implemented on the ground.

3.3. Pharmaceutical Supply chain and Market Segmentation

3.3.1. Regulation of the Pharmaceutical Sector in Mali

Pharmaceutical sector in Mali is governed by a series of legislation that govern the supply of medicines in both the public and the private sectors. Concerning the public sector, Mali formally applied the distribution of essential medicines in 1995 and from the following year, a comprehensive mechanism called the "Master Plan for the Supply and Distribution of Essential Medicines" (SDADME) was developed and implemented (SDADME, 2010). SDADME describes the role and responsibilities of actors at different levels of pharmaceutical management in the public sector.

On a broader level, Mali adopted its first national pharmaceutical policy in 1999 with the objective to ensure the quality of medicines and other pharmaceutical products and improve the implementation of pharmaceutical legislation and regulation. In 2002, the pharmaceutical policy was integrated within the multisectoral health policy framework permitting an active coordination between the stakeholders – government, civil society, and donors – in financing, implementation, and monitoring of programs (Paul, 2011).

Three primary structures share regulatory functions of the pharmaceutical sector in Mali. They include The Department of Pharmacy and Medicines (la Direction de la Pharmacie et du

Médicament or DPM), The National Health Laboratory (le Laboratoire Nationale de la Santé or LNS), and The Department for Health Inspection (l'Inspection de la Santéor IS) *(source: interviews with DPM, LNS, IS)*.

i. **DPM** was created as the national regulatory authority by the Ordinance N° 00-039 /P-RM of 20 September 2000. DPM's mission is to develop the national drug policy, to ensure its implementation and to facilitate coordination and control of the services concerned in the implementation of this policy. Among its other functions, it is in charge of setting pharmaceutical regulations, overseeing market authorization of pharmaceutical products, preparation of national essential medicines list and development of tools for the rational use of drugs *(source: interview DPM)*.

ii. **LNS** was created by the Ordinance N° 00-040/P-RM on the same day as the DPM with the mission to control the quality of medicines, food products or drinks imported or produced in Mali. It is also a member of the committee of reception of medicines and committee for granting market authorization. LNS is independent both financially and juridically and is managed by a board of directors. It has three sources of revenues in its budget: subvention from the state, fee from clients, and support from donors through financial or in-kind contribution. The LNS controls the medicines at different points in the supply chain. First, it is responsible for asserting the quality of products before granting the market authorization. Second, it also tests samples for quality at the time of importation and before distribution for public procurements made by the Central Medical Store of Mali. Third, the LNS is also responsible for post-marketing inspections at the points of sale and distribution. Inspections are obligatory and made by surprise and at random. Once poor-quality medicines are found then the LNS reports them to the DPM which issues a notification to remove the concerned lot. Finally, it also checks for quality when any organization signals a problem *(source: interview LNS)*.

iii. **IS** came into existence by the Ordonnance N° 00-058/P-RM of 28 September 2000. It is responsible for monitoring all pharmaceutical establishments at all levels of the supply chain. It ensures that the good manufacturing, distribution, and storage practices are followed by the manufacturers, wholesalers, distributors and public or private pharmacies. Nevertheless, it is difficult for IS to operate efficiently due to insufficient

staffing and a lack of regulatory means *(source: interview IS)*. Their role thus is mostly limited as reminders of regulation and providers of information

3.3.2. Market Authorization

Marketing authorization (MA) or product registration is the first step towards the launch of a pharmaceutical product in the market. It warrants that all the pharmaceutical products used in a country are registered and involves a technical assessment of the product for safety, efficacy, and quality. Further, the manufacturer is required to provide all information related to the product like the form, dosage, mode of administration, its composition in active ingredients and excipients, therapeutic indications as well as side-effects, and the wholesale price before tax among others. To be imported and distributed in Mali, a pharmaceutical product must have a marketing authorization (l'Autorisation de Mise Sur le Marché or AMM) the conditions of which are strictly defined by the inter-ministerial order No. 05-2203/MS-MEF-SG of 20 September 2005. The ministry of health grants marketing authorization upon the recommendation of a national committee for the registration of medicines which is headed by the DPM and includes the LNS and IS among its members *(source: interviews with DPM, LNS, IS)*. In theory, any medicine distributed in the country must have a marketing authorization. However, the reality is more complex, and multiple procedural arrangements do exist. The minister of health can give special authorization to import medicines for international aid purposes. Further, a fast track authorization procedure exists for specific treatments or in case of an emergency. Also, a special temporary import authorization may be given to legal manufacturers or importers under the well-defined conditions of product specification and criteria for quality control for drugs that have passed the open tender for procurement by the CMS. The supplier, in this case, has six months following the notification of contract award date to apply for product registration *(source: multiple interviews)*.

The market authorization is granted for five years after which it can be renewed. As of December 2014, there were 2806 specialty (branded or originator), and 414 non-proprietary generic products had market authorization in Mali *(source: List of products with a market authorization in Mali, version December 2014)*. For the moment market authorization granted in another country is not recognized in Mali but all such certificates are demanded along with

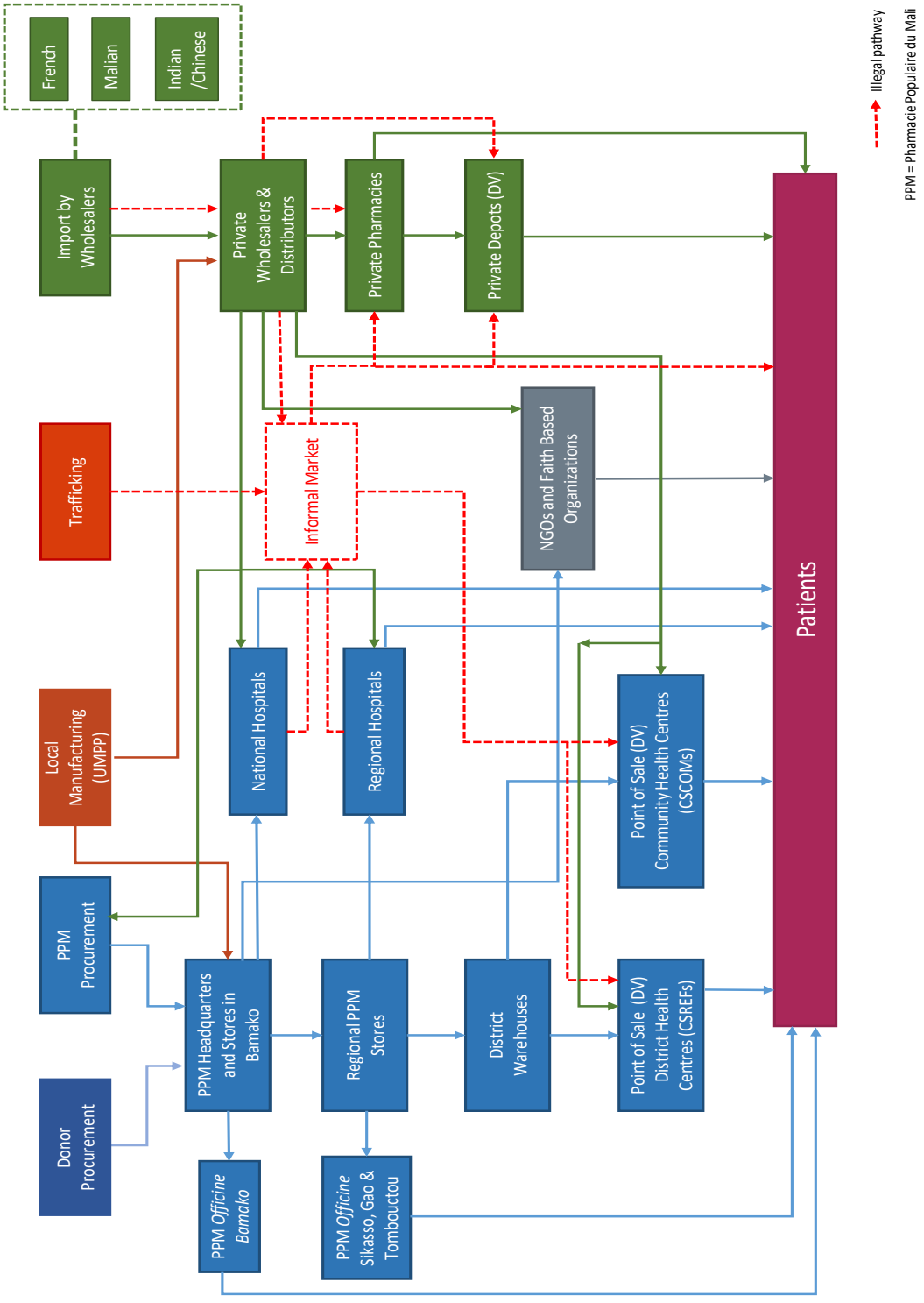
the application. However, the harmonization among the West African countries is under negotiation *(source: interview LNS)*.

3.3.3. Local Pharmaceutical Production

The pharmaceutical industry in Mali is not well developed. The state-owned "Usine Malienne de Produits Pharmaceutiques" (UMPP) is the only functioning enterprise, but it is in a dire situation *(source: interview UMPP)*. It produces basic molecules like paracetamol and some syrups. Recently, a private Chinese pharmaceutical firm, 'Humanwell Pharma" has been established in Sanankoroba, 30 km from Bamako. However, the unit had not started functioning at the time this study was conducted.

Thus, Mali is nearly 100% import dependent for the medicinal needs of its citizens. Pharmaceutical import in Mali is done by both public and private sectors. The public sector can be further divided between government and donor-funded markets where pharmaceutical import is carried out by the central medical store of Mali (Pharmacie Populaire du Mali or PPM) and international agencies, respectively. The private sector comprises the formal and informal sectors. A comprehension of this differentiation and organization of supply chain and regulatory framework in each segment will help us to understand the options open to firms for their operations in these markets. We discuss each of them briefly in the following sections

Figure 3.3: Pharmaceutical circuit in Mali



Source: Adapted from (McCabe et al., 2011) and information from various interviews

3.3.4. Pharmaceutical Supply chain in the Government Funded Public Sector

Two main texts regulate the management of supply chain in the government-funded public sector. The first is the master plan for the management of procurement and distribution of essential drugs (SDADME) that was adopted in 1995 and put to practice in 1996. The current version of the document was revised in 2010. The goal of SDADME is to ensure a proper supply of quality essential medicines throughout Mali at a price that is affordable by the population (SDADME, 2010). The second is the contract between the state and the PPM that outlines their roles to ensure the availability, accessibility, and affordability of essential medicines within the country. The contract is renewed every three years (SIAPS, 2014).

The PPM is responsible for the procurement and distribution of essential medicines in the public sector throughout the country on behalf of the government. The PPM is a semi-autonomous organization under the ministry of health which gives it more flexibility to operate and make strategic decisions. It is a strategic entity with special privileges that acts towards the realization of the national pharmaceutical policy. It is responsible for the procurement, storage and distribution of pharmaceutical products throughout the country from the central to regional and even sub-regional levels on behalf of the government and often international organizations. It primarily procures generics listed on the national essential medicines list (NEML) through an international competitive bidding. The 2014 version of the Malian NEML consists of 366 molecules that correspond to 566 products in different dosage and forms

PPM has 16 points of sale (point de vent), eight of which are located in Bamako. Of these eight stores, seven shops (Magasin) act as wholesale points while one pharmacy (Officine) sales directly to patients. Another five wholesale stores of PPM are located in different regions namely: Kayes, Koulikoro, Sikasso, Ségou, and Mopti. Additionally, three pharmacies (Officines) are located, one each in the regions of Sikasso (Koutiala), Gao and Tombouctou. This network of stores extends the coverage of PPM throughout the national territory except for the region of Kidal where the product is supplied through the store in Gao.

PPM supplies medicines to national and regional hospitals, national programs against various diseases, district health centers of Bamako and other regions (CSREFs), CSCOMs, NGOs, faith-based organizations, private wholesalers and pharmacies, and patients.

3.3.4.1. Process of Procurement by the PPM

The process of procurement starts with the PPM receiving the estimation of the need of essential medicines. According to the contract between the state and the PPM, the DPM is responsible for providing the PPM with the total need of essential medicines of the country for the forthcoming year by the end of September of the ongoing year. DPM achieves this through a technical committee on coordination and monitoring of drugs of which PPM is also a member. The committee consists of members from government agencies (such as the DPM, LNS, and IS.) as well as private sector (La Fédération Nationale des Associations de Santé Communautaire du Mali or FENASCOM) and development partners (such as the WHO, United Nations Population Fund, United Nations Development Programme, Population Services International, Catholic Relief Services, and Management Sciences for Health),

After receiving the estimation of need, the PPM prepares the specifications of the tender which is sent to the Directorate of Public Procurement (DGMP) for approval. Once approved by the DGMP, the PPM issues an annual call for tenders for required medicines. After the bids for tender arrive, they are evaluated, and the results are notified to the suppliers who are awarded the contract for one year. Suppliers then take nearly four months to fulfill the demand. In its usual course, the whole process can take a minimum of six months, but in reality is longer.

On arrival, shipments are received by a national committee of reception made up of DPM, PPM, and LNS. LNS, analyses samples from shipments to check their quality. Once tested and approved by the LNS, medicines are ready for distribution in the public market. Figure 3.4 summarizes the whole process *(source: interview PPM)*. According to officials, the PPM procures medicines from suppliers across the globe, but Indian and Chines products make up nearly 60% and 30% of the total import, respectively *(source: interview PPM)*. Nevertheless, PPM represents less than 50% of the public pharmaceutical market in Mali (in terms of value) (McCabe et al., 2011).

3.3.4.2. Distribution of Pharmaceutical Products in the Government-Funded Market

At the central level, the PPM supplies pharmaceutical products to national hospitals, district health centers (CSREFs) and special programs such as immunization. Further, at the national level, it also provides logistics and distribution support to disease-specific programs such as

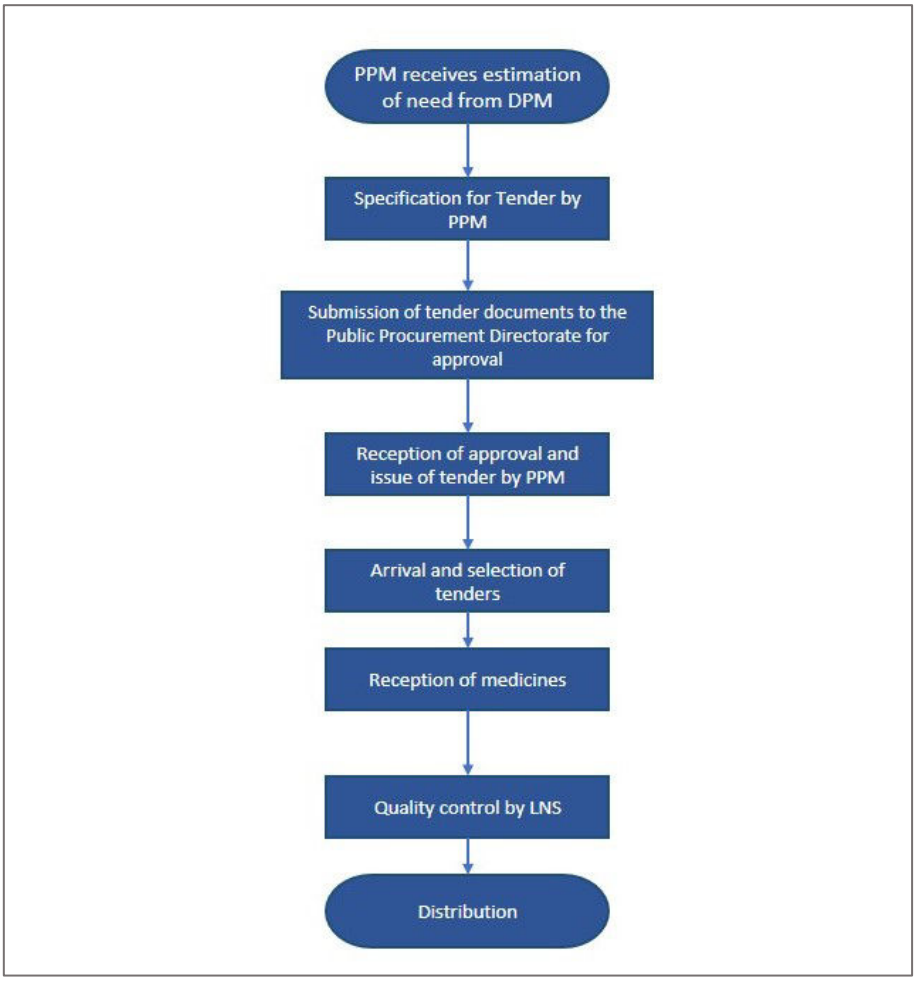
those concerning HIV, tuberculosis, malaria, and also to the national family planning and the national maternal, newborn and child health programs.

At the regional level, hospitals and district warehouses (Dépôt Répartiteur de Cercle or DRC) come to buy from the regional PPM stores. At the sub-regional or health district level, CSREFs and CSCOMs buy medicines from the DRC. In fact, the DRC is located within a CSREF and acts as the point of storage for essential medicines. Its purpose is not to sell medicines to patients but pharmacies or point of sale (Dépôts de Ventes) of CSREFs and CSCOMs of the concerning district. CSCOMs must pay the cost of transport to carry medicine from DRC. Thus, the PPM controls and manages the procurement **a**nd supply only until the regional level after which the management is passed to the DRC.

Nevertheless, for products that are distributed for free as a part of the national fight against malaria, the PPM provides distributional support until the DRC. Similarly, the PPM ensures the distribution of ARVs until the support centers. Further, according to the SDADME (2010), public sector organizations including CSCOMS (who as we discussed are private in origin but integrated within the public healthcare delivery system) are required to buy their supplies first from the PPM and only when there is a rupture of stock at the PPM that they can buy medicines from the private wholesalers. However, this condition is often not respected, and there is no provision of sanction in the SDADME.

Various reasons explain why public entities buy medicines and other supplies in the private sector. First, PPM suffers from frequent ruptures and in this case, in accordance with the SDADME public and community-based organizations (Hospitals, CSCOMs and CSREFs) can procure medicines in the private sector. Second, public pharmacies often lack funds and private wholesalers supply product on credit which the PPM does not do. Also, they can get more stock from multiple wholesalers on credit. Third, sometimes private wholesalers offer products at cheaper rates. Finally, private wholesalers deliver the product at the point of sale which saves transportation cost.

Figure 3.4: Procurement process of the PPM



Source: Interview with PPM

3.3.5. Donor Procurement in Public Sector

Finally, as discussed in chapter 2, international organizations determine the governance structure of the donor-funded market segment. One the one hand, they create demand for medicines by providing funds to developing countries. On the other, they make market attractive for manufacturers for supplying medicines at negotiated prices by consolidating the demand through pooled procurement. Also, institutional intermediaries such as the WHO prequalification program allow for providing a rigorous quality assurance mechanism which is often lacking in most developing countries.

In Mali, international partners or donors work mainly for diseases specific national programs such as HIV/AIDS, tuberculosis, malaria, maternal, newborn and child health and family

planning. These programs get substantial financial and technical support from international donors for their smooth functioning. Each disease targeting national program has specific quantification committees and sub-committees that are responsible for estimating the medicinal need and make annual demand forecasts. Follwing a multi-sectoral approach, these committees are comprised of government agencies, donors, development organizations and procurement agents and work under the supervision of the DPM. Figure 3.5 shows the sub-committees for quantification for HIV, tuberculosis, and malaria. On the one hand, such quantification allows knowing the national need for program-specific medicines while on the other, it ensures better coordination among partners. It also permits the government to know which part of the national need will be contributed by the partners and thus allowing it to focus its resources on the remainder.

Product specifications for the donor-funded market are laid down by the funding agency or other development partners in charge of procurement and are different from those specified in the government led public market or the formal private market. The program buys the medicines that are recommended in the national therapeutic guidelines but their criteria for the selection of products (such as strength and packaging) and manufacturers are rigorous, and the standards for quality are much higher. Most funding agencies such as the Global Fund and the PEPFAR only entertain products that are certified by the WHO prequalification program or approved for use by a stringent drug regulatory authority (SRA) such as the USFDA, or the European Medicines Agency. In addition, some organizations such as MSF have their own qualification scheme especially for products which are not prequalified or approved by an SRA (MSF, 2016). Procurements for these programs are usually undertaken by the donors or a third party representing them.

For example, Global Fund encourages its principal recipients (PRs) to use its Pooled Procurement Mechanism. However, subscribing to the pooled procurement mechanism is not mandatory for PRs (GFATM, 2015b). They may use their own procurement and supply management systems, rules, processes, and procedures. PRs also have the freedom to employ third-party procurement agents as long as the Global Fund purchasing policies like those pertaining to quality and pricing are met (GFATM, 2017b). Nevertheless, in some instances, the Global Fund itself determines the procurement mechanism that PRs should follow. For example, The Global Fund puts special conditions for medicines against multidrug-resistant TB which can only be procured through agents approved by the Global Drug Facility of the

Stop TB Partnership[55]. Similarly, pediatric ARVs can only be procured through entities who are members of ARV Procurement Working Group which consist of multiple development partners and donors (GFATM, 2017b). Similarly, procurement for ARVs for the PEPFAR is done by the Supply Chain Management System (SCMS) project under the supervision of Partnership for Supply Chain Management (PFSCM)[56] (JSI, 2017).

Example 1: Population Services International (PSI) is the principal recipient of the Global Fund malaria grant in Mali since 2011. PSI does not use the Global Fund pooled procurement mechanism but instead uses its own procurement channel to buy the products for the national malaria control program. The first step involves the estimation of country's need, product specifications and technical guidelines which is provided by the quantification committee. The requirements are then passed on to the PSI headquarters in Washington D.C, USA, which then issues an international tender with technical specifications to select the supplier *(source: interview PSI)*.

Example 2: Achieving Catalytic Expansion of Seasonal Malaria Chemoprevention in the Sahel (ACCESS-SMC) is a Unitaid funded project that targets children under five years of age in seven countries: Burkina Faso, Chad, Gambia Guinea, Mali, Niger, and Nigeria. Catholic Relief Services (CRS) is the implementing partner in Mali (and additionally in Gambia, Niger, and Guinea). CRS communicates the estimation of need to the Malaria Consortium who is responsible for procurements under the guidelines issued by the Unitaid. Malaria consortium further takes the services of specific procurement agencies like Crown Agents for purchasing medicines through competitive tenders. The procurement agent is responsible for handling and shipping the medicines to CRS in Mali *(source: interview CRS)*.

In both the examples cited above, once medicines enter Mali, they are handed over to the PPM for warehousing and distribution. PPM receives a key of distribution schedules and quantities from the respective programs. The process is monitored by the concerning partner, and it pays an amount to the PPM for its services *(source: multiple interviews)*.

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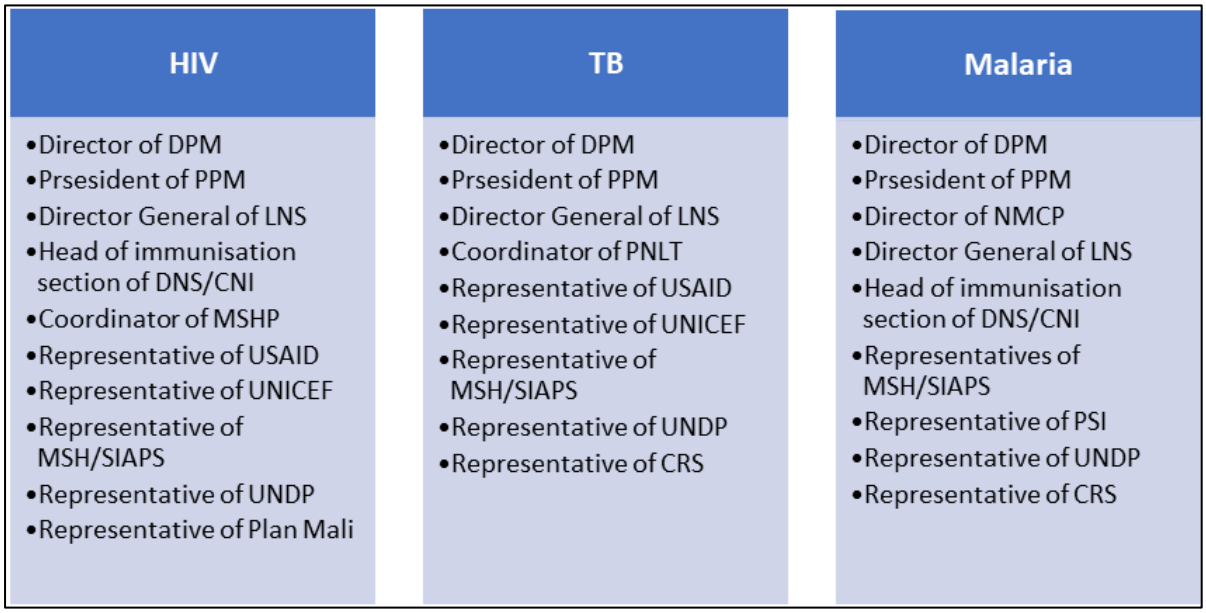
[55] Stop TB Partnership is a Global Health Initiative of 1500 partners to eliminate tuberculosis. For more details see website: http://www.stoptb.org

[56] PFSCM is a nonprofit organization established by the Management Sciences for Health (MSH) and John Snow, Inc. For further details check organization website: https://pfscm.org

Figure 3.5: Subcommittees for quantification of medicines for HIV, TB and malaria in Mali



3.3.6. Pharmaceutical Supply chain Circuit in the Formal Private Sector

3.3.6.1. Makeup of the Private Market

The formal private sector is comprised of all importers, wholesalers, pharmacies and pharmaceutical depots (dépôts pharmaceutiques)[57] that work within the legally defined framework of the country. Historically, pharmaceutical sector in Mali was under the monopoly of the PPM that mainly imported branded medicines sourced from European companies (Johnson et al., 1999). Private practice in the field of medicine was allowed by the law N° 85-41/AN.RM of 1985. The revised policy opened new modes of import of medicines in the country led by private importers. The competition that came out of this reform was one of the reasons that resulted in PPM procuring generic medicines in the early 1990s thereby reducing prices and increasing availability (Johnson et al., 1999).

Almost 100 percent of the pharmaceutical supply in the private sector is imported. The law permits only registered wholesalers to import medicines in Mali. For every shipment, the

[57] Pharmaceutical depots (dépôts pharmaceutiques) are dispensing structures under the responsibility of a pharmacy but without the effective and constant presence of a pharmacist.

Department of Customs requires the wholesalers to present an authorization by the DPM to import medicines within the country.

In 2016, the private sector comprised of 66 registered importers and wholesalers, a number that has more than doubled since 2009 (Personal communication with the National Council of the Order of Pharmacists of Mali; Table 3.1). This large number of private wholesalers is a unique feature of the Malian pharmaceutical supply system. In fact, Yadav (2015) notes that francophone African countries are typically characterized by the presence few importers and wholesalers. Indeed, as of 2014, there were only six registered wholesalers in Senegal (OECD, 2014). Similarly, studies by the World Bank (2012) and Mahamé and Baxerres (2015) reported the presence of eight wholesalers in Burkina Faso and five in Benin, respectively.

Malian wholesalers can be grouped into three categories based on the ownership structure. The first group consists of pure Malian enterprises whose shareholders are exclusively Malian pharmacists. This group includes the majority of the wholesalers in Mali. The second group includes two wholesalers – Laborex and Ubipharm – whose capital is partially held by French companies. The presence of these subsidiaries of French companies is a distinctive feature of francophone African countries where they control most of the private market. For example, Laborex and Ubipharma control more than 85% of the private market in Mali (McCabe et al., 2011). The third group is made up of those commercial enterprises where ownership is partially held by the entrepreneurs of Indian and Chinese origin. Table 3.2 shows the some of the top importers of pharmaceutical products in Mali in each category.

The two biggest wholesalers, Laborex and Ubipharm, have their own extensive supply and distribution channels with well-functioning cold-chain. Their procurement is managed through company headquarters in France and mainly consists of specialty products, i.e., originator brands and branded generics. Small wholesalers in group 1 and group 2 mainly concentrate on the branded and non-proprietary generics segment and purchase their stock directly from the manufacturer.

Pharmacies are the primary clients for wholesalers and act as the link between wholesalers and patients. In 2016, there were 536 pharmacies and 132 pharmaceutical depots in Mali (Table 3.1). However, most of the pharmacies are concentrated in urban areas, primarily Bamako (Lamiaux et al., 2011; McCabe et al., 2011). Also, the majority of them have direct ties with Laborex and Ubipharm who supply most of their need. Private wholesalers also supply to

public hospitals and district and community health centers. According to an estimate private sector supplies nearly 50% of the demand in the public sector in Mali (SIAPS, 2014).

Further, wholesalers can purchase medicines from each other at a preferential rate. This is a win-win situation for everyone because all wholesalers do not have all the products which have a demand at all times. Further, small wholesalers who do not have financial means to import medicines themselves, work with those who can. This also helps medium-sized wholesalers who though have the means to import the drugs but not the logistics to distribute. Having tied up with other wholesalers allows them to achieve a broader coverage of their products. For example, one of the wholesalers, SOPROPHA directly supplies to 60-65 pharmacies but using intermediate wholesalers allows their product to reach some 200 pharmacies *(source: interview)*.

Table 3.1 Number of wholesalers and pharmacies in Mali

Statistics	**2009**	**2016**
Wholesaler	32	66
Pharmacies	401	536
Pharmaceutical Depots	109	132
Total	542	734

Source: Conseil National De L'ordre Des Pharmaciens Du Mali

Table 3.2: Top private importers of pharmaceutical product for human use in Mali

Group1	**Group 2**	**Group 3**
CAMED	Laborex	SOPROPHA
Pharma Plus	Ubipharm	Da Hai Co
Africa Lab		Sino Pharma
SVPP		K Pharma
Mapropharm		Humanwell Pharma

Source: Department of Commerce and Concurrence, Mali

3.3.6.2. French Wholesalers in Francophone Africa

A distinct feature of the formal private market in Francophone Africa is the presence of multinational French importers and wholesalers. These companies play multiple roles and provide vertically integrated services to pharmaceutical firms for their business operations in Francophone countries. They act as pre-wholesaler, provide logistics, warehousing, marketing, and promotion and have also entered manufacturing. They consolidate the demand from individual countries into large procurements which are centrally managed through their headquarters in France. Their simultaneous operation in multiple countries and connection with an extensive network of pharmacies for distribution allows them to exert substantial market power. Laborex, a subsidiary of the Eurapharma and Ubipharm are the two most prominent wholesalers active in Francophone Africa.

Eurapharma is a large organization with a widespread geographical coverage. It is a part of CFAO – a multi-billion conglomerate registered in France (Eurapharma, 2016). It supplies medicines in 23 African countries and seven French overseas territories with its network of pre-wholesalers, logistics companies, and distributional channels. At the country level, it has local subsidiaries who act as wholesalers and distributors. For example, it operates as Laborex in Mali, Senegal, and Burkina Faso, as Promopharma in Benin, Copharmed in Ivory Coast and Uniphart in Togo. The group serves over 5000 pharmacies and supplies medicines from 450 pharmaceutical companies. It had a revenue of 1.3 billion euros in 2016 of which 41% came from 14 francophone countries in Sub-Saharan Africa and another 30% from French overseas territories. Eurapharma also owns Missionpharma and Fazzini which are dedicated to supplying to institutional customers such as international organizations and governments (Eurapharma, 2016).

The order placed by country level subsidiaries like Laborex-Mali goes to ‘Continental Pharmaceutique’ which is located in Rouen, France and serves as the central purchasing platform for Eurapharma. Continental does not stock products but instead facilitates regrouping and distribution for country-level subsidiaries. Once orders are received by Continental, then it uses its network to get products directly from many multinational companies and/or pre-wholesalers such as EPDIS which is also a part of the Eurapharma group. Pre-wholesalers such as EPDIS and Planetpharma provide a platform for pharmaceutical companies to outsource and subcontract their logistics and export operations for African countries. Pre-wholesalers then

manage the storage and distribution of their products intended for sale in Africa. Once Continental receives orders, it consolidates and sends them from France to respective wholesalers in Africa through the air or maritime freight depending upon the value of consignment and also manages to clear the product from customs. These findings support those noted by McCabe et al. (2011) in their analysis of Malian pharmaceutical market.

A similar model is used by Ubipharm which works in 11 Francophone countries and 3 French overseas territories. It has a network of 3500 pharmacies and works with over 400 pharmaceutical companies. Its 2016 revenue was 665 million euros (Ubipharm, 2017). The consignment order of Ubipharm-Mali is automatically generated through software and sent to Planetpharma on a weekly basis. Planetpharma is Ubipharm's principal pre-wholesaler and regrouper. It groups the order from different country-level subsidiaries and gets the product from manufacturers and suppliers based in Europe and Asia. Some of the products are already stocked by the planet because it acts also as pre-wholesaler for many companies. It can also source its products from other pre-wholesalers like EPDIS.

The supply chain of Laborex and Ubipharm is centrally managed from France. It takes approximately two months for the order to arrive at specific countries if sent by maritime transport and 45 days if sent by air. Together, Eurapharma and Ubipharm control nearly 80-90% of the private market in countries like Mali and Senegal (McCabe et al., 2011; OECD, 2014). Both Laborex and Ubipharm deliver the order to pharmacies located in Bamako within 24 hours and within 2-3 days to pharmacies located in other regions.

3.3.7. Informal Sector[58]

Baxerres (2011) designates that formal and informal are mutually exclusive, i.e., informal markets fall outside the forms imposed by the government. Thus, we can define the informal pharmaceutical market as the sum of all the activities including importation, storage, distribution and dispensing that violates the national law. Medicines in the informal market reach the patients through unlicensed pharmacies, street vendors, and kiosks.

The informal sector is a major source of poor quality medicines which according to the new definition adopted by the Seventieth World Health Assembly can be categorized as substandard, falsified and unregistered or unlicensed medical products. Substandard medicines are authorized by national regulatory authorities but fail to meet either national or international quality standards or in some cases, both. Falsified medicines are the outcome of deliberate or fraudulent activities and misrepresent their identity, composition or source. Finally, unauthorized or unlicensed medicines refer to those products that have not been approved by the appropriate regulatory authority for the market in which they are marketed, distributed or used (WHO, 2017b).

In fact, poor medicine quality has become a pandemic, and a significant threat to global health. The Lancet reported that up to 15% of all drugs sold worldwide are estimated to be falsified (The Lancet, 2011, 2012). While the circulation of falsified medicines is increasing in the industrialized world, it is kept in check due to strict standards and control measures exerted by national medicine regulatory authority (Caudron et al., 2008). On the contrary, the impact is disproportionately high in resource-poor countries (Dégardin, Roggo, & Margot, 2014). Studies suggest that many developing countries of Africa, Asia and Latin America may have regions where more than 30% of medicines on the market can be of poor quality (Almuzani, Choonara, & Sammons, 2013; Ambroise-Thomas, 2012; Dondorp et al., 2004; G. M. L. Nayyar, Breman, & Herrington, 2015; G. M. L. Nayyar, Breman, Newton, & Herrington, 2012;

[58] This study does not take into account the informal market for examining entry strategies of Indian firms because a variety of sources facilitate the entry of medicines into this segment. Such sources include trafficking, pilferage, and corruption in the public sector among others. Thus, the presence of a firm's products into informal market does not reflect its active involvement. However, there may be certain firms who trade in the informal sector but such activities are criminal offences and tracking and studying those firms was beyond the scope of this work.

Newton, Green, & Fernández, 2010; Newton, Green, Fernández, Day, & White, 2006). Such imbalances can partially be attributed to ineffectual drug regulation and inadequate or limited technical capacity that is common in resource-poor countries (Chaccour, Kaur, & Del Pozo, 2015; Kaur et al., 2016; Mackey & Liang, 2011).

Poor quality medicine can lead to treatment failure, serious health conditions, drug misuse and resistance to molecules (Bassat, Tanner, Guerin, Stricker, & Hamed, 2016; Dégardin et al., 2014; Johnston & Holt, 2014). Further, there may be good quality medicines present in the informal sector. Such products may have leaked from the official circuit or maybe not yet authorized by the national regulatory authority. In any case, these medicines are stored and sold under poor conditions which are aggravated by high tropical temperature leading to degradation (Gaudiano et al., 2007).

Medicines enter the informal market through a variety of channels such as cross-border trafficking and import of unregistered products by registered wholesalers (Baxerres & Le Hesran, 2011; McCabe et al., 2011). Expired products and products stolen from the official circuit can also enter the informal market due to corruption and complicity of government officials (Dégardin et al., 2014; Erhun Babalola & Erhun, 2001; Kaur et al., 2016; Mukhopadhyay, 2007).

However, the existence of informal market also suggests that there is an unmet pharmaceutical need that the formal sector is unable to fulfill. There are various reasons that explain the existence of such markets. First, for many patients, informal sector is the only means to get access to treatment and is financially more attractive (Derriennic & Mensah, 2003; Gaudiano et al., 2007). Drugs are either cheap or may be perceived as such due to the possibility of buying per unit. Second, informal vendors are easily accessible, provide quicker services, and have flexible working hours (Goodman et al., 2007). Third, there is no need of prescription to buy any medicine in the informal sector which on the one hand saves fees for consultation and transport and on the other saves time (Baxerres & Le Hesran, 2006). It is crucial, as most people live with less than a dollar per day and time spent in going to see a doctor is foregone income. Fourth, it offers a wide variety of choices including generic and branded products. Sometimes medicines that have a rupture in the formal sector can be found in the informal sector (Baxerres & Le Hesran, 2011; Goodman et al., 2007). Last but not the least, ignorance regarding the

harms of poor quality medicines also leads patients to buy medicines in the informal sector (Erhun Babalola & Erhun, 2001; Newton et al., 2010).

3.3.7.1. Informal Sector in Mali

During the interviews conducted in Mali, every participant without exception was aware of the presence of the informal market. The exact value of the informal trade is difficult to find due to lack of market quantification studies, but according to a recent estimate, the informal market may account for nearly 15% of the pharmaceutical trade in Mali (SIAPS, 2014). In the interviews, the LNS reported that it has found expired, degraded, falsified, and sub-standard products and also those lacking market authorizations.

In their study, McCabe et al. (2011) suspected that some wholesalers in Mali might be involved in supplying to the informal sector. Indeed, one Malian distributor in our interview reported of importing unregistered branded-generic version of an antimalarial medicine (Artemether + Lumefantrine) from an Indian manufacturer. Further, officials also stated that donations that do not follow the official circuit are yet another source of unaccounted medicines whose quality is not guaranteed. Such medicines can be given by faith-based organizations or governments through bilateral aid. These medicines are channeled through the community health centers (CSCOMs) or distributed directly to the population. They may not possess the market authorization and might not be on the national essential medicines list.

Cross-border trafficking remains one of the primary source of poor quality medicines in Mali, but the customs personnel is inadequately trained to differentiate between authorized and illegal drugs. Customs officers only look for basic papers for import and market authorization and if the importer is qualified by the government. However, they do know not much about medicines. Wholesalers can have papers for one drug but along with it they can bring other drugs without authorization and inspector has no clue. Additionally, Mali lacks a computer-based information system to manage the registry of pharmaceutical products *(source: interview LNS, DPM)*. This has far-reaching consequences because granting of import visas involves checking the validity of market authorization for each medicinal product and the same needs to be verified by the customs at the point of entry but it cannot be carried out efficiently without an up-to-date listing.

Also, Mali has no regulations defining the different causes of non-quality like falsified and substandard and for penalizing intentional importation and sale of poor quality medicines. The legislative arsenal is limited to few activities such as import and sale of counterfeit products with specific connotations to intellectual property violations, import and sale of prohibited substances and the illegal practice of pharmacy (Law N° 01-075 of 18 July, 2001 on customs code; Law N° 01-079 of 20 August, 2001 on the penal code). So, the law fails to discourage the actors in the informal market. Indeed, during the fieldwork, we had informal interactions with four pharmaceutical vendors in the market of Dabanani, Bamako. When asked about the possibility of a raid by authorities, one vendor replied that *"police rarely come here"*. One government official explains this as,

"Everyone knows everyone in Mali and when everyone knows everyone then it is difficult to enforce the law".

Further, the functioning of the informal market is also aided by the lack of political will, corruption, and complicity of government officials at different levels in the pharmaceutical supply chain. This is particularly evident from the following statement of a government official,

"Medicines from illegal routes, if found, are destroyed. However, sometimes medicines that were supposed to be destroyed can be found in the parallel market!"

This was further reflected in conversation with a custom official who remarked,

"fermer les yeux et serrer les mains (close your eyes and shake hands) is the normal practice".

Another factor that prohibits the containment of informal market is its cognitive and normative features in the sense that it is taken for granted and is accepted or rather supported by members of the society.

Once a medicine has entered the country through the informal route, it can find a way to contaminate the formal sector as well. This can happen in several ways. First, wholesalers who import medicines illegally sell their products to pharmacies in the official sector. Second, we were also informed by officials that some pharmacies, depots and community health centers frequently buy medicines from street vendors at a cheaper rate and then sell them to their patients through the official channel *(source: multiple interviews)*. This contamination of formal sector is a matter of immense concern. It spoils the effort made to sensitize the population regarding the harms of buying medicines in the unofficial network. Even an

informed patient who is willing to buy medicine from authorized sellers will not know that the quality of product might be compromised.

3.3.8. Summarizing Market Segmentation

The discussion so far has made it clear that the regulatory framework and the organization of the four market segments are different. They **vary regarding source of financing, procurement agency, criteria of quality, size, and distribution channel (Table 3.3).**

In the government-funded sector, the Central Medical Store of Mali (Pharmacie Populaire du Mali or PPM) finances and procures medicines for the government. PPM primarily procures non-proprietary generic medicines listed on the national essential medicines list of Mali. The only criteria of quality for importation is that the medicines must have a market authorization. Once in the country, PPM facilitates the distribution of these medicines through its own channel.

Another part of pharmaceutical imports in the public sector is taken care of by international organizations who mainly supply medicines to national programs against diseases such as HIV/AIDS, TB, and malaria. Major international donors only procure those medicines that are on the national treatment guidelines of the country and have a market authorization. In addition, medicines must be either prequalified by the WHO or a stringent regulatory authority to be eligible for procurement. The procurement in this segment is done either by the donor itself or a third-party representing the donor. They primarily purchase non-proprietary and branded generics, but they can also procure originator products in certain situations where there are no alternatives. Once in the country, the medicines are distributed by employing the services of the CMS.

On the other hand, in the private sector, only the authorized wholesalers have the right to import pharmaceutical products. They are permitted to import most medicines that have a market authorization. For example, there is no private market for antiretroviral drugs, which is mainly supplied by donors and government for free of charge. Also, opioids can only be imported by the PPM. Private importers and wholesalers mainly deal in specialty products that include originator products and branded generics. The medicines are distributed through wholesalers' own channel. Another part of the private sector is the informal market that dwells on illegal

trafficking and spillage from the public sector. These market segments can also differ vis-à-vis their size. For example, In Mali private sector is estimated to account for nearly 80% of the market in terms of value (McCabe et al., 2011). The informal sector is accounted for 15% of the total market (SIAPS, 2014).

Table 3.3: Comparison of regulatory framework and organization of public and private market segments

	Public Market		**Private Market**	
Characteristic	Government Funded	Donor Funded	Formal	Informal
Financing for Procurement	Government through the CMS	Bilateral & multilateral donors	Government authorized importers	Illegal
Procuring Agency	CMS	Donors or their representative which is usually a third party	Government authorized importers	Cross-border trafficking & spillage from public sector
Type of Medicines	Medicines on NEML; mainly generics	Generics; branded generics and to a lesser extent, innovator products for diseases specific national programs	Mainly specialty: branded generics and originator products	All
Quality Regulation	Products with MA	MA + WHO prequalification or SRA approval	Products with MA	Unregulated
Market-Size (Ex. Mali)	20%	Data Unavailable	80%	15%
Distribution Channel	CMS	CMS	Wholesaler's network	Informal street market; penetration into formal distribution circuit

CMS = Central Medicines Store; MA = Market Authorization; NEML = National Essential Medicines List
"" = Informal market is unquantified*

3.4. Market Entry and Operation Strategies of Indian Pharmaceutical Firms

3.4.1. Characteristics of Indian Firms Present in Mali

Analysis of the market authorization data (version: December 2014) reveals that there were 3,216 pharmaceutical products registered in Mali at the end of 2014 supplied by 265 firms (Table 3.4). Of these, 2,802 were either originator brands or branded generics, and remaining 414 were non-proprietary products. 50% (1621) of products belonged to 139 companies from Europe and North America. We identified 889 branded and 162 non-proprietary generics from 66 Indian manufacturers accounting for 33% (1056) of the total registration. 30 Firms from Asia and another 22 firms from the Middle East and North Africa (MENA) accounted for 8% each of the total registration (Figure 3.6). 36 remaining products belonged to 8 other firms from South America and Africa.

Table 3.4: Type of pharmaceutical products registered in Mali grouped by firm origin

Region	Number of Firms	Branded Generics or Originator	Non-Proprietary Generics	Total Products	Percentage of Total
Asia	30	152	86	238	7
Europe & North America	139	1459	162	1621	50
India	66	889	162	1051	33
MENA	22	266	4	270	8
South America & Africa	8	36	-	36	1
Total in Database	265	2802	414	3216	100

Source: Analysis of market authorization data (version December 2014)

The 66 identified Indian pharmaceutical companies have different firm characteristics in terms of size and global presence. Table 3.5 presents a list of selected Indian firms with active product registration in Mali.

Products from eight of the top-20 Indian firms (Cipla Ltd, Sun Pharma, Aurobindo Pharma, Hetero Labs, Serum Institute India, Macleods Pharma, Alkem Laboratories Ltd. And Ipca Laboratories) are present in Mali. Further, ANDA certifications are a good indicator of a firm's

presence in the developed country market such the US. We identified at least twelve Indian firms having one or more ANDAs to their name to be present in Mali. We also found twelve firms who have two or more of their products prequalified by the WHO (Table 3.5).

In fact, ten Indian firms who have an ANDA also have a WHO prequalification. Only two firms (Serum Institute of India and Shantha Biotechnics Ltd.) who have a WHO prequalification but for which we could not trace an ANDA are the manufacturers of vaccines. Given that WHO prequalification has become the minimum criteria of quality acceptance by international organizations, we can argue that firms who are active in donor-funded markets of developing countries are also actively pursuing developed countries. It also points out that the general idea that the overall regulatory environment of the African pharmaceutical market is weak is not valid (Chaudhuri et al., 2010; Yeoh, 2011). The barrier to entry within the donor-funded market is high and only a few firms that have developed capabilities to meet the stringent regulatory and quality norms can enter this segment.

On the other hand, Chaudhuri et al. (2010) rightly note that most Indian companies cannot afford the costly and time-consuming requirements of the US market. Similar logic can be extended to the donor-funded segment which necessitates the WHO prequalification. Most Indian firms either do not have resources or technical capabilities or both to meet the requirements for WHO prequalification.

On the other hand, government-funded public and formal private sectors have a more comprehensive disease coverage and a much lower entry-barrier due to simple market authorization requirements. Moreover, in case of Mali, a test of bio-equivalence is not mandatory for granting market authorization to generic products, making the entry of Indian manufacturers even easier. To put this into perspective, there are only 53 Indian formulation companies with US FDA approval compared to 66 in Mali which has a much smaller market in terms of value (Pharmexcil, 2017). Indeed, 52 of the 66 Indian firms active in Mali do not have either WHO prequalification or ANDA certification. Nevertheless, some of these firms have a strong presence in Mali, which is evident from the number of product registration. Caplin Point (79), S Kant (45), Solitaire Trade Link Pvt. Ltd. (43), and Troikaa Pharmaceuticals Ltd. (42) are among the top-10 Indian firms in Mali.

Table 3.5: Characteristics of selected Indian firms with active products in Mali

Firm Name	Products in Mali	Revenue FY15 (INR Billion)§	India Ranking	ANDA Certification	WHO Prequalification
Ipca Laboratories	85	31.2	20	Yes	Yes
Caplin Point	79	2.4	99	-	-
Ajanta Pharma Ltd.	77	13.9	36	Yes	Yes
Strides Shashun	77	5.1	58	Yes	Yes
S Kant	45	-	-	-	-
Solitaire Trade Link Pvt. Ltd	43	-	-	-	-
Cipla Ltd.	42	102.8	1	Yes	Yes
Fourrts Laboratories Pvt. Ltd.	42	3.3	80	-	-
Troikaa Pharmaceuticals Ltd.	42	-	-	-	-
Sun Pharma	39	82.4	5	Yes	Yes
Ronak Exim Pvt Ltd.	34	-	-	-	-
Alkem Laboratories Ltd.	32	33.2	17	Yes	Yes
Hetero Labs	27	45.5	11	Yes	Yes
BDA Pharma Pvt. Ltd.	21	-	-	-	-
Syncom Formulations	19	1.8	114	-	-
Sixer Trading Pvt. Ltd.	19	-	-	-	-
Macleods Pharma	15	35.6	15	Yes	Yes
Aurobindo Pharma	13	81.6	6	Yes	Yes
Biocon	9	23.9	24	Yes	-
Micro Labs	8	24.3	22	Yes	Yes
Serum Institute India	7	39.4	13	-	Yes*
Indoco Remedies Ltd.	7	8.6	50	Yes	-
Bliss GVS Pharma	7	3.3	78	-	-
Sirmaxo Chemicals Pvt.	5	-	-	-	-
TFC Pharma	5	-	-	-	-
Tablets India Ltd.	3	2.5	95	-	-
Shantha Biotechnics Ltd.*	2	-	-	-	Yes*
Indus Pharmaceuticals	2	-	-	-	-
Saga Labs	2	-	-	-	-
Bharat Serums	1	5	60	-	-
Flamingo Pharmaceuticals	1	2.7	91	-	-
Ciel Pharma Pvt. Ltd.	1	-	-	-	-
Pure Pharma Ltd.	1	-	-	-	-
Swiss Parenterals Pvt Ltd	1	-	-	-	-

§Data based on Dun & Bradstreet report on India's leading pharmaceutical companies (2016)
**Prequalified for vaccines only*

3.4.2. Export as Entry Mode in Mali and Other Francophone West African Countries

Indian firms rely exclusively on export to enter the Malian market. In fact, we found this to be true not only for Mali but other countries in francophone West Africa as well. These countries include all members of the West African Economic and Monetary Union (WAEMU): Benin, Burkina Faso, Ivory Coast, Guinea-Bissau[59], Mali, Niger, Senegal, and Togo. The value of pharmaceutical exports from India to WAEMU countries grew over eight folds from an estimated USD 20 million in 2001 to over USD 174 million in 2011 (Figure 3.6). Since then revenues gained from this market has decreased and become relatively stable at around USD 152 million since 2014. However, this trend can be explained by the decrease in demand from Benin. It is worth noting that Indian firms have steadily become the one of the biggest suppliers of pharmaceutical products to these countries second only to France. Indeed, the data reflects that Indian firms have registered a significant growth by taking up space previously dominated by European, especially, French firms due to old colonial ties. Market share of Indian firms has expanded from 3% in 2001 to 12% in 2016 reflecting they have substantially penetrated Francophone West African Countries by pushing existing players (Figure 3.7).

Use of export as an active entry strategy by Indian firms is not surprising. Indeed they have relied on export to enter both developing counties as well regulated markets of Europe and the US (Dixit & Yadav, 2015; Pradhan, 2006). In fact, in 2016, India had 700 manufacturing plants for bulk drugs and formulations approved by the US FDA and another 666 plants compliant with the EU GMP. Additionally, 1400 companies have WHO GMP certifications (Pharmexcil, 2017). These certifications are primarily targeted towards exports rather than the domestic market in India where firms are only required to comply with the Indian GMP (Schedule M). Concerning Sub-Saharan Africa, market entry through export is further facilitated by the prevailing free trade regime as most countries do not impose tariffs on imports of finished formulations (Chaudhuri, 2015a).

Exporting allows Indian firms to take advantage of their low-cost domestic production (Mahajan et al., 2015). Also, it is a low-risk entry mode and does not necessitate a firm to undertake direct investment in host countries which is costlier, and firms risk losing the capital if the foreign market engagement fails (Laufs & Schwens, 2014b; Pan & Tse, 2000). In the

[59] Guinea-Bissau is a Portuguese speaking country but it was included as it is a member of the WAEMU.

case of exports, the biggest risk involved is losing the money for a consignment if dealing in credit with the foreign partner. However, if such a situation arises, Indian firms can stop supplying to that partner in future. Also, many firms choose to work only on advance payments mitigating the risks even further.

While this study only focused on the francophone countries in West Africa where Indian firms are relying solely on exports to enter the pharmaceutical market, the situation is comparatively different in few commonwealth African countries and calls for our attention. Some Indian firms are supplementing exports with local manufacturing in countries like Nigeria, Ethiopia, Uganda and South Africa using a variety of mechanisms such as joint-venture, acquisition and greenfield investment. The large market-size can partially explain the attractiveness of these countries for investing in local production. In 2016, Indian firms exported pharmaceutical products worth $418 million to South Africa, second only to the US and the UK. In the same year, exports to Nigeria, Kenya, Uganda, Ghana, Ethiopia, and Mozambique were $355 million, $319 million, $154 million, $145 million, $133 million and $124 million respectively *(source: trademap)*. This data on exports indicates that each of these countries offers larger market-size for carrying out profitable manufacturing operations compared to the combined market of WAEMU countries. Also, it is interesting to note that firms are starting in local production in Sub-Saharan countries not only as a preceding step before entering highly regulated markets. It seems like their expansion in Africa is a part of the strategy to capture a fast-growing market in an attempt to become truly global players. This is explicit from the evidence that many new ventures in Africa started after these firms had successfully penetrated the US and European market.

Figure 3.6: India's Export of Pharmaceutical Products to WAEMU[60]

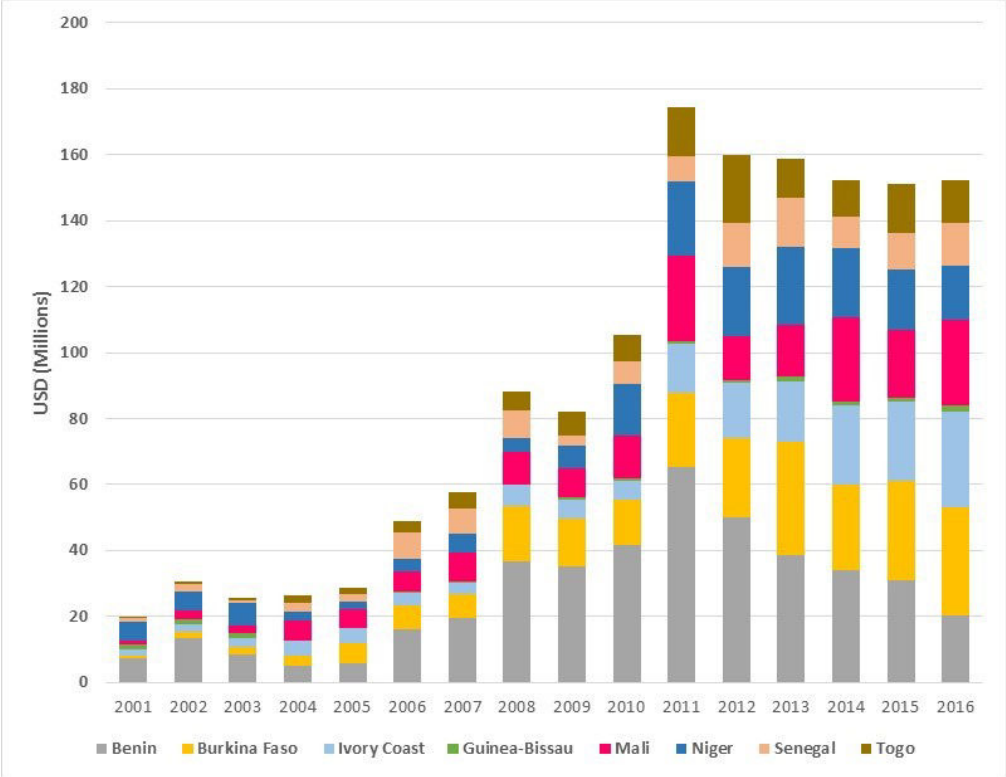
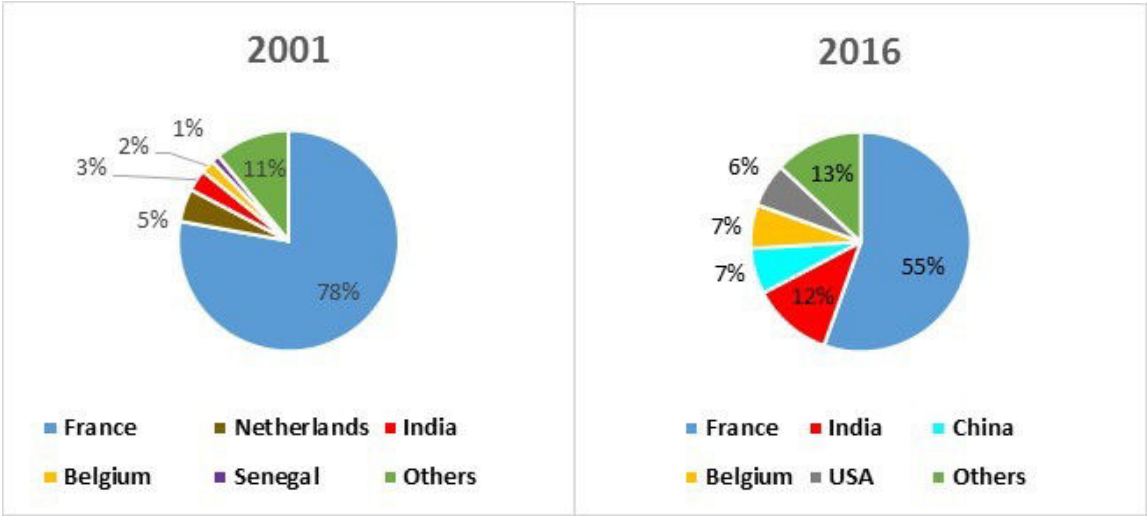


Figure 3.7: Top Supplier of Pharmaceutical Products to WAEMU countries



Note: Total value of import in by WAEMU in 2001 = USD 271 million; 2016 = USD 1128 million

[60] Analysis based on international pharmaceutical trade data retrieved from http://www.trademap.org.

Erstwhile Ranbaxy (Now Sun Pharma) was the first Indian firm to enter local manufacturing in Sub-Saharan Africa through a minority joint-venture (10%) in 1977 in Nigeria (Pradhan & Alakshendra, 2006). In 2007, Ranbaxy expanded its African operations by acquiring BE-Tabs in South Africa (Kale, 2010a; Yeoh, 2011). Similarly, Cipla formed Quality Chemicals Industries Ltd (QCIL) as a joint-venture with Ugandan firm Quality Chemicals Ltd in 2005. The idea was to locally manufacture antiretroviral and antimalarial drugs under the license from Cipla. Seven years later, in 2013, Cipla acquired a majority stake in the QCIL. In the same year, Cipla also completed the acquisition of Cipla Medpro in South Africa. Cipla Medpro was the distribution partner for Cipla and the third largest company in South Africa (VCCircle, 2013). It manufactures a wide range of chronic care medicines and over the counter products. It also provides contract manufacturing services to local and multinational companies.

In 2008, Lupin, another top Indian player, entered a majority joint-venture (60%) with South African firm, Pharma Dynamics (PD). In 2015, it acquired the remaining 40% shares to make Pharma Dynamics a fully-owned subsidiary (Lupin, 2015). Taking a different path, Cadila Pharmaceuticals started a greenfield manufacturing plant in Ethiopia in 2007 (Cadila Pharmaceuticals, 2017).

All four companies – Sun Pharma, Cipla, Lupin, and Cadila – show some common trends. They are relatively large Indian pharmaceutical companies with sufficient financial, technological and human resource capabilities. They are leading players in the domestic market, and at the same time, their export and manufacturing operations span multiple countries across the globe. More importantly, their entry into the African market was not a one-time event but rather the outcome of tactical decision making that happened in different phases. All four firms were already established players in the American and European markets where they had undertaken multiple acquisitions by the time they expanded their production activities in Africa. These findings provide credence to the argument that not all firms are using Africa as the first step in internationalization. It is true that most Indian firms are small and medium-sized enterprises who do not have access to resources for undertaking local production. These firms will rely only on exports. However, for large Indian firms, African market is not just a step to gain experience, but rather their investments are targeted towards becoming genuinely global players.

3.4.3. Entry Strategies are Specific to Market Segments

3.4.3.1. Entry to the Formal Private Market

While Indian firms use export as a mode of entry to the West African Francophone Countries, the organization of export and firm strategy varies from one market segment to another. Further, even within the same market segment firms can use different strategies.

To approach the formal private market the most common strategy is to enter into a contractual alliance with a local wholesaler/distributor and a product promotion agency. These alliances are designed to exploit the specific assets of each partner (Peng, 2001; Petersen et al., 2008). The primary advantage of Indian firms is their low-cost production abilities, but they lack market information, distribution channel and human resources for product promotion in host countries. Local operators, on the other hand, are well aware of the specificities of their home country market. They possess assets in the form of local marketing and distribution networks, market intelligence and can easily access local labor market. Further, they are familiar with regulatory frameworks, have connections in government offices and know the right approach to get things done. Thus, alliances also allow firms to deal with the complexities of local political and regulatory environments and facilitates firm performance (Peng, 2001). According to one Indian manager, when it comes to developing country markets, liaising and relationships matter and the expertise of the local distributor acts to fill the knowledge void about the functioning of the local market. Partnership with local wholesalers is a must for launching products in the formal private market, but the same partner can be used to fill tenders in the government-funded public sector as well.

The Internet has made it easy for firms willing to enter an African country to identify a list of potential distributors through trade directories. The first contact is usually made through emails and phones to discuss the products and prices. Once quotation and rates are fixed then company representatives visit the country to meet the partner (in some cases even that is not required). Alternatively, company representatives can visit the country as the first step and meet the potential distributors personally. Managers identify the financial stability and reach of distributors in terms of relationships and geographical coverage as primary criteria for entering a contractual relationship. Once the partner is selected, then the company can go for product registration which can take up to 18 months depending on the target country.

3.4.3.1.1. Entering Through Subsidiaries of French Firms

As discussed earlier, the formal private market in Francophone countries in Africa is largely controlled by wholesalers who are subsidiaries of French companies. Firms like Eurapharma (Laborex in Mali) and Ubipharm have substantial bargaining power due to their sheer size and scope of operations in all francophone countries and French overseas territories. They also create a substantial barrier to entry for firms given that francophone countries in Africa are characterized by the presence of only a few wholesalers (Baxerres, 2012; OECD, 2014; Yadav, 2015). This is in sharp contrast to most Anglophone countries where there are hundreds of wholesalers and firms have multiple possibilities of partnerships. For example, there are about 700 registered wholesalers in Kenya (Africa Business Pages, 2017). The corresponding numbers are over 640 in Ghana and over 500 in Nigeria (Baxerres, 2012; Mahamé & Baxerres, 2015).

So**, if a firm wants to approach the Francophone African market comprehensively and aggressively, then it needs to use wholesalers who are French subsidiaries as a means of entry**. Thus, this model is particularly suited to large Indian players who want to cover a broader geographical area. In fact, major Indian firms like Cipla, Ajanta, Ipca, and Alkem work with the Ubipharm group to access the private market in Mali and other Francophone countries. This strategic alliance can be regarded as a mean to overcome the barrier to entry (Dunning, 1995). Further, by partnering with French subsidiaries, Indian firms do not have to deal with the logistics of transporting to multiple countries. Supply chain and delivery to specific countries are managed by the partner. We must note that companies like Ajanta, do not supply their products directly to Mali but rather products are procured by Planetpharma (part of the Ubipharm group) which diverts it to Ubipharm-Mali or other countries based on the demand. So, Firms also do not need to enter into numerous contractual agreements with wholesalers in each country. Moreover, these distributors are reliable regarding payment, and the supply of products is continuous.

On the downside, the business is always dominated by the French partner who has the upper hand in negotiation. There is also a delay of approximately 240 days between the first delivery of the product (document assigned after delivery in the country) and payment to the manufacturer. Furthermore, French subsidiaries often work with the clause that if anything is not sold in the country and if products reach expiration then firms have to replace them for free

of cost. If the product is in a competitive disease class, then it is difficult to deal with this model because there are many firms present in the market and margins are low. Also, if the corporate strategy of a firm is different, i.e., it wants to work with advance payments or through a letter of credit then this model is not suitable. Additionally, the presence of multiple layers of intermediaries increases the transaction cost. Direct trade between a firm in India and a distributor in Francophone country can reduce the expenses and increase the profit by cutting the middle layer. Lastly, this model is not suitable for most Indian firms which are small and medium-sized enterprises and do not have sufficiently large product portfolio and resources to operate in multiple countries simultaneously. Also, because French subsidiaries do not pay in advance, cash crunch smaller firms cannot sustain in this model.

3.4.3.1.2. Direct-to-Distributor Model

The second option to enter the formal private market is to enter into alliance with wholesalers other than French subsidiaries (wholesalers from group 1 and 3 described before). In fact, supplying directly to distributors is the preferred mode of Indian firms in Anglophone African countries which are marked with numerous importers/distributors (Baxerres, 2012; Mahamé & Baxerres, 2015). This model of penetrating the market is steadily growing in West African Francophone countries as well. This is particularly true for Mali where the number of wholesalers (66 in 2016) is several times higher than the average number in other countries in the Francophone West Africa (Senegal - 6 in 2014; Burkina Faso - 8 & Benin - 5 in 2012) (Mahamé & Baxerres, 2015; OECD, 2014; World Bank, 2012).

In this mode, the manufacturer supplies its products directly to wholesalers in the host country under some specified terms. It is the main option of choice for small and medium-sized firms. These wholesalers are usually much smaller in terms of size compared to the France based wholesalers as they are mainly active in their home country. Further, even within the home country, these wholesalers have a smaller number of pharmacies in their distribution network, but most of them are located in the country capital where the demand is high. However, working with small wholesalers offers greater flexibility to manufacturers in negotiating the terms of payment and business arrangements. For example, a firm can choose to work with advance payments, letter of credit or a combination of the two to avoid the risk of default by wholesalers. Payment conditions also depend on the relationship with the wholesaler.

The arrangement of business with distributors can take multiple forms. The most common form is for the manufacturer to enter into an exclusive agreement with the wholesaler. The firm only supplies its products to the agreed partner in the given country and in most cases also takes the responsibility of product promotion. For example, Pharma Plus, a pure Malian wholesaler (Group 1) has an agreement with *Caplin Point* which was ranked 99 in India in 2006 (Dun & Bradstreet, 2016). The company is among the leading players in Mali and has market authorization for 79 products, second only to Ipca.

Further, a new type of distributor model can be observed in Mali[61] where **Indian and Chinese people in business have started their import and wholesale enterprises by partnering with local pharmacists (group 3 wholesalers)**. They are taking advantage of the recent growth in the demand for generic drugs. They source their product mainly from their home countries using either exclusive licenses with firms or using contract manufacturing to create their brand in Mali. *Sopropha* and *K-Pharma* are two Indian wholesalers who procure various products directly from Indian manufacturers and also have their own products registered. S.Kant, Fourrts Laboratories (Fourrts) and Indus Pharmaceuticals (Indus) have exclusive agreements with Sopropha. Both S.Kant and Fourrts are among the top-10 firms in Mali in terms of product registration, each having a portfolio of over 40 products.

K-Pharma is a part of a trading company called Tarachand & Sons (TCS) which is run by an Indian businessman. The company is headquartered in Dubai and has several branches located in Mali, Niger, Burkina Faso and Guinea and the Republic of the Congo. It deals in trading a wide range of products including foodstuffs, textile, automobile, electronics, pharmaceuticals, furniture, plywood, and utensils among others. K-Pharma is the Malian subsidiary dealing in the importation and distribution of pharmaceutical and veterinary products. It has exclusive licenses with Indian companies like Syncom Formulations Ltd (Syncom) and Ahlcon Parenterals India Ltd (Ahlcon). The two companies have respectively 19 and two products registered in Mali.

[61] Study could not confirm if these forms are also rising in other WAFCs.

3.4.3.1.3. Contract manufacturing

A third option for Indian firms to enter the private market is to undertake contract manufacturing for distributors. Few wholesalers like Ubipharm, Pharma Plus, Pharma Globe and Sopropha use Indian firms to get products manufactured and then register them with a new name in Mali. For example, Ubipharm uses contract manufacturing to get products manufactured through its subsidiary Ubithera under the brand Ubigen and which are then sold through Ubipharm's network in multiple francophone countries.

This mode is advantageous for both the firms and wholesalers. Firms benefit from not investing in product promotion and marketing activities. Wholesalers, on the other hand, get market exclusivity over the product by owning the trademark and registration. This arrangement forbids both the manufacturer and other wholesalers from entering the market by bypassing the original wholesaler once the product becomes popular in the market. Interviews suggest that few firms are using both exclusive distributor and contract manufacturing modes together and with the same manufacturer.

3.4.3.2. Market Entry Specificities of the Public Market Segments

To enter the government-funded market segment, **any firm is obliged to supply its product to the country-specific Central Medical Stores (CMS).** The CMS issues call for tenders based on national requirements mainly for non-proprietary generics listed on the NEML. In Mali, this role is played by the Pharmacie Populaire du Mali (PPM). Indian firms use different options to participate in biddings. They can answer the call directly or use a local representative who can be the distributor or the liaising agent. The tenders are internationally open which make them highly competitive, and price becomes a determining factor for the award of the contract. However, the segment is characterized by high volume orders which compensate for lower margins. Further, CMSs' are the single largest buyers of certain kind of medicines such as antimalarials, intravenous fluids, and hospital care products.

In fact, some companies are only interested in government tenders for various reasons. First, government tender based market needs less effort in terms of promotion and marketing compared to the private segment. So, if the size of the private market is small, then there is no reason for a firm to concentrate on it. It would instead look at the public market where

promotion is simple. A firm can send its representatives to the country once or twice a year to meet the national tendering and pharmaceutical regulatory authorities. This is the easiest way to build relationships and get relevant information needed to apply for tenders. Also, because there are no intermediaries, companies can offer competitive rates in the tender. According to the manager of an Indian pharmaceutical firm, if this strategy can get one tender worth $2-3 million with 25-30% margin then it is sufficient. Second, product registration is a costly and time-consuming process. However, if a company is awarded the tender, then it is given a timeframe to get the registration done. So, the company does not need to invest before it is sure about the award of the contract. Third, if the firm is supplying only a small range of products like those needed in hospital care, then the government market is a natural choice.

Another dimension of the public sector, i.e., the donor-funded market has substantially high entry barrier as most donors have strict criteria of product quality to ensure safety and efficacy. Thus, only manufacturers whose products are either prequalified by the WHO and/or have been approved for use by a stringent regulatory authority such as the US FDA are eligible for supplying to the donor-funded segment. In this respect, the donor-funded segment resembles developed country markets due to stringent regulatory requirements of product authorization. However, once a firm manages to pass the barrier of product authorization, it faces low competition due to the presence of a smaller number of firms. As of July 2017, 16 Indian pharmaceutical firms had a combined portfolio of 322 WHO prequalified pharmaceutical products (excluding vaccines, diagnostics, and active pharmaceutical ingredients) across seven disease classes (Table 3.6). Ten of these 16 manufacturers – Alkem, Aurobindo, Cipla, Ipca, Macleods, Micro Labs, Strides, and Ranbaxy (Now, Sun Pharma) – were present in Mali at the end of 2014 (Tables 3.5 and 3.6).

The **donor-funded market is also tender based** and which Indian firms have evolved as prominent players (See chapter 2 for details). The organization of export in this market is also different than those in the formal private market (alliance with a distributor) or government-funded market (supplying to the CMS). **Here the tendering authority is either the donors themselves or a third party appointed by the donor**. Further, tenders are not organized at country levels. Purchasing agencies pool the demand from individual countries into large-volume orders which are procured centrally at international level. Thus, to access this segment firms do not need to target each country separately. Indeed, the country level operations concerning donor-funded market are limited mainly to product registration. In fact, Strides won

the tender administered by the PSI, the principal recipient of the Global Fund malaria grant in Mali, to supply antimalarial medicine to the national malaria control program. The tender was not based in Mali but rather managed from the PSI headquarters in Washington DC. Firms apply to these tenders directly from their headquarters in India and continuously work in association with international donors like the Global Fund and PEPFAR to negotiate and optimize the terms of procurement (GFATM, 2014b, 2016a).

3.4.4. Support of Business Operations

Indian firms not only export their products to Mali but also use a variety of strategies to support their operations, this is particularly true for firms who actively want to pursue the market. So, **even if all firms use a low-risk entry mode like export, there exists a considerable difference among them when it comes to the market commitment in a given host country**. We can arguably say that the higher the in-country support operations, the more the market commitment. Such commitments are reflected in the number of products registered by a firm and the involvement in business support strategies. Ipca, Caplin Point, Ajanta, and Stride have nearly 80 products registered in Mali (Table 3.5). Such product portfolios need active field support for the better realization of return on investment.

In fact, market support strategies are mainly targeted to tackle administrative hurdles like product registration, establishing and maintaining relationships with wholesalers and product promotion activities. For obtaining market authorization or product registration, a firm can submit the dossier by itself, or it has to search a local representative who can either be a local wholesaler or partner. Ranbaxy, for example, had its representative in Mali who is different from the wholesaler and looks after administrative issues such as product registration. To establish contact with wholesalers and to find new business opportunities firms regularly send their representatives in the field. Some Indian companies prefer to put an expat country manager who looks after the firm's business operations in one or more neighboring countries and acts as the link between the foreign market and the company headquarters. The country manager looks for new business opportunities, maintains relationships with government officials and wholesalers, and coordinates with promotion activities.

Finally, product promotion is a significant component of foreign operation strategies especially for the business in the private market and firms can use different models. They can create a

subsidiary, use a specialized agency or use distributor's network. Interviews conducted during fieldworks reveal that most big firms active in Mali have contractual agreements with specialized agencies that look after the promotion and communication of their pharmaceutical products. The medical representatives are on the payroll of the promotion agency which works for a specific fee or a commission on sales or both. Promopharma is one such Malian promotion agency which is responsible for promotional activities for Indian firms like Ajanta and Caplin Point. Finally, firms can also rely on wholesalers for the promotion of their products. For example, Sopropha engages local medical representatives for promoting products. In case of contract manufacturing, it is usually the responsibility of the wholesaler to do the marketing and promotion.

3.4.5. Case of Ajanta Pharma in Ivory Coast

Ajanta Pharma Limited (Ajanta) is an Indian multinational pharmaceutical firm with headquarters in Mumbai and business operations in India, USA and 30 emerging countries across Asia, Africa, Middle East and CIS. Ajanta was started in 1973 as a re-packing company for generic products and established its first manufacturing facility in 1979 at Chikalthana, (Maharashtra) India (Ajanta Pharma, 2017b). Currently, the company owns six manufacturing units – 5 in India and one in Mauritius. Additionally, it has one active pharmaceutical ingredient plant in India, mainly for captive consumption. It has six subsidiaries (USA, Nigeria, Philippines, Mauritius, and the UK) including one step-down subsidiary in Mauritius (Ajanta Pharma, 2017a).

Ajanta focuses on the branded generic market for a wide range of therapeutic segments like antibiotics, antimalarials, anti-diabetics, cardiology, and orthopedics. In 2009, Ajanta became the first generic company to receive a WHO prequalification for antimalarial medicine making the company eligible to supply to the donor-funded malaria programs (WHO, 2017c). Today, Ajanta has eight prequalified antimalarial products – the largest portfolio compared to any other Indian firm (Cipla - 6, Ipca - 4, Strides - 2, and Mcleods - 1).

It has started sales in the US market since 2013 and has already received 17 final and two tentative ANDAs while additional 15 ANDAs are under review (Ajanta Pharma, 2017a). Nevertheless, the majority of Ajanta's revenue comes from its exports to emerging markets, particularly Africa. Its total revenue and profit in FY 2017 were INR 20.26 and INR 5.07 billion

respectively. Export of formulations accounted for 65% of the total turnover. The majority (54%) of the export was directed to Africa followed by Asia (32%) and USA (14%). In fact, Ajanta ranked among the top 10 pharmaceutical firms in Francophone Africa in 2012 (Ajanta Pharma, 2017a). In this section, we will analyze the market entry and operation strategies of Ajanta pharma in WAFCs by focusing on its activities in Ivory Coast. WAFC countries have relatively similar structure and organization of the pharmaceutical market. All countries have a national central medical store which is responsible for importing and distributing medicines for the government (Govindaraj & Herbst, 2010; Mahamé & Baxerres, 2015; Yadav, 2015). They also have a structured formal private market and an active presence of international donor organizations such as the Global Fund *(source: The Global Fund website)*.

In Ivory Coast, Ajanta operates in the formal private sector through an alliance with Ubipharm and Planet Pharma group. Ubipharm is the partner of choice for Ajanta to enter the private market in 14 Francophone countries. This is in contrast to Ajanta's operation in Anglophone Africa where consignments need to be sent separately to each country *(source: interview)*. Choosing Ubipharm as the partner allows Ajanta to have a structured logistics and distribution channel in Francophone countries. Terms of payment with Ubipharm are different depending on the situation. For example, for a new product launch, Ubipharm pays Ajanta under the condition of "Dépot payable après vente (DPV)", i.e., payments are made after the sales. However, terms are more negotiable for a successful product already on the market.

To provide support to its business operations, Ajanta has placed an Indian country manager in place. The country manager acts as the coordinating link between the host country and headquarters and plays multiple roles. He is responsible for monitoring the flow of stocks, assessing market evolution and competition, keeping track of disease epidemiology and suggesting products accordingly. He is also responsible for building a relationship with health regulatory authorities and for carrying on product registration. In fact, the presence of a country manager shows firm's commitment and support towards the market which is vital for imbibing confidence and building trust with partners. It also guarantees smooth functioning of business activities and ensures initiatives are taken and necessary measures are implemented promptly.

Moreover, Ajanta has outsourced its product promotion and marketing activities to Nobel Pharma based in Abidjan (Similarly, in Mali it has outsourced its promotion activities to Promo Pharma). The country manager plays an active role there too. One of his primary coordinating

function is to recruit and train medical representative. In fact, this is an example of how firms can extend certain advantages that they have developed owing to the institutional context of the home country to foreign markets (Aulakh, 2007). Indeed, as explained by one of the managers in our interview, French West Africa is similar to India regarding pharmaceutical marketing and promotion activities and Indian firms have years of experience in this domain. In the simplest form, a medical representative goes to meet doctors and explains them about company's products and its benefits so that doctors can prescribe those products.

However, during our interview, we were told that a significant challenge is to find skilled sales personnel. The presence of the country manager allows Ajanta to cope up with the institutional void resulting due to lack of specialized human capital (Khanna & Palepu, 2006). Currently, the sales team in Ivory Coast consists of 54 local medical representatives who are on the payroll of Nobel Pharma, but Ajanta provides all the training and promotional material through the country manager.

In the case of the public market, Ajanta is not participating in government tenders either in Ivory Coast or any other country in Francophone West Africa. Nevertheless, it is interesting to note that Ajanta was participating in the tenders of the Ivorian CMS (Pharmacie de la Santé Publique, PSP) 6/7 years ago, though on a limited scale. However, tenders did not come easily, and margins were minimal. Additionally, payments were untimely and only came after many efforts and follow-up. From Ajanta's point of view, this was much work for a lot less return. Nevertheless, payment conditions have recently improved. So, Ajanta is rethinking to participate in the PSP tenders for high volume products like artemisinin based combination therapies (ACTs) and painkillers.

In the donor-funded segment, Ajanta primarily supplies ACTs to international organizations like the Global Fund, WHO, and the Clinton Foundation. This segment is not under the charge of country manager who is only responsible for the private market. The institutional sector is handled by a separate team at Ajanta based in India which is responsible for applying to calls for tenders and coordinating the logistics with the procuring agency.

From our discussion regarding the organization of business operations of Indian firms in Mali and the case of Ajanta in Ivory Coast we can get a general idea about the entry and operation strategies of Indian firms. While Indian firms use only export as the means of entry, the subtleties of export organization present a more complicated picture. In the private market, they

are using an alliance with distributors to launch their product and are involved in active promotion and marketing activities through specialized intermediaries. In the government-funded segment, they export to the CMS by participating in the call for tenders either directly or through the local partner. Only few WHO prequalified manufacturers are active in the donor-funded market where they export directly to the procurement agencies. **Thus, Indian firms utilize a combination of different export strategies targeted to specific market segments.** These findings support the claim of Petersen & Welch (2002) and Benito et al. (2009) that firms use "mode packages" as a way of more efficiently serving the foreign market. Each export mode in the package is used in a different way but towards the overall objective of penetrating the foreign market which could not have been possible through a single mode.

Further, Petersen & Welch (2002) point out that "mode use is a dynamic process and may be subject to transition through alterations such as mode additions or subtractions through a period of time changing the existence and form of mode packages". Indeed, the case of Ajanta in Ivory Coast provides credence to this argument. The company chose to withdraw from participating in government tenders due to unfavorable institutional condition namely the inability of the PSP to pay in a timely and efficient manner. However, by doing so, it only changed the configuration of its mode package. The company did not withdraw from the pharmaceutical market in Ivory Coast as a whole but rather from a specific market segment. However, as the payment conditions improved and the demand rose, Ajanta is considering to re-enter the market. Thus, the prevailing institutional environment became the guiding factor in determining firm strategy.

3.4.6. Market Segment Specific Product Strategy

We analyzed the product registration data to get a better understanding of firm strategy in the Malian market. In fact, information regarding the types of products and associated regulatory approval can provide valuable insights regarding the strategy of Indian firms in the African market. In particular, it can indicate which market segments a given firm is trying to penetrate.

An Indian firm entering a country in Africa is free to register products which are only approved by the Drug Controller General of India (DCGI) as long as the product satisfies the market authorization guidelines of the host country. However, it may also choose to register products which are not only approved by the DCGI but also by other stringent regulatory authorities

which would allow it to supply to the donor-funded segment. Further, even if a firm has WHO prequalified products it can choose not to register them, indicating its intention to stay out of the donor-funded segment.

Here we must emphasize that market authorization data provides only a snapshot of active products at a particular time. Firm behavior is dynamic and susceptible to institutional factors and therefore, may change over time. Also, product registration data in itself is not evidence that the company has launched the product in the market, but it indeed is an essential condition for a firm to be able to do so. The following subsections will shed light on how Indian firms are targeting specific market segments in Mali. **We have only selected firms with WHO prequalified products because these firms have the strategic advantage to pursue all the market segments (government, donor or private) or choose not to do so**.

Without exception, all Indian firms are actively pursuing the private market which is evident from the numerous branded products registered by them. Tables 3.7 to 3.14 provide a detailed description of products registered by eight Indian pharmaceutical firms in Mali.[62] Anti-infectives such as antibiotics, antifungals, antimalarial and antituberculosis medicines, antiretrovirals seems to be a major focus of Indian firms. In fact, antibiotics are the most targeted therapeutic class. For Example, 11 of the 13 products marketed by Aurobindo are antibiotics (Table 3.7). Similarly, the majority of the medicines offered by Macleods (7 of 15), Cipla (10 of 42), Alkem (24 of 32) and Strides (23 of 77) are antibiotics (Tables 3.9, 3.10, 3.13, and 3.14 respectively). Indian firms also offer medications for an array of chronic conditions like hypertension, asthma, diabetes, cardiovascular diseases and even cancer. They also provide treatment for common conditions like fever, cough, pain, and nutritional and vitamin deficiency among others.

Concerning the donor-funded segment, only 7 of the ten firms have registered one or more WHO prequalified products in Mali. Three firms – Aurobindo, Microlabs, and Alkem – are not at all active in the donor segment. Here we are particularly concerned with the medicines for HIV, TB, and malaria that have been the primary focus of international organizations.

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[62] Detailed analysis is not presented for Ajanta and Ipca. We included these firms in the analysis of antimalarial medicine. This is the only category where they have a WHO prequalification.

In fact, we get a broader picture of the market when we look into the medicines registered for each of these specific diseases. Currently, there are 12 Indian manufacturers (Table 3.6) that have ARVs prequalified by the WHO or the USFDA (This we can know because WHO prequalification information also mentions if a product is approved by the USFDA). Eight of these manufacturers – Alkem, Aurobindo, Cipla, Hetero, Macleods, Microlabs, Strides and Sun Pharma (Ranbaxy) are active in Mali. However, a closer analysis reveals that only 3 of these firms (Cipla, Hetero, and Sun Pharma) have registered monotherapies and fixed-dose ARV formulations in Mali. Hetero seems to be the most aggressive player in the HIV medicines market. It has market authorizations for 27 products of which 18 are ARVs (Table 3.11). 12 of these formulations are approved by the WHO or USFDA or both. However, another five formulations do not have approval from SRA (Table 3.11). On the other hand, Cipla and Sun Pharma each have 7 WHO prequalified ARV formulations and additional three which are not prequalified (Tables 3.10 and 3.12). Here a formulation or dosage form refers to a unique pharmaceutical product with specific active pharmaceutical ingredients, excipients, administrable form (such as a tablet, capsule, syrup, & injection) and strength. So, two pharmaceutical products both consisting of "Ibuprofen" as the active pharmaceutical ingredient but with strengths of 250 mg and 500 mg, respectively are two different formulations. This is important because the same firm may have one dosage form of a molecule(s) prequalified by the WHO but not the others.

Looking at the market for antituberculosis medicines we find that 6 of the 9 Indian manufacturers, who have one or more WHO prequalified products, are present in Mali (Table 3.6). However, only three companies – Cipla, Macleods, and Sun Pharma are actively pursuing the donor-funded segment. Cipla has 4 WHO prequalified medicines for TB registered in Mali (Table 3.10) while Macleods (Table 3.9) and Sun Pharma (Table 3.12) each have one.

This information points out two interesting findings. First, **it confirms the hypothesis that effective competition in the donor-funded segment is not only low, but it can further decrease due to some players not being active in a given country**. In fact, for some molecules, there might not even be any real competition at all. For example, Only Cipla, Lupin, Macleods and Micro Labs have WHO prequalification for different formulations of the TB

medicine "Ethionamide" *(source: WHO prequalification database)*[63]. However, Lupin is not active in Mali, whereas Micro Labs has registered a single TB molecule "Levofloxacin - 750 mg", but the product is not approved by the WHO (Table 3.8). On the Other hand, Macleods has registered a single product (Ofloxacin - 200 mg") which is WHO prequalified. So, for Cipla there is practically no competition for this specific molecule as no other company is supplying a WHO prequalified formulation of "Ethionamide" (Table 3.10). However, there is a possibility that firms only register these products in the country after they have been awarded the tender for supplying in the government or donor-funded segment.

Second, as noted earlier, few ARVs are not prequalified by the WHO or any other SRA. This means that these products are ineligible for purchase by using the Global Fund or PEPFAR grants. Also, there is no private market for HIV medicines in West African Francophone countries. This was confirmed during our interviews with private wholesalers in Mali. Thus **indicating that not-prequalified products may be targeted towards government-funded segment or to those institutional donors who have a more relaxed quality requirement for procurement of pharmaceutical products**.

Lastly, we look at antimalarial medicines by focusing on artemisinin-based combination therapies (ACTs) which are recommended by the WHO for the treatment of malaria. Mali adopted two ACTs, namely "artemether + lumefantrine" (AL) and "artesunate + amodiaquine" (ASAQ) as the first line of treatment against *p. falciparum* malaria in 2007 (WHO, 2011b). All five Indian manufacturers – Ajanta, Cipla, Ipca, Macleods, and Strides – who have one or more type of WHO prequalified ACTs, have registered their products in Mali. Indeed, malaria seems to be high on the agenda of these firms who have a combined portfolio of 31 ACT products in different dosage forms of both AL and ASAQ (Table 3.15). Ajanta, Cipla, and Ipca have registered dosage forms of both AL and ASAQ while Macleods and Strides have registered only AL formulations (Table 3.15). In fact, 14 of Ipca's 85 products in Mali are ACT formulations (Table 3.5 and 3.15). This is not surprising because malaria is the leading cause of morbidity in Mali where 2.3 million clinical cases of malaria were reported in 2013 and accounted for 42% of all outpatient visits (USAID, 2015). So, the demand for ACTs is high.

[63] https://extranet.who.int/prequal/content/prequalified-lists/medicines

All five firms have registered only branded ACTs except for Ipca which has registered both branded and unbranded generics (Table 3.15). Branded generics are non-originator products bearing a trade name given by the manufacturer. On the other hand, unbranded generics are sold under an international non-proprietary name (INN), i.e., the generic name of the ingredient molecule(s) rather than a brand name (Kaplan, 2013). Moreover, while all registered dosage forms of ASAQ are WHO prequalified, the same is not true for AL.

In fact, until July 2015, the WHO had only approved AL in the form of either dispersible or non-dispersible tablets with the strength of "20 mg + 120 mg", available in various pack-sizes. However, we find that Indian firms have not only registered WHO prequalified formulations, but they also hold authorizations for not-prequalified dosage forms such as oral suspensions, injections, suppositories, and novel formulations of higher strengths. This indicates firm strategy also to target private market where, according to a Unitaid estimate, 40% of all malaria patients seek treatment (UNITAID, 2013).

There are no patents on the active pharmaceutical ingredients used in ACTs (Orsi & Zimmerman, 2015) and Indian firms have used their R&D capabilities in re-formulating pharmaceutical drugs to **develop novel dosage forms adapted to the need of target populations.** Indeed, over 70% of malaria mortality is concentrated in children less than five years of age (WHO, 2016d). It is difficult for small children to swallow a tablet. We find that three firms (Ajanta, Cipla, and Macleods) have oral suspensions and additionally, Cipla also has rectal suppositories targeting small children with malaria (Table 3.15). We also notice that Ajanta[64], Ipca, and Strides have registered one or more AL dosage forms with higher strengths ("40 mg + 240 mg", "60 mg + 360 mg" or "80 mg + 480 mg") particularly to target adult patients. The advantage of using higher strength is that it reduces the number of pills a patient has to take to treat malaria. For example, adult patients of over 14 years of age have to take 24 tablets of "AL-20 mg + 120 mg" (4 tablets, twice daily) over three days as a part of the treatment (WHO, 2010). However, they only need six tablets of "AL-80 mg + 480 mg" (1 tablet, twice daily) over the same period. Higher strength AL tablets are more convenient to use and can also promote adherence to treatment in adults. The evidence suggests that firms

[64] Ajanta got a WHO prequalification for all three dosage forms in April 2017.

are using novel dosage forms to be more responsive to patient needs which in turn can help them to penetrate the market.

Further, we can also observe that all five firms use the same brand name for WHO prequalified and not-prequalified AL formulations (Table 3.15). To clarify this point, **firms are using the same brand name for products which are approved by a rigorous regulatory authority and those which are not.** This behavior can be a part of the firm strategy to gain legitimacy. Indeed, researchers have argued that firms not only need to conform to regulatory norms of the host country, but they also need to be consistent with the established cognitive structures in the society (Dunning & Lundan, 2008; Kostova & Zaheer, 1999; Laufs & Schwens, 2014a).

International donors purchase WHO prequalified ACTs which are distributed free of charge through the public healthcare delivery system in Mali and many other countries. If a firm's product is distributed in this way then people not only get familiar with its brand but they also put their trust. Especially because organizations like the Global Fund are widely known and highly reputed and supplying to them may bring reputational value to firms as well. The advantage resulting from the trust in the brand can then spillover not only to not-prequalified dosage forms of the same molecule(s) but to other products of the company too. Indeed, Strides not only had a contract with PSI to supply for the national malaria program in Mali through the Global Fund grants but it was also marketing ACTs in the private sector.

Table 3.6: Indian Firms with WHO Prequalified Pharmaceutical Products Across Diseases

SN	Firm Name	Diarrhea	HIV/AIDS	Influenza	Malaria	NTD	RH	TB	Total
1	Acme Formulation						1		1
2	Ajanta Pharma*				8				8
3	Alkem Laboratories*	1	1						2
4	Aurobindo Pharma*		44						44
5	Cadila Pharmaceutical		2					4	6
6	Cipla Ltd*		44	3	6	1	4	8	66
7	Emcure Pharmaceutical		10						10
8	Hetero Labs Ltd*		32					3	35
9	Ipca Laboratories*				4				4
10	Lupin		2				6	11	19
11	Macleods*	1	20	3	1			27	52
12	Meditab		2						2
13	Micro Labs*		15					13	28
14	Strides Shasun*		19	1	2			1	23
15	Sun Pharma*		18					1	19
16	Svizera							3	3
	Total	2	209	7	21	1	11	71	322

*Source: Analysis of WHO Prequalification Database as on July 2017[65]. In all WHO has approved 540 pharmaceutical products from 70 manufacturers. RH = Reproductive Health; TB = Tuberculosis. *Firms present in Mali.*

[65] Link to WHO prequalification Website: https://extranet.who.int/prequal/

Table 3.7: Products Registered by Aurobindo Pharma in Mali

SN	Product Name	INN	Form	Strength	Target Disease
1	Auro-Metformin	Metformin	Tablet	850 mg	Diabetes
2	Auro-Metformin	Metformin	Tablet	1000 mg	Diabetes
3	Auro-Podox 200	Cefpodoxime	Tablet	200 mg	BI
4	Auro-Xetil 250	Cefuroxime	Injection	250 mg	BI
5	Auro-Xetil 500	Cefuroxime	Tablet	500 mg	BI
6	Auro-Xetil 750	Cefuroxime	Injection	750 mg	BI
7	Drox 250	Cefadroxil	Syrup	250mg/5ml	BI
8	Drox 500	Cefadroxil	Capsule	500 mg	BI
9	Koact 156.25	Co-amoxiclav	Syrup	156.25 mg/5ml	BI
10	Koact 312.50	Co-amoxiclav	Syrup	312.5 mg/5ml	BI
11	Koact 625	Co-amoxiclav	Tablet	625 mg	BI
12	Pozineg 1000	Cefepime	Injection	1000 mg	BI
13	Pozineg 2000	Cefepime	Injection	2000 mg	BI

Note: BI=Bacterial Infection

No WHO prequalified products registered in Mali

Table 3.8: Products Registered by Micro Labs in Mali

SN	Product Name	INN	Form	Strength	Target Disease
1	Levobact 750	Levofloxacin	Tablet	750 mg	TB
2	Allercet	Cetirizine	Tablet	10 mg	Allergy
3	Amlong 10	Amlodipine	Tablet	10 mg	BP
4	Amlong 5	Amlodipine	Tablet	5 mg	BP
5	Angizaar-H	Losartan+ Hydrochlorothiazide	Tablet	50 mg/12.5 mg	BP
6	Avas 20	Atorvastatin	Tablet	20 mg	High Cholesterol
7	Gramocef-O	Cefixime	Capsule	200 mg	BI
8	Phytoral	Ketoconazole	Shampoo	NA	Dandruff

Note: BI = Bacterial Infection; TB = Tuberculosis; BP = Blood Pressure

No WHO prequalified products registered in Mali.

Table 3.9: Products Registered by Macleods Pharmaceuticals in Mali

SN	Product Name	INN	Form	Strength	Target Disease
1	Accuzon	Ceftriaxone	Injection	1 g	BI
2	Accuzon 250	Ceftriaxone	Injection	250 mg	BI
3	Accuzon 500	Ceftriaxone	Injection	500 mg	BI
4	Azicure	Azithromycin	Syrup	200 mg/5 ml	BI
5	Azicure 250	Azithromycin	Tablet	250 mg	BI
6	Azicure 500	Azithromycin	Tablet	500 mg	BI
7	Amapine 10	Amlodipine	Tablet	10 mg	BP
8	Amapine 5	Amlodipine	Tablet	5mg	BP
9	Amapine-H	Amlodipine/Hydrochloroyhiazide	tablet	5 mg/12.5 mg	BP
10	Fluomac 150	Fluconazole	Tablet	150mg	FI
11	Lumiter	Artemether+ Lumefantrine	Syrup	suspension	Malaria
12	Lumiter	Artemether+ Lumefantrine	Tablet	20 mg + 120 mg	Malaria*
13	Oflomac	Ofloxacin	Tablet	200 mg	TB**
14	Rabemac 20	Rabeprazole	Capsule	20 mg	SU
15	Rabemac DSR	Rabeprazole+ Domperidone	Capsule	30 mg + 20 mg	SU

*Note: BI = Bacterial Infection; BP = Blood Pressure; FI = Fungal Infection; SU = Stomach Ulcer; TB = Tuberculosis; *WHO prequalified product; Reference MA091; **WHO Prequalified Product; Reference TB218*

Table 3.10: Products Registered by Cipla in Mali

SN	Brand Name/ INN	INN	Form	Strength	Target Disease	WHO Ref.
1	Abamune	Abacavir dispersible	Tablet	60 mg	HIV*	HA488
2	Nelvir	Nelfinavir	Powder		HIV	No
3	Viraday	Efavirenz/Emtricitabine /Tenofovir Disoproxil Fumarate	Tablet	(600 + 200 + 300) mg	HIV*	HA500
4	Zidovir	Zidovudine	Tablet	100 mg	HIV*	No
5	Zidovir	Zidovudine	Capsule	100 mg	HIV*	HA052#
6	Zidovir	Zidovudine	Tablet	300 mg	HIV*	HA051#
7	Duovir	Lamivudine/Zidovudine	Tablet	150 mg + 50 mg	HIV*	HA060#
8	Lamivudine	Lamivudine	Tablet	30 mg	HIV*	HA502
9	Lamivir S-30	Lamivudine + Stavudine	Tablet	150 mg + 30 mg	HIV	No
10	Tenvir Em	Emtricitabine/ Tenofovir Disoproxil Fumarate	Tablet	300 mg+200 mg	HIV*	HA439
11	Ethionamide 250	Ethionamide	Tablet	250 mg	TB*	TB215
12	Moxicip	Moxifloxacin	Tablet	400 mg	TB*	TB210
13	Oflox-200	Ofloxacin	Tablet	200 mg	TB*	TB224
14	Oflox-400	Ofloxacin	Tablet	400 mg	TB*	TB225
15	Falcimon Kit	Artesunate+Amodiaquine	Tablet	50 mg+135 mg	Malaria*	MA103
16	Falcimon Kit Adult	Artesunate+Amodiaquine	Tablet	100 mg + 270 mg	Malaria*	MA104
17	Lumartem	Artemether+Lumefantrine	Suppository	20 mg + 120 mg	Malaria	No
18	Lumartem	Artemether+Lumefantrine	Oral suspension		Malaria	No
19	Lumartem	Artemether+Lumefantrine	Tablet	20 mg + 120 mg	Malaria*	MA064
20	Ciplacef-250	Ceftriaxone	Injection	250 mg	BI	NA
21	Ciplox 0,3%	Ciprofloxacin	Eyewash	0.3% w/v	BI	NA
22	Ciplox -750	Ciprofloxacin	Tablet	750 mg	BI	NA
23	Azee 500	Azithromycin	Tablet	500 mg	BI	NA
24	Norflox -400	Norfloxacin	Tablet	400 mg	BI	NA
25	Pylokit,	Tinidazole, Clarithromycin, Lansoprazole	Tablet	(500 + 250 + 30) mg	BI; PI	NA
26	Forcan - 50	Fluconazole	Capsule	50 mg	FI	NA
27	Photericin-B	Amphotericin B	Injection	50 mg	FI	NA
28	Nystatin 100000	Nystatin	Syrup	100,000 Units per ml	FI	NA
29	Bendex	Albendazole	Syrup		Worms	NA
30	Alerid	Cetirizine	Tablet	10 mg	Allergy	NA
31	Asthalin Inhalateur	Salbutamol	Inhaler	100 µg/Dose	Asthma	NA
32	Asthalin	Salbutamol	Syrup	2mg/5ml	Asthma	NA
33	Flohale-125	Fluticasone	Inhaler	125 µg/dose	Asthma	NA
34	Flomist 50	Fluticasone	NasalSpray	50 µg	Asthma	NA
35	Budenase AQ	Budesonide	Nasal Spray	64 µg/Dose	Asthma	NA
36	Carloc 12.5	Carvedilol	Tablet	12.5 mg	HF	NA
37	Carloc 6.25	Carvedilol	Tablet	6.25 mg	HF	NA

38	Lansec-30	Lansoprazole	Capsule	30 mg	SU	NA
39	Lomac 20	Omeprazole	Capsule	20 mg	SU	NA
40	Lomac Iv 40	Omeprazole	Injection	40 mg	SU	NA
41	Lomac-20	Omeprazole	Capsule	20 mg	SU	NA
42	Tramacip	Tramadol	Capsule	50 mg	Pain	NA

*Note: BI = Bacterial Infection; BP = Blood Pressure; FI = Fungal Infection; HF = Heart Failure; PI = Parasitic Infection; SU = Stomach Ulcer; TB = Tuberculosis; *WHO prequalified product; # Approved by both WHO and US FDA; No = Not prequalified Product; N/A = WHO prequalification program is not applicable to the disease area.*

Table 3.11: Products Registered by Hetero in Mali

SN	Brand/INN	INN	Form	Strength	Target Disease	WHO Ref.
1	Zido-H	Zidovudine	Tablet	300 mg	HIV	No
2	Zidolam	Lamivudine/Zidovudine	Tablet	150 mg/300 mg	HIV*	HA521
3	Abacavir Sulfate	Abacavir Sulfate	Tablet	300 mg	HIV*	HA575#
4	Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate	Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate	Tablet	600 mg/200 mg/300 mg	HIV*	HA538#
5	Efavirenz/Lamivudine/ Tenofovir Disoproxil Fumarate	Efavirenz/Lamivudine/ Tenofovir Disoproxil Fumarate	Tablet	600 mg/300 mg/300 mg	HIV*	HA549
6	Tenofovir Disoproxil Fumarate	Tenofovir Disoproxil Fumarate	Tablet	300 mg	HIV*	HA508#
7	Lamivudine/Zidovudine/ Nevirapine	Lamivudine/Zidovudine/ Nevirapine	Tablet	150 mg/300 mg/200 mg	HIV*	HA275
8	Lamivudine	Lamivudine	Tablet	150 mg	HIV*	HA153#
9	Lamivudine	Lamivudine	Syrup	10 mg/ml	HIV*	ANDA 091475 USFDA2
10	Ritonavir	Ritonavir	Tablet	100 mg	HIV*	HA565
11	Atazanavir Sulfate + Ritonavir	Atazanavir Sulfate + Ritonavir	Tablet	300 mg/100 mg	HIV	No
12	Abacavir sulfate	Abacavir sulfate	Syrup	20 mg/ml	HIV*	HA493
13	Zidovudine	Zidovudine	Syrup	50 mg/5 ml	HIV*	HA486
14	Darunavir	Darunavir	Tablet	400 mg	HIV	No
15	Darunavir	Darunavir	Tablet	600 mg	HIV	No
16	Heptavir	Lamivudine	Tablet	150 mg	HIV*	HA153#
17	Indivir-400	Indinavirs	Capsule	400 mg	HIV	No
18	Nevivir	Nevirapine	Tablet	200 mg	HIV/AIDS*	HA155#
19	Anatero	Anastrozole	Tablet	1 mg	BC	NA
20	Letero	Letrozole	Tablet	2.5 mg	BC	NA
21	Gemtero	Gemcitabine	Injection	1000 mg	Cancer	NA
22	Gemtero	Gemcitabine	Injection	200 mg	Cancer	NA
23	Glimed-2	Glimepiride	Tablet	2 mg	Diabetes	NA
24	Glimed-1	Glimepiride	Tablet	1 mg	Diabetes	NA
25	Monte-H	Montelukas	Tablet	10 mg	Asthma	NA
26	Yesom-20	Esomeprazole	Tablet	20 mg	GI	NA
27	Yesom-40	Esomeprazole	Tablet	40 mg	GI	NA

*Note: GI = Gastrointestinal; BC = Breast Cancer; *WHO prequalified product; # Approved by both WHO and US FDA; No = Not prequalified Product; N/A = WHO prequalification program is not applicable to the disease area.*

Table 3.12: Products Registered by Ranbaxy (Sun Pharma) in Mali

SN	Brand/INN	INN	Form	Strength	Target Disease	WHO Ref.
1	Abac 300	Abacavir	Tablet	300 mg	HIV	HA322
2	Abac-LZ	Abacavir+Lamivudine+Zidovudine	Tablet	300mg+150mg+300mg	HIV	HA324
3	Adosine DR	Didanosine	Capsule	250 mg	HIV	No
4	Adosine DR	Didanosine	Capsule	400 mg	HIV	No
5	Aviranz Kid 100	Efavirenz Dispersible	Tablet	100 mg	HIV	HA509
6	Avocomb Kid	Lamivudine + Zidovudine	Tablet	30mg/60 mg	HIV	No
7	Avocomb Kid	Lamivudine + Zidovudine	Tablet	150 mg/300 mg	HIV	HA286
8	Tenolam	Lamivudine + Tenofovir Disoproxil Fumarate	Tablet	300 mg+ 300 mg	HIV	HA525
9	Tevir-Em	Emtricitabine + Tenofovir Disoproxil Fumarate	Tablet	200 mg + 300 mg	HIV	HA551
10	Tevir	Tenofovir Disoproxil Fumarate	Tablet	300 mg	HIV	HA423
11	Staxom	Moxifloxacin	Tablet	400 mg	TB	TB253
12	Lomeran	Artemether+Lumefantrine	Tablet	20 mg+120 mg	Malaria	No
13	Avoiroday EM	Untracable	Untracable	Untracable	Untracable	NA
14	Ceruvin	Clopidogrel	Tablet	75 mg	HF	NA
15	Chericof	Phenylephrine+ Chlorpheniramine+Dextromethorphan	Syrup	(5+ 2+10) mg/ 5ml	Cough	NA
16	Ranoxyl 250	Amoxicillin	Syrup	250 mg/5 ml	BI	NA
17	Ranoxyl 500	Amoxicillin	Capsule	500 mg	BI	NA
18	Cifran	Ciprofloxacin	Tablet	500 mg	BI	NA
19	Cilentra	Escitalopram	Tablet	20 mg	Depression	NA
20	Cilentra	Escitalopram	Tablet	10 mg	Depression	NA
21	Ketanov MD	Ketorolac	Tablet	10 mg	Fever	NA
22	Olmetec 40	Olmesartan	Tablet	40 mg	BP	NA
23	Olmetec 20	Olmesartan	Tablet	20 mg	BP	NA
24	Olmetec 10	Olmesartan	Tablet	10 mg	BP	NA
25	Coolmetec	Olmesartan+ Hydrochlorothiazide	Tablet	20 mg/25 mg	BP	NA
26	Coolmetec	Olmesartan+ Hydrochlorothiazide	Tablet	20 mg/12.5 mg	BP	NA
27	Raciper 20	Esomeprazole	Tablet	20 mg	SU	NA
28	Raciper 40	Esomeprazole	Tablet	40 mg	SU	NA
29	Raciper 40	Esomeprazole	Injection	40 mg	SU	NA
30	Gestid	Aluminium Hydroxyde + Magnesium Hydroxyde + Simethicone	Syrup	250 mg + 250 mg + 50 mg	Acidity	NA
31	Ranferon-12	Ferric Ammonium Citrate	Capsule		Anemia	NA
32	Ranferon-12	Ferric Ammonium Citrate	Syrup	(200+15+0.05) mg/5 ml	Anemia	NA
33	Ranferon Plus	Ferric Ammonium Citrate	Capsule		Anemia	NA
34	Revital	Multivitamin	Capsule		VD	NA
35	Trambax	Tramadol	Tablet	50 mg	Pain	NA
36	Trambax	Tramadol	Injection	100/2 ml	Pain	NA
37	VOLINI Gel	Diclofenac Diethylamine	Gel		Pain	NA
38	Brustan	Ibuprofen+Paracetamol	Syrup		Pain	NA
39	Brustan	Ibuprofen+Paracetamol	Tablet	400 mg/325 mg	Pain	NA

*Note: BI = Bacterial Infection; BP = Blood Pressure; HF = Heart Failure; SU = Stomach Ulcer; TB = Tuberculosis; VD = Vitamin Deficiency; *WHO prequalified product; No = Not prequalified Product; N/A = WHO prequalification program is not applicable to the disease area.*

Table 3.13: Products Registered by Alkem in Mali

SN	Brand/INN	INN	Form	Strength	Target Disease
1	Chinther	Artemether + Lumefantrine	Tablet	80 mg + 480 mg	Malaria
2	Chinther	Artemether + Lumefantrine	Tablet	40 mg + 240 mg	Malaria
3	Chinther	Artemether + Lumefantrine	Tablet	20 mg + 120 mg	Malaria
4	Dip 10	Amlodipine	Tablet	10 mg	BP
5	Dip 5	Amlodipine	Tablet	5 mg	BP
6	Mecam 7.5	Meloxicam	Tablet	7.5 mg	Pain
7	Mecam 15	Meloxicam	Tablet	15 mg	Pain
8	Sodrol	Methylprednisolone	Injection	40 mg	Inflammation
9	Alcipro	Ciprofloxacin	Tablet	500 mg	BI
10	Alevo 250	Levofloxacin	Tablet	250 mg	BI
11	Alevo 500	Levofloxacin	Tablet	500 mg	BI
12	Clavam	Co-amoxiclav	Tablet	1125 mg	BI
13	Clavam	Co-amoxiclav	Tablet	1125 mg	BI
14	Clavam	Co-amoxiclav	Syrup	281.25 mg/5ml	BI
15	Clavam	Co-amoxiclav	Syrup	562.5 mg/5 ml	BI
16	Clavam	Co-amoxiclav	Tablet	562.5 mg	BI
17	Clavam	Co-amoxiclav	Injection	600 mg	BI
18	Clavam	Co-amoxiclav	Injection	1.2 g	BI
19	Magtam	Cefoperazone + Sulbactam	Injection	2 g	BI
20	Magtam	Cefoperazone + Sulbactam	Injection	1 g	BI
21	Swich	Cefpodoxime	Tablet	200 mg	BI
22	Taxim-O	Cefixime	Tablet	200 mg	BI
23	Unozit	Azithromycin	Tablet	500 mg	BI
24	Unozit	Azithromycin	Tablet	250 mg	BI
25	Xone	Ceftriaxone	Injection	500 mg	BI
26	Xone	Ceftriaxone	Injection	1 g	BI
27	Zaxter	Meropenem	Injection	1 g	BI
28	Zaxter	Meropenem	Injection	500 mg	BI
29	Zocef	Cefuroxime	Injection	1.5 g	BI
30	Zocef	Cefuroxime	Injection	750 mg	BI
31	Zocef	Cefuroxime	Tablet	500 mg	BI
32	Zocef	Cefuroxime	Tablet	250 mg	BI

Note: BI = Bacterial Infection; BP = Blood Pressure

No WHO prequalified products registered in Mali.

Table 3.14: Products Registered by Strides in Mali

SN	Brand/INN	INN	Form	Strength	Target Disease
1	Combiart	Artemether + Lumefantrine	Tablet	20 mg + 120 mg	Malaria*
2	Combiart	Artemether + Lumefantrine	Tablet	80 mg + 480 mg	Malaria
3	Quinine	Quinine	Tablet	300 mg	Malaria
4	Sulfadoxine+Pyrimethamine	Sulfadoxine + Pyrimethamine	Tablet	500 mg + 25 mg	Malaria
5	Cefotaxime	Cefotaxime	Injection	1 g	BI
6	Cefotaxime	Cefotaxime	Injection	1 g	BI
7	Celltriaxon	Ceftriaxone	Injection	1 g	BI
8	Clariton	Clarithromycin	Tablet	500 mg	BI
9	Clavicin	Co-amoxiclav	Injection	1000 mg + 200 mg	BI
10	Clavicin XR	Co-amoxiclav	Tablet	1000 mg + 625 mg	BI
11	Azithrin	Azithromycin	Capsule	500 mg	BI
12	Betazidim	Ceftazidime	Injection	1 g	BI
13	Amoxicilline	Amoxicillin	Capsule	250 mg	BI
14	Amoxicilline	Amoxicillin	Capsule	500 mg	BI
15	Ampicilline Sodium	Ampicillin	Injection	1 g	BI
16	Ceftriaxone	Ceftriaxone	Injection	1 g	BI
17	Ciprofloxacine	Ciprofloxacin	Tablet	500 mg	BI
18	Cloxacilline	Cloxacillin	Capsule	500 mg	BI
19	COTIMOXAZOLE (10x10)	Co-trimoxazole	Tablet	480 mg	BI
20	Cotrimoxazole (Box Of 1000)	Co-trimoxazole	Tablet	480 mg	BI
21	Cotricel	Co-trimoxazole	Syrup	240 mg/5 ml.5 ml	BI
22	Erycel	Erythromycin	Syrup	125 mg/5 ml	BI
23	Erythromycin Stearate	Erythromycin Stearate	Tablet	500 mg	BI
24	Doxycycline	Doxycycline	Capsule	100 mg	BI; PI
25	Metronidazole	Metronidazole	Tablet	250 mg	BI; PI
26	Metronidazole	Metronidazole	Tablet	500 mg	BI; PI
27	Metcel	Metronidazole	Syrup	125 mg/5 ml	BI; PI
28	Nyscel	Nystatin	Syrup	100000 UI/5 ml	FI
29	Knz 200	Ketoconazole	Tablet	200 mg	FI
30	Albendazole	Albendazole	Tablet	400 mg	Worms
31	Bendacel	Albendazole	Syrup	200 mg/5 ml	Worms
32	Iscept-800	Glibenclamide + Metformin	Tablet	5 mg + 800 mg	Diabetes
33	Adride 4	Glimepiride	Tablet	4 mg	Diabetes
34	Adride 2	Glimepiride	Tablet	2 mg	Diabetes
35	Adride-M	Glimepiride + Metformin	Tablet	1 mg + 500 mg	Diabetes
36	Glim Forte	Gliclazide + Metformin	Tablet	80 mg + 800 mg	Diabetes
37	Metformin	Metformin	Tablet	500 mg	Diabetes
38	Amlostar Plus	Amlodipine + Atenolol	Tablet	5 mg + 50 mg	BP
39	Arconifed SR	Nifedipine	Tablet	20 mg	BP
40	Stripril 10	Lisinopril	Tablet	10 mg	BP
41	Stripril 5	Lisinopril	Tablet	5 mg	BP
42	Strimide	Indapamide	Tablet	2.5 mg	BP
43	Lorhist 10	Loratadine	Tablet	10 mg	Allergy
44	Lorhist	Loratadine	Syrup		Allergy

45	Hydrocortisone Succinate Sodium	Hydrocortisone Sodium Succinate	Injection	100 mg	Allergy
46	Carcel 2%	Carbocisteine	Syrup	0.02	Bronchiectasis
47	Carcel 5%	Carbocisteine	Syrup	0.05	Bronchiectasis
48	Erecta	Sildenafil	Tablet		Sexual Dysfunction
49	Lipovas 10	Atorvastatin	Tablet	10 mg	CVD
50	Lipovas 20	Atorvastatin	Tablet	20 mg	CVD
51	Solcer	Omeprazole	Injection	40 mg	SU
52	Excegin	Aluminum Hydroxide + Magnesium Hydroxide + Simethicone	Syrup		Heartburn
53	Parexcel	Paracetamol	Syrup	120 mg/5 ml	Fever
54	Strimol Extra (5x4)	Paracetamol + Caffine	Tablet	500 mg + 30 mg	Fever
55	Strimol Extra (50x4)	Paracetamol + Caffine	Tablet	500 mg + 30 mg	Fever
56	Paracetamol (10x10)	Paracetamol	Tablet	500 mg	Fever
57	Paracetamol (Box Of 1000)	Paracetamol	Tablet	500 mg	Fever
58	Ferrous Sulfate + Folic Acid (10x10)	Ferrous Sulfate + Folic Acid	Tablet	100 mg + 0.5 mg	Anemia
59	Ferrous Sulfate + Folic Acid (Box Of 1000)	Ferrous Sulfate + Folic Acid	Tablet	100 mg + 0.5 mg	Anemia
60	Vitafer	Ferrous Sulfate + Folic Acid	Capsule	150 mg + 500 mg	Anemia
61	Vitafer Forte	Ferric Ammonium Citrate+ Folic Acid + Vitamin B 12	Syrup	200 mg + 1.5 mg + 50 µg	Anemia
62	Renerve Plus-Bt	Multivitamine	Capsule		VD
63	Renerve Plus Softgel	Multivitamine	Capsule		VD
64	Vitacel	Multivitamin	Syrup		VD
65	Camvit Plus	Multivitamine	Capsule		VD
66	Megaza	Omega-3 Fatty Acid	Capsule	1 g	ND
67	Ostriol	Calcitriol	Capsule	0.5 µg	ND
68	Ostriol	Calcitriol	Capsule	0.25 µg	ND
69	Xytinin	Oxybutynin Hydrochloride	Tablet	5 mg	Muscular Spasms
70	Melonax	Meloxicam	Tablet	15 mg	Inflammation
71	Melonax	Meloxicam	Tablet	7.5 mg	Inflammation
72	Diclofenac	Diclofenac	Tablet	50 mg	Inflammation
73	Ibuprofen (Box Of 1000)	Ibuprofen	Tablet	400 mg	Pain
74	Ibuprofene	Ibuprofen	Tablet	400 mg	Pain
75	Ibucel Suspension	Ibuprofen	Syrup		Pain
76	Nouric	Allopurinol	Tablet	100 mg	Gouts
77	Worcel	Product Not Tracable	Product Not Tracable	Product Not Tracable	Product Not Tracable

*Note: BI = Bacterial Infection; BP = Blood Pressure; CVD = Cardiovascular Diseases; FI = Fungal Infection; HF = Heart Failure; PI = Parasitic Infection; SU = Stomach Ulcer; TB = Tuberculosis; VD = Vitamin Deficiency; ND = Nutritional Deficiency; *WHO prequalified product, Reference MA088*

Table 3.15: Product Portfolio of WHO Prequalified Manufacturers for Antimalarial Medicines in Mali

SN	Firm	Brand Name/ INN	INN	Form	Strength	Pack-Size	WHO Ref.
1	Ajanta	Apmod	ASAQ	Tablet	25 mg + 67.5 mg	3 Tablets	MA095
2	Ajanta	Apmod	ASAQ	Tablet	50 mg + 135 mg	3 Tablets	MA096
3	Ajanta	Apmod	ASAQ	Tablet	100 mg + 270 mg	3 Tablets	MA097
4	Ajanta	Apmod	ASAQ	Tablet	100 mg + 270 mg	6 Tablets	MA097
5	Ajanta	Artefan	AL	Tablet	20 mg + 120 mg	24 Tablets	MA052
6	Ajanta	Artefan	AL	Tablet	40 mg + 240 mg	12 Tablets	MA128*
7	Ajanta	Artefan	AL	Tablet	80 mg + 480 mg	6 Tablets	MA130*
8	Ajanta	Artefan Dispersible	AL	Tablet	20 mg + 120 mg	6 Tablets	MA092
9	Ajanta	Artefan	AL	Suspension	180 mg + 1080 mg	Bottle - 60 ml	No
10	Cipla	Falcimon Kit Adult	ASAQ	Tablet	100 mg + 270 mg	6 Tablets	MA104
11	Cipla	Lumartem	AL	Tablet	20 mg + 120 mg	24 Tablets	MA064
12	Cipla	Lumartem	AL	Suppository	20 mg + 120 mg	6 Suppositories	No
13	Cipla	Lumartem	AL	Suspension	180 mg + 1080 mg	Bottle - 60 ml	No
14	Ipca	IASAQ	ASAQ	Tablet	25 mg + 67.5 mg	3 Tablets	MA080
15	Ipca	IASAQ	ASAQ	Tablet	100 mg + 270 mg	3 Tablets	MA082
16	Ipca	IASAQ	ASAQ	Tablet	100 mg + 270 mg	6 Tablets	MA082
17	Ipca	Artesunate Amodiaquine	ASAQ	Tablet	25 mg + 67.5 mg	30 Tablets	MA080
18	Ipca	Artesunate Amodiaquine	ASAQ	Tablet	50 mg + 135 mg	30 Tablets	MA081
19	Ipca	Laritem	AL	Tablet	20 mg + 120 mg	6 Tablets	MA062
20	Ipca	Laritem	AL	Tablet	40 mg + 240 mg	12 Tablets	No
21	Ipca	Laritem	AL	Tablet	40 mg + 240 mg	6 Tablets	No
22	Ipca	Laritem	AL	Tablet	80 mg + 480 mg	6 Tablets	No
23	Ipca	Larither	AL	Injection	40 mg /ml	Bottle - 1 ml	No
24	Ipca	Larither	AL	Injection	80 mg/ml	Bottle - 1 ml	No
25	Ipca	Artemether Lumefantrine	AL	Tablet	20 mg + 120 mg	12 Tablets	MA062
26	Ipca	Artemether Lumefantrine	AL	Tablet	20 mg + 120 mg	18 Tablets	MA062
27	Ipca	Artemether Lumefantrine	AL	Tablet	20 mg + 120 mg	6 Tablets	MA062
28	Macleods	Lumiter	AL	Tablet	20 mg + 120 mg	24 Tablets	MA091
29	Macleods	Lumiter	AL	Suspension	180 mg + 1080 mg	Bottle - 60 ml	No
30	Strides	Combiart	AL	Tablet	20 mg + 120 mg	24 Tablets	MA088
31	Strides	Combiart	AL	Tablet	80 mg + 480 mg	6 Tablets	No

Note: AL = Artemether + Lumefantrine; ASAQ = Artesunate + Amodiaquine

** Products were only approved on April 21, 2017.*

3.5. Conclusion

This chapter aimed to show the market entry and operation strategies of Indian pharmaceutical firms in Francophone West African countries by focusing on the case of Mali. It highlights that the Malian pharmaceutical market is comprised of four market segments: government-funded, donor-funded, formal private and the informal sector. It also shows that the organization of pharmaceutical supply chain in the four segments and the regulatory framework governing their functioning are different. These market segments are characterized by the presence of different economic actors, funding sources, the requirement of product quality and distributional channel.

The chapter further demonstrates that market entry and operation strategies of Indian firms are determined by the institutional setting of each market segments. While they depend on export to supply the Malian market, the organization of export varies with the market segments – government-funded, donor-funded and the formal private sector.[66] Further, even within the same market segment, firms have the different strategic options. This is particularly true for the private sector where firms can enter into partnership either with French subsidiaries who have operations in multiple countries or with other small country-level importers and distributors. Thus, firms have the possibility to use a combination of modes, i.e., "mode packages" as suggested by researchers like Benito et al. (2009). Further, few firms who actively want to pursue the market also support their foreign engagement through supporting activities such product promotion.

However, not all firms can be active in all market segments. This is especially true for the donor-funded segment as only a few Indian firms satisfy the stringent quality requirements such as the WHO product prequalification demanded by most donors and procurement agencies. Moreover, looking at the market authorization data also reveals that even if a firm has the capabilities to be active in multiple segments, it can make a strategic choice of not doing so.

The study is not without limitations. The first limitation concerns the extent to which the findings can be generalized to other countries. We can definitely argue that Indian firms might

[66] Informal sector was not included for examining the entry strategies of Indian firms.

be using the same general operation strategy in Francophone West African countries because the evidence from the literature and fieldworks suggests that the general architecture of the pharmaceutical market in West African Francophone countries is similar and made up of four market segments. This was also confirmed by the case study of Ajanta in Ivory Coast. Nevertheless, strategies may need to be modified to suit country-specific structural differences and regulations. For example, compared to Mali, the formal private market in other West African Francophone countries is characterized by relatively few wholesalers (section 3.4.3.1.2). This leaves Indians firms with few strategic options to enter the private sector. Similarly, Burkina Faso requires the test of bio-equivalence as an essential condition for granting market authorization to generic medicines. Therefore, less quality conscious companies will find it difficult to operate in such environment.

The question of generalizability becomes more demanding on a broader scale of Sub-Saharan Africa where the results may not be entirely applicable as significant variability can exist in the choice of entry modes across Indian firms. This is particularly true for their operation in English speaking Commonwealth countries like South Africa, Nigeria, Uganda, Ethiopia and Mozambique where Indian firms have already entered into local production in addition to exports. Further, while it is worth noting that the existing literature indicates the existence of all four types of market segments in African countries their organization, regulatory norms and market-size among other can significantly vary. For example, countries like Nigeria, Ghana, and Kenya have each over 500 registered wholesalers in the formal private market. So, Indian firms can have more bargaining power compared to countries in Francophone West Africa with few wholesalers with greater market power. In another example, we can take the case of Nigeria which as noted by Baxerres (2012) does not have a central medical store. So, the public-sector procurement is done for health structures at the level of states and national health programs which obtain medicines from Nigerian producers as well as wholesalers. As such, the strategy of Indian manufacturers towards the public sector may change as the market is not consolidated and they might target private wholesalers to supply their products to public entities.

Second, while the fieldwork in Mali confirmed the presence of a deeply rooted informal market, the did not take into account to examine the strategies of Indian firms. This choice was logical because only the presence of a firm's product in the informal market does not mean that it is involved in illegal transactions. This is not to say such activities do not take place as one wholesaler in our interview reported importing a product without the market authorization. So,

we can reasonably say that the manufacturer exporting the product in this case must be aware of the choice it made. However, the arrival and distribution of medicines through informal routes is a multifactorial issue and often possible due to corruption and complicity of government officials. Moreover, the issue is a sensitive one and only few participants talked about it but even so they avoided the details.

Lastly, other than understanding the operations of Ajanta Pharma in Ivory Coast, the study did not did not rely on firm-specific cases studies. As such it does not capture the perspective of firms towards the markets. For example, while our examination confirms that the organization of export in the donor-funded market is different, we do not know the subtleties of strategies used by firms towards this segment. Also, we could not gather information on the role and extent of lobbying and illegal relation building activities such as bribes and gifts employed by firms to ease their entry and penetration in the market.

Thus, to sum up, while this study is the first step towards the understanding of market-entry and operation strategies of Indian firms in the African context, more case studies focusing on multiple countries and multiple firms are needed to provide a comprehensive picture of the phenomenon.

4. Firm Strategy under the Opportunities and Constraints Posed by International Organizations: An Explorative Study of the Development and Launch of Synriam™ by Ranbaxy

4.1. Introduction

In the previous chapter, we took a broader vision of the market entry process of Indian pharmaceutical firms by examining the organization of pharmaceutical market into four different market segments and observed that firms adapt their strategies according to the institutional environment of the segments in which they intend to operate. In the present chapter we take a different, albeit complementary approach towards market entry in Africa by analyzing how new products targeted to the need of patients in the global south is being shaped by the action of international organizations from product development to delivery.

To recall, market entry according to Root (1994), is "an institutional arrangement that makes possible the entry of a company's products, technology, human skills, management or other resources into a foreign country". A firm can undertake such initiatives either by itself or in alliance with some other organization. For example, a firm can use its internal resources for developing, manufacturing, exporting, marketing, and/or distributing its product in a foreign country but it can also do perform one or more such initiatives by collaborating with other firms. International business researchers have noted that alliances can help a firm to gain access to new and complementary technologies, fasten the process of innovation and learning, and upgrade efficiency in R&D, manufacturing and marketing (Dunning, 1995; Eisenhardt & Schoonhoven, 1996; Luo & Tung, 2007; Peng, 2001). Further, there is not a rigid and dichotomous choice that firms have to use either alliance or work independently in a given foreign market. It can choose to perform some of the activities targeting a foreign market in collaboration while others it can do itself (Benito et al., 2009; Petersen et al., 2008; Petersen & Welch, 2002).

There are numerous instances where Indian pharmaceutical firms have used strategic alliances with foreign multinationals as a means to gain new resources and capabilities and to increase their penetration in the foreign market. These alliances have targeted diverse activities like R&D, contract manufacturing, and marketing. For example, Ranbaxy and GlaxoSmithKline (GSK) had signed a multi-year joint research alliance in 2003 (Kedron & Bagchi-Sen, 2011). Similarly, Dr. Reddy's and GSK entered into an alliance in 2009 in which the latter gained exclusive access to over 100 formulations in Dr. Reddy's future pipeline. The drugs were to be manufactured by Dr. Reddy's and licensed and supplied by GSK in numerous developing countries in Asia, Africa, Middle-East, and Latin America (Joseph, 2011). Likewise, Dishman Pharmaceuticals signed a partnership with Merck to manufacture intermediate for the high blood pressure drug – Losartan – to be supplied to its contract manufacturers in Japan (Joseph, 2011). Nevertheless, researchers have primarily focused on the alliances of Indian firms with developed country multinationals (Joseph, 2011; Kale, 2010a; Kedron & Bagchi-Sen, 2011, 2012; Pradhan, 2006; Pradhan & Alakshendra, 2006).

Interestingly and pertinent to our study, few Indian firms[67] like Cipla, S.Kant, Zydus Cadila, Strides, Macleods, and Syngene are not only working with other multinational companies but they also entered into collaborative alliances with international organizations dedicated to developing pharmaceutical products targeting infectious diseases prevalent in southern countries, especially Sub-Saharan Africa. These include the big three – HIV/AIDS[68], tuberculosis (TB), and malaria and various tropical diseases such as leishmaniasis, human African trypanosomiasis (sleeping sickness), filaria, Buruli ulcer, and trachoma among many others (Bhutta, Sommerfeld, Lassi, Salam, & Das, 2014; Harper, 2007; Hotez, Fenwick, Savioli, & Molyneux, 2009). These diseases are characterized by a disproportionately high

[67] Information obtained from : https://www.dndi.org/partnership/partners/

https://www.mmv.org/research-development/mmv-supported-projects

https://www.tballiance.org/portfolio/partners

[68] HIV is neither a tropical disease nor is neglected by pharmaceutical companies. However, it is often included among neglected tropical diseases because of its extremely high burden in the global South and lack of investment in research for developing formulations dedicated to children (Policy Cures Research, 2016).

disease burden in the South. WHO reports that together these diseases cause 32% of the burden of ill health in Africa and severely impact health outcomes in every region of the world (WHO, 2016b). Most of these diseases require new pharmaceutical technologies because either there is no existing product or improved products adapted to patients are needed (Hotez et al., 2016; Policy Cures Research, 2016). However, the insufficient commercial market has led to underinvestment of private R&D addressing these diseases.

To respond to this neglect, several public-private partnerships have emerged to stimulate the R&D for new vaccines, treatments, and diagnostics to combat diseases that primarily affect Southern countries. These so-called product development partnerships (PDPs) have brought a new culture of collaborative R&D by bringing together various actors of the innovation system such as funding agencies, academia, public laboratories, contract research organizations, and pharmaceutical companies (Chataway et al., 2007). Remarkably, PDPs are not only entering into alliances with Western multinationals[69] but are providing opportunities to developing country firms as well. For example, DNDi partnered with the Indian firm Cipla to launch a fixed-dose combination of "artesunate-mefloquine" (DNDi, 2012; S. Wells et al., 2013). However, such alliances as firm strategy have not received the attention of international business researchers.

To understand the interaction of firms with PDPs, we must take into account the broader context of market creation for pharmaceutical products. The most notable success of PDPs has been in the field of HIV, TB, and malaria (J. P. Cohen et al., 2014). The creation of market for medicines for these diseases is a multilayered and complex political process which is complicated by the diversity of social actors (See sections 2.5 and 2.6). For example, the WHO plays the role of an international prescriber by publishing evidence-based disease-specific treatment guidelines mainly targeting policymakers in developing countries. It is one of the core functions of the WHO (WHO, 2018) and central to the process of market construction as countries align their national treatment guidelines for a given disease in line with the WHO recommendations. WHO recommendation also means that medicine is eligible for inclusion in

[69] For example, Drugs for Neglected Diseases Initiative (DNDi) partnered with Sanofi to launch the fixed-dose formulation of "artesunate-amodiaquine" in multiple countries globally (DNDi, 2005). Similarly, Medicines for Malaria Venture (MMV), joined hands with Novartis to develop a child-friendly dispersible formulation of "artemether-lumefantrine" (Abdulla & Sagara, 2009).

the WHO Essential Medicines List (EML) which in turn serves as the basis for national EML (Laing et al., 2003). Thus, WHO recommendation is crucial for inducing the demand for a new pharmaceutical product, especially in developing countries. Moreover, WHO also assures the quality of medicines to guarantee their safety and efficacy and it has become a minimum requirement for procurement by international financing agencies like the the Global Fund, PEPFAR, PMI, and Unitaid.

So, in light with the discussion so far, this chapter aims to examine how PDPs and the regulatory framework put in place by international organizations shapes the market entry strategy of a firm. To answer the above question, a case study approach following the recommendations of Eisenhardt (1989) and Yin (2003) was employed. A case study is an empirical inquiry of a contemporary phenomenon within the real-life context of its occurrence (Yin, 2003). It focuses on why a particular set of decisions were taken and how they were implemented allowing all contextual conditions and social processes to be a part of the analysis (Eisenhardt, 1989; Kale, 2010b; Yin, 2003). Further, a case-based investigation is particularly appropriate for answering questions which are not thoroughly researched (Eisenhardt & Graebner, 2007; Leonard-Barton, 1990).

Synriam, a new antimalarial drug was selected as the case of interest. It is a fixed-dose combination (FDC) product that combines two parasiticidal drugs with independent modes of action – faster-acting arterolane maleate (arterolane) and longer acting piperaquine phosphate (piperaquine). It offers a "three days-three tablets" treatment regimen where each tablet consists of 150 mg of arterolane and 750 mg of piperaquine.

The selection of Synriam followed a "theoretical sampling" approach where cases "are chosen because they are unusually revelatory, extreme exemplars, or opportunities for unusual research access" (Eisenhardt & Graebner, 2007). Indeed, Synriam is unique in many respects. One of its components, arterolane, is the outcome of PDP-funded research by Medicines for Malaria Venture (MMV). For the further development of the molecule, MMV partnered with an Indian firm Ranbaxy[70]. The goal of Ranbaxy's alliance with the MMV was to develop and launch a new product in a specific disease segment (malaria in this case). As nearly 90% of

[70] Ranbaxy was acquired by Sun Pharma in a landmark deal on 25th March 2015.

malaria cases are concentrated in Sub-Saharan Africa (WHO, 2016d), it is logical to assume that the largest market for the potential product was outside India.

However, unsatisfied with the early clinical trial outcomes of arterolane, MMV left the partnership, but it gave Ranbaxy an exclusive license over intellectual property rights (IPR) to continue product development. After the withdrawal of MMV from the project, Ranbaxy partnered with the Government of India to complete the clinical trials of the combination of arterolane and piperaquine, trademarked under the brand name of Synriam. The drug was first approved by the Drug Controller General of India (DCGI) in 2011 for treating acute, uncomplicated *P. falciparum* malaria in patients from 12 to 65 years of age. This made Ranbaxy the first Indian company to bring an NCE (arterolane) to the market. By 2015, Ranbaxy had already managed to launch the product in 9 Sub-Saharan countries. **Thus, the case of Synriam provides the opportunity to investigate "why" Ranbaxy partnered with MMV and "how" it adapted its strategies to launch the product in India and other African countries after the partnership was broken.**

Data was collected through semi-structured interviews between September 2016 and August 2017 following the guidelines of Barriball and While (1994) and Harrell and Bradley (2009) to design and conduct semi-structured interviews (See section 3.1). In the preparatory phase, we searched the published literature and online resources to identify people who had been involved in the development of Synriam. Emails or LinkedIn messages were sent to over twenty potential participants describing the project and requesting participation. We also unsuccessfully contacted Sun Pharma requesting its participation in the study. Finally, we managed to conduct five interviews. Three participants were ex-employees[71] of the erstwhile Ranbaxy and were closely associated with the Synriam project. One of them was a vice president at Ranbaxy who started working on Synriam from early clinical phase and steered its launch in India and Africa. Another participant was a senior manager who dealt with the regulatory approvals and product registration in several African countries. The last employee was a marketing manager mainly involved in the launch process of Synriam.

[71] We were informed during the interviews that many of the key resource persons who were engaged with the Synriam project had left Ranbaxy after its acquisition by Sun Pharma.

Another interview was carried out with a senior scientist from the Indian Council of Malaria Research which was the partner organization for conducting clinical trials for Synriam in Indiana and Africa. The last participant is a Vice President the MMV and was involved with the arterolane project until the withdrawal of MMV. We surely had a limited number of participants but their diversity and knowledge gained through their involvement in the Synriam project at senior level positions allowed capturing a detailed understanding of its development process.

An interview guide (See appendix 6.5) was prepared to provide a framework for respondents. Each interview started with a brief inquiry about the professional profile of the respondent and their level of involvement in the development of Synriam. On the one hand, this approach allowed building up a rapport with the participants, and on the other, it allowed focusing on the most relevant questions related to their domain of specialization. Further, broad and open-ended questions were asked to allow participants to express their understanding and conceptualization of the phenomenon and followed-by probing on specific issues. The central themes included the history of Synriam, project management, collaboration, market launch and challenges. Additional information was gathered from a review of scientific literature, reports, websites, and news articles.

Lastly, the study also benefitted from participation in an expert panel titled "Access to essential medicines - the commons in the face of globalization". The event was organized by the French Development Agency (AFD) on October 4, 2017 and was attended by the delegates from DNDi, MMV, Unitaid, MSF Access Campaign, and several senior economists. Participation to this panel not only helped to better understand of the organization and functioning of PDPs but it also benefitted from presenting and discussing an initial version of the study.

Rest of the chapter is organized as follows: In section 4.2, we start by explaining the PDP model of drug development by focusing on its underlying functional features that includes funding, organization of R&D and processing of intellectual property rights. Section 4.3 provides a detailed account of the development of Synriam and strategies of Ranbaxy to bring the product to market in India and later in Africa. Section 4.4 is a brief conclusion.

4.2. An Introduction to PDPs

4.2.1. TDR: The Precursor of Modern PDPs

Product Development Partnerships (PDPs) are self-governing, private, not-for-profit organizations that rely on active collaboration with multiple stakeholders such as academia and industry to deliver new drugs, vaccines, and diagnostics. They are regarded as social experiments and organizational innovations dedicated to addressing the unmet medical needs of the South (Chataway et al., 2007; Chataway, Hanlin, Mugwagwa, & Muraguri, 2010).

However, the use of public-private collaboration to foster pharmaceutical R&D for tropical diseases is not entirely new. TDR, the Special Programme for Research and Training in Tropical Diseases can be regarded as a predecessor of modern PDPs. It was established in 1974 with the objective of intensifying tropical diseases R&D and strengthening research capabilities in endemic countries (Reeder & Guth, 2015). It was initially sponsored by the WHO but gradually joined by other partners including the United Nations Development Programme (UNDP) in 1976, the World Bank in 1977 and the United Nations Children's Fund in 2003. Initially, TDR focused only on basic research, but it soon realized that developing new products was crucial for improving health outcomes in developing countries (Reeder & Guth, 2015). One of the first public-private partnerships was the development of "mefloquine" for the treatment of malaria which resulted out of a collaboration between the Walter Reed Army Institute of Research, Hoffman-La Roche (Roche) and TDR (Olliaro, Kuesel, & Reeder, 2015).

By the1990s it was clear that relying solely on the private sector will not lead to the development of new medicines needed for diseases troubling developing countries as the pharmaceutical industry was withdrawing from tropical diseases research. So, TDR created a product development unit for advancing additional public-private partnerships for new product R&D targeting tropical diseases. These initial partnerships by the TDR were crucial for the development of several new medicines against diseases like malaria, leishmaniasis, and sleeping sickness. Nevertheless, TDR had its limitations. It lacked the narrow product focus and fundraising capabilities needed for successful drug development (Olliaro, Kuesel, & Reeder, 2015). Moreover, active engagement with pharmaceutical companies seemed not only costly and complicated to be implemented by TDR but also lied beyond its mandate (Muñoz et al., 2014).

It was in this scenario that independent, disease-focused organizations were envisioned as alternative solutions to accelerate the development of new medical technologies for tropical diseases (Muñoz et al., 2014; Olliaro et al., 2015). The experience of TDR proved valuable for guiding the creation of various PDPs. It provided initial mentorship to some of the most prominent PDPs such as the Medicines for Malaria Venture (MMV), the Drugs for Neglected Diseases Initiative (DNDi) and the Foundation for Innovative New Diagnostics (FIND).

4.2.2. Organization and Functioning of PDPs

PDPs differ regarding their target disease and the type of product such as medicines, vaccines, and diagnostics they intend to develop. Table 4.1 categorizes selected PDPs based on their scope concerning diseases and product. Most PDPs focus on a single disease and a single product type. For example, MMV focuses on developing new drugs for malaria while the efforts of the International AIDS Vaccine Initiative (IVAI) is directed towards developing vaccines for HIV/AIDS. However, few organizations like DNDi and FIND target six diseases or more.

Each disease has a specific epidemiological profile such as incidence, prevalence, mortality and geographical coverage. For example, diseases like HIV, TB, and malaria that have a significantly high burden and substantial geographical coverage, have been the central focus of PDPs. The three diseases draw the majority of the funding from governments and philanthropies for the procurement of pharmaceutical products as well as for the development of new medical technologies (Policy Cures Research, 2016; Unaids, 2017; WHO, 2016d, 2017a). Thus, PDPs have a wider space for negotiation with the industrial partners as the incentives to enter the market are higher.

Further, there is a considerable variation across PDPs regarding business organization and operational design. They differ in terms of size, number of products in the portfolio, organization of R&D, and outsourcing and intellectual property (IP) practices among others (Muñoz et al., 2014). Nevertheless, some fundamental similarities guide the business model of most PDPs. We shall discuss them in subsequent sub-sections.

Table 4.1 Classification of selected PDPs based on target disease and product type

Name	Target Disease(s)	Target Product	Year
Aeras	TB	Vaccine	2003
Dengue Vaccine Initiative (DVI)	Dengue	Vaccine	2010
Drugs for Neglected Diseases Initiative (DNDi)	Leishmaniasis, Sleeping Sickness, Chagas Disease, Pediatric HIV, Filaria, Hepatitis C, & Mycetoma	Drug	2003
European Vaccine Initiative (EVI)	Dengue, Influenza, Leishmaniasis, Malaria, Zika	Vaccine	1998
Fund for Innovative New Diagnostics (FIND)	Hepatitis C, HIV, Malaria, NTDs, TB, Sleeping Sickness	Diagnostic	2003
Infectious Disease Research Institute (IDRI)	Leishmaniasis, Leprosy, TB	Diagnostic, Drug, Vaccine	1993
Innovative Vector Control Consortium (IVCC)	Malaria, Dengue, and other NTDs	Vector Control Products	2005
Institute for OneWorld Health* (OWH)	NTDs	Drug	2000
International AIDS Vaccine Initiative (IAVI)	HIV/AIDS	Vaccine	1996
International Partnership for Microbicides (IPM)	HIV/AIDS	Microbicides	2002
International Vaccine Institute (IVI)	Cholera, Dengue, Typhoid, MERS	Vaccine	1997
Medicine Development for Global Health (MDGH)	Onchocerciasis, Diarrhea, Hepatitis B & C, Scabies, Pertussis, Rheumatic Fever	Drugs, Vaccine	2005
Medicines for Malaria Venture (MMV)	Malaria	Drug	1999
PATH's Malaria Vaccine Initiative (MVI)	Malaria	Vaccine	1999
TB Alliance	TB	Drug	2000
Tuberculosis Vaccine Initiative (TVI)	TB	Vaccine	2008

Source: Information taken from Kiddle-Monroe, Greenberg, & Basey (2016) and PDP websites.
Note: NTD = Neglected Tropical Diseases; PATH = Program for Appropriate Technology in Health.
**OWH is a part of PATH Drug Discovery Program since December 2011.*

4.2.2.1. Funding Independent of Financial Return

PDPs are not guided by financial return on investment into R&D. Instead, they are motivated by the need of patients in developing countries for safe and effective medical technologies which are adequately available and acceptable to end-users. They are mainly financed through grants from governments and philanthropic organizations which allows them to adopt a not-for-profit business model (Chataway et al., 2007; Grace, 2010; Muñoz et al., 2014; Policy

Cures Research, 2016). As described by Munoz et al. (2014), this nature of the origin of funds is crucial for operating on a not-for-profit business model. Unlike shareholder in pharmaceutical companies, public and philanthropic organizations do not measure the return on investment in terms of profit maximization. Rather, these organizations are more concerned with the ability of PDPs to deliver successful medicinal products that can make a public health impact. The charitable nature of funding allows PDPs to make attractive propositions to industrial partners. They can reduce the risk of product development for companies by entirely or partially paying for services throughout the product development value chain. For example, they pay to contract research organizations for clinical trials. This cost-sharing, which PDP themselves do not want to recover, gives them the ability to negotiate the pricing conditions with the industrial partner and is crucial for delinking the price of final products from R&D costs. Moreover, for large multinationals, alliances with alternative pharmaceutical R&D organizations may not primarily be motivated by commercial returns, but they also serve towards improving their public image and a part of their corporate social responsibility. Moreover, such partnerships are also valuable for strategic considerations like positioning themselves in developing country markets (Moran, 2005). On the other hand, small firms have not only commercial interests but also the incentive to build capabilities and gain legitimacy by associating with reputed agencies (Eisenhardt & Schoonhoven, 1996; J. F. Li & Garnsey, 2014; Moran, 2005).

A report by Policy Cures Research (2016) found that, in 2015, PDPs received combined funding of $450 million. Of this, philanthropic organizations accounted for 59% ($268 million), and 36% ($164 million) came from high-income country governments primarily routed through their aid agencies ($145 million). Nearly all of the remaining funding came from multilateral public-sector organizations ($17 million, 3.9%), mainly Unitaid which invested $16 million through PDPs to support the development of pediatric formulations for HIV/AIDS, TB, and malaria.

4.2.2.2. Open and Collaborative Innovation

Another common aspect of PDPs originates from their collaborative action with a diverse set of partners which requires integrating the various parts of the innovation process (Chataway et al., 2007). Medicines are the outcome of a complex and expensive research and development

process involving multiple steps that can span over a decade and is highly uncertain (Lipsky & Sharp, 2001; Scherer, 2010). However, most PDPs do not have in-house R&D or production capabilities (Chataway et al., 2007; Munos, 2006; Muñoz et al., 2014).

The uniqueness of PDPs lies in the ability to overcome this challenge by employing "open innovation" approach. According to Chesbrough (2003; Chesbrough & Crowther, 2006), open innovation allows a firm to look for new sources of innovation beyond its boundaries. Thus, the boundary of the firm becomes permeable, and knowledge can flow both ways, i.e., from inside the firm to outside and from outside to inside.

In fact, PDPs rely on a diverse set of actors like government and private philanthropic donors, universities, public research laboratories, contract organizations and pharmaceutical companies working in collaboration. PDPs slice and dice the development project into small packets and outsource it to partners throughout the value-chain. Thus, PDPs engage and leverage diverse resources and capabilities of partners to mimic like vertically integrated pharmaceutical companies (Hughes & Wareham, 2010).

The collaboration also results in the formation of an innovation ecosystem consisting of a variety of actors involved in knowledge generation. The ecosystem functions towards the specific goal of discovering, developing and delivering a selected pharmaceutical product at affordable prices to patients in the global South. All actors in such an ecosystem have different organizational identities, and each actor adds some unique resource or capability to the system (Brinkerhoff & Brinkerhoff, 2004; J. F. Li & Garnsey, 2014; Moran, 2005). Academia and other public health institutions do not have all the necessary capabilities needed for bringing a pharmaceutical product to market even if there is a will to do so. Research organizations are involved primarily in making early phase discovery and optimization of medicines which are limited to laboratory scale. However, successful product development involves further steps that include passing through clinical trials, regulatory approvals, and scale-up from laboratory to industrial manufacturing, sales, and distribution. These capabilities lie with pharmaceutical firms. Working as an ecosystem allows the participating agents to create values and attain goals that none of them could have achieved alone (Adner, 2006; J. F. Li & Garnsey, 2014).

Moreover, each ecosystem is a unique and sophisticated unit dedicated to a single product with specific partners. Since the organization of research, development, and delivery is oriented around a target product, the same PDP can have numerous sets of ecosystem depending upon

their product portfolio. For example, two major PDPs, MMV and DNDi have 47 and 30 products respectively in their portfolio which are at different stages of development. This leads to a complex and intricated network of relationships between a given PDP and its partners some of which can be working on multiple projects. The complexity of such relationships is further increased if we take into account that few pharmaceutical companies, donors, research labs and contract research organizations work across PDPs.

Thus, PDPs act as hubs and integrators by bringing disparate actors together to work towards a common goal (Chataway et al., 2007). They assume the central role of integration and coordination in the ecosystem and use private sector management practices to drive product development. Most PDPs manage a portfolio of projects that allow them to pursue multiple avenues of innovation while diversifying risk and increasing the chance of success (Grace, 2010; Muñoz et al., 2014). Their main managerial task is the selection of projects and partners, management of R&D portfolio and coordination of information throughout the R&D chain. PDPs have independent scientific-advisory boards which are tasked with the selection of projects and partners based on the scientific merit, technical feasibility and ability to meet the priority health needs of developing countries.

Further, the ecosystem created by PDPs is not a geographically localized cluster but rather a global network of partners allowing them to trap the knowledge infrastructure surpassing national boundaries. Here the knowledge infrastructure refers to the way in which R&D is done, IPRs processed, human capital is managed, and funding is secured.

However, PDP ecosystems operate within the framework of existing institutions such as safety and efficacy rules for drug development, medical ethics, IPR regime but simultaneously creating space for new constitutive and regulatory rules as to how pharmaceutical R&D should be conducted and how its fruits should be distributed.

4.2.2.3. Access to End Product through IPR Negotiation

PDPs are working not only to bring products to market but also to guarantee affordability. Their non-profit investment creates space to de-link R&D costs from product pricing. They ensure that the final product is brought to the market with a pricing structure that warrants equitable access. They actively negotiate the process management of intellectual property with academic

and institutional partners often with flexibilities that allow for easier technology transfer and licensing agreements to developing country manufacturers. In fact, distribution of the terms of use associated with intellectual property has emerged as a distinctive and recurring feature of PDPs. For example, the fixed-dose combination of "artesunate-amodiaquine" was developed by DNDi-Sanofi partnership as a "non-exclusive, not-patented, not-for-profit public good" (Pécoul et al., 2008). Similarly, the fixed-dose combination of "artesunate-mefloquine" was developed by DNDi and the Brazilian government company Farmanguinhos/Fiocruz. Later, DNDi assisted an agreement between Farmanguinhos/Fiocruz and Cipla which agreed to supply the medicine at pre-agreed affordable prices to developing countries (S. Wells et al., 2013).

This way of managing IPR is contrary to the prevailing practice by pharmaceutical firms who prefer exclusive property rights and aggressively defend their position through litigations (Correa, 2004). Pharmaceutical firms emphasize market valuation and capital accumulation over public interest (D'Mello, 2002). Exclusive rights over intellectual property pertaining to pharmaceutical research not only deters further innovation by blocking valuable inputs but it also creates barriers to access to treatments (Orsi & Coriat, 2005; Orsi, Hasenclever, Fialho, Tigre, & Coriat, 2003; Sampat, 2009). A Federal Trade Commission (FTC) inquiry in 2002 reported that in the US, nearly 75 percent of the new drug application by generic manufacturers experienced legal actions under the patent law by the originator patent holder. They claimed that these litigations were driving the cost of drugs in the US by keeping the cheaper generic versions out of the market (Wroblewski, 2002).

On the contrary, PDPs are breaking the norm by redefining rights in a way which ensures their functioning in line with the objective of their creation of optimal social outcome (Arrow, 1962; Nelson, 1959). PDPs' management of IPR is unique because it is not rooted in the absence of rights. Instead, it is more subtle and related to how the patent is intended to be used, i.e., how these rights can be used to ensure equitable access. It involves deciding the how the rights over the knowledge and products created during the research will be shared, whether the product can be commercialized and if so by whom and under what conditions. Moreover, each product under the portfolio of a PDP is unique and different PDPs have different subjective conceptualizations of the right way to get to their objective. As such, there is not a single path. The scope of distribution of rights may vary from one product to another and from one PDP to another, but on a broader scale, it is always oriented towards the objective of making safe and

effective medical technologies available in sufficient quantities at affordable prices for patients in developing countries.

For example, the IPR policy of MMV explicitly states that,

"If IP is generated during a given research programme, it is not essential that MMV will take an ownership position in it to accomplish its mission. If, however, ownership of IP does not vest in MMV, MMV will insist on appropriate license rights to any compound(s) being developed under its portfolio (Italics added)."[72]

Similarly, the objective of DNDi's IPR is t*o*

"ensure that drugs are affordable to and access is equitable for patients who need them and at the same time to develop drugs as public goods swhen possible."[73]

Pharmaceutical products are tangible goods, and as such, there is an inherent cost of their production and distribution. Any pharmaceutical partner will need to recover these costs and make profits. PDPs draw definite boundaries within which the possibility of making a profit by an industrial partner, if any, is marginal. However, outside these boundaries, partner firms have the possibility of making profits. In this regards, PDPs actively negotiate with their industrial partner(s), which territories (disease-endemic countries) and which sectors (public or private) within territories will get preferential access to technology and at what prices (Grace, 2010). They also put in place mechanisms to monitor that the technology is developed and put in the market under the mutually agreed terms. Thus, PDPs offer a unique approach by demonstrating that IPRs can be used as an instrument to achieve the goal of equitable access to safe and effective medicines. They show that it is possible to get over the dilemma that arises when IPRs conflict with human welfare rights (Reisel & Sama, 2003). By including the terms of use of IPR in contractual agreements with partners they highlight the possibility of achieving a delicate balance between creating incentives for innovation and socially desirable outcomes.

Nevertheless, PDPs are not without limitations. A biggest concern for PDPs is their financial sustainability. In 2015, nearly half of the PDPs received more than half of their funding from a single funding agency, The Bill and Melinda Gates Foundation (Policy Cures Research,

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[72] https://www.mmv.org/sites/default/files/uploads/docs/policy_documents/MMV_and_Intellectual_Property_Rights.pdf

[73] https://www.dndi.org/wp-content/uploads/2009/03/ip%20policy.pdf

2016). For a long-term survival PDPs would need new avenues of funding. Even more so, dependence on a single large funding source can also influence the direction of research from what is needed and acceptable to patients and governments in developing countries to what is the priority of the donor (Muñoz et al., 2014).

Further, there is an inherent question linked transparency. PDPs play a role of facilitators across partners including donors, universities and the private sector who do not necessarily share the similar worldview. However, PDPs do not disclose the conditions of their agreement with partners (Muñoz et al., 2014). This becomes even more important as PDPs have a strong presence of the pharmaceutical industry on their board and scientific committees (Branciard, 2012) which may lead to conflicts of interest.

Another criticism of PDPs emanates from their success by targeting low-hanging fruits in neglected diseases research (Munos, 2006; Muñoz et al., 2014). They have delivered products by investing on developing new formulations and applications of existing molecules and developing novel dosage forms such as fixed-dose combinations and child-friendly treatments. PDPs like MMV and DNDi have already started investing in NCE research and maintain a rich a portfolio of NCEs several of which are in later stages of development. In fact, the present study investigates the development of one case but how far they can go towards delivering treatments based on new chemical entities (NCE) remains a question as the process is long, complex, expensive and full of uncertainties.

4.3. The Story of Synriam

4.3.1. MMV: A PDP Dedicated to the Development of Antimalarial Medicines

By the late 1990s, malaria has reemerged as a global public health threat and was killing over a million people most of them located in Sub-Saharan Africa (Krogstad, 1996; Malakooti et al., 1998; Murray et al., 2012; Nchinda, 1998). Most of the classic treatments like quinine, chloroquine, proguanil, and mefloquine were already ineffective due to the rise of parasitic resistance (Lin et al., 2010; Wongsrichanalai, 2002). At the time artemisinin derivatives such as “artemether”, “artesunate” and “Dihydroartemisinin” were the only group of molecules that was highly effective against malaria parasites. However, there was growing fear that using these molecules as monotherapies may lead to a quicker emergence of resistance rendering

them useless. Researchers suggested using artemisinin derivatives in combination with other parasitic drugs with antimalarial action, i.e., the use of artemisinin-based combination therapies (ACTs), to delay the onset of resistance (Bloland, 2001; Bloland, Ettling, & Meek, 2000; White, 1999).[74]

However, there were two problems with the use of ACTs. First, combination treatment can be offered either as a fixed-dose combination (FDC), where two active ingredients are combined in the same pill or as co-blister where two different molecules are presented separately but in the same pack. FDCs are considered more useful than co-blisters for adherence to treatment by patients. By 2000, there was only one ACT, "artemether-lumefantrine" that was available as FDC (Spar & Delacey, 2008). Second, most of the malaria incidence and mortality is concentrated in children less than five years of age (Carneiro et al., 2010; Hay et al., 2010) but artemisinin derivatives were developed during the Vietnam War by the Chinese (Miller & Su, 2011). So, these drugs specifically targeted adults.

Moreover, despite breakthroughs in medical sciences, investment into R&D for new antimalarial drugs by the US government had reduced post-Vietnam conflict significantly, and private sector had no interest in developing medicines for which return on investment was low (Arrow et al., 2004, p. 305). As such, there was an immediate need for new and more adapted treatments to combat malaria.

It was in this lack of antimalarial pipeline that several public and private stakeholders joined hands to create Medicines for Malaria Venture (MMV) to catalyze the development of new medicines. MMV was among the first public-private partnership to address the lack of pharmaceutical R&D for a dominant global disease. Among the partners in the initial discussion were the TDR, the Rockefeller Foundation, the Wellcome Trust, the Global Forum for Health Research, the World Bank, the Swiss Agency for Development and Cooperation, the Association of the British Pharmaceutical Industry, the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), Glaxo Wellcome and Hoffmann-La Roche (Roche) (MMV, 2000). MMV was conceptualized with the idea to bring the relative strengths of pharmaceutical industry in drug discovery and development and public sector in

[74] It would not be until 2006 that WHO would recommend the use of ACTs as the first line treatment against malaria in all endemic countries. For more details on ACTs please see Chapter 2, Section 6.

basic biology, clinical medicine, chemistry, and field experience to create a dynamic partnership to handle malaria drug discovery *for public health as a global public good* (Arrow et al., 2004, p. 305; MMV, 2000). MMV underwent an incubation period (1998-1999) at the WHO/TDR until it was officially launched as an independent Swiss foundation in November 1999. The initial seed finance of $4 million came from the Government of Switzerland, UK Department for International Development, the Government of the Netherlands, The World Bank and Rockefeller Foundation.

MMV pursues a not-for-profit business model. Each year it launches a call for research proposals which are reviewed by an Expert Scientific Advisory Committee (ESAC) consisting of members from both industry and academia covering a full range of expertise needed to assess the complex drug development process. Selected projects are included in MMV's portfolio, and R&D is outsourced to a consortium of partners. Each project is handled by a specific project manager who is responsible for its monitoring and coordinating with partners. Further, all projects undergo an annual review process by the ESAC which decides their continuation or termination. MMV collaborates with an industrial partner with good manufacturing and distribution capabilities, ideally before phase III clinical trials, for clinical development and bringing the final product to market. The contractual agreement is negotiated to ensure that medicines will be adequately available and affordable in endemic malaria countries (MMV, 2016).

The business operation of MMV is funded through donations from governments and philanthropic organizations, the most notable being the Bill and Melinda Gates Foundation. Since its establishment, MMV has spent $778 million to create a dynamic portfolio of 47 projects including six already in the market (MMV, 2017).

4.3.2. Discovery of Arterolane: Outcome of a Multi-Stakeholder Partnership

Origin of Synriam lies in the research project that investigated the potential to synthesize and develop synthetic peroxides as potential antimalarial candidates. The project was started by Roche in the early 1990s. Roche collaborated with a group of chemists under Prof. Jonathan Vennerstrom at the University of Nebraska. However, it stopped all antimalarial development in the mid-1990s (1996/97) but not before transferring some of its equipment and even technicians to the Swiss Tropical and Public Health Institute (Swiss TPH).

In 2000, when MMV became truly operational, the synthetic peroxide research was one of the first projects that it started to support and manage. A consortium was formed between three academic partners under the guidance and funding from the MMV: University of Nebraska Medical Center under Prof. Vennerstrom's group to do the chemistry, Swiss TPH (Prof. Reto Brun) to do parasitology work, and the team of Prof. William Charman at Monash University to do key pharmacokinetic and metabolism studies. The project also received pro bono support from Roche during the project.[75] The combined expertise of these research groups led to the discovery of arterolane (OZ277 and later RBx-11160), and the patent was filed in 2002[76]. The molecule exhibited structural simplicity, economically feasible and scalable synthesis, superior antimalarial activity and enhanced biopharmaceutical profile (Vennerstrom et al., 2004). As such, arterolane was selected as an optimal candidate to go into Good Laboratories Practices (GLP) compliant pre-clinical testing and first-in-human trials.

4.3.3. Ranbaxy: An Industrial Partner Looking for Opportunity

To take the molecule through clinical development and manufacturing an industrial partner was needed. Roche, which was associated with the arterolane development since the beginning, had already indicated its intention of not re-entering the malaria market even though the molecule resulted from its initial work. MMV intended to engage with a company from a malaria-endemic country, and Ranbaxy was identified as an ideal partner.

The company was incorporated in 1961 and was the first Indian pharmaceutical company to internationalize. It started exporting in 1975 (Bartlett & Ghoshal, 2000) and soon established subsidiaries in other developing countries, primarily in Asia and Africa. It formed a minority joint venture (10%) in Nigeria in 1977 followed by a majority joint venture (53%) in Malaysia in 1984 (Kale, 2010a). However, Ranbaxy was at the bottom of the pharmaceutical value curve.

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[75] Heinrich Urwyler who used to work on anti-infectives in Roche as pre-clinical toxicology expert moved to Basilea Pharmaceutica Ltd. (A spin-off from Roche). He had a greenlight from the Baselia management that he could spend a certain amount of his time supporting the MMV collaboration. There was also a parasitologist scientist from Roche who spent 10-15% of his time on this project.

[76] https://www.google.com/patents/US6906205

While it its formulation business was growing in India, its foreign exports mainly consisted of bulk drugs and intermediaries (Athreye & Godley, 2009; Bartlett & Ghoshal, 2000).

Ranbaxy's foreign market strategy received a significant push in 1993 when Parvinder Singh became the CEO and chairman and restructured the company with the new corporate mission to "become a research based international pharmaceutical company" (Bartlett & Ghoshal, 2000; B. R. Kumar & Satish, 2007). The primary focus of the renewed strategy, which was also influenced by the prospects of the arrival of a stringent patent regime in India in the form of impending TRIPS agreement, was developed country markets (Athreye & Godley, 2009; Kale, 2010b). By 2002, Ranbaxy had acquired subsidiaries in prominent markets like the US, the UK, Canada Germany and Japan and more than half of its revenue was coming from international operations (Bartlett & Ghoshal, 2000; Bowonder & Mastakar, 2005; Kale, 2010a; Mowla et al., 2014; Yeoh, 2011).

Ranbaxy's motivation to become a genuine research-based company also lead it to invest in developing technical capabilities mainly in new drug discovery research (NDDR) and novel drug delivery systems (NDDS). This early decision to invest in R&D turned out to be productive and valuable. Ranbaxy developed a novel oral dosage form of "ciprofloxacin" – antibiotic medicine originally developed by Bayer AG. The blockbuster drug was marketed as "Cipron" had a turnover of around $1.5 billion in 1998 (Evaluate Group, 1999). Ranbaxy's once-a-day oral formulation was an improvement over Bayer's twice-daily dosage form in terms of patient compliance and convenience. In September 1999, Bayer entered into a $65 million licensing agreement with Ranbaxy to get exclusive development and worldwide marketing rights. The agreement also secured a 10% royalty on sales of the product (Basant, 2010; Evaluate Group, 1999). In the same year, its first proprietary NCE, RBx-2258 for Benign Prostate Hyperplasia had received DCGI approval for conducting clinical phase I (B. R. Kumar & Satish, 2007). The molecule was subsequently out-licensed to Schwarz Pharma in 2002 for further development (Bowonder & Mastakar, 2005). It had also filed Investigational New Drug (IND) applications for asthma molecule RBx-4638 in 2000 and antibacterial RBx-7644 in 2002 (Bowonder & Mastakar, 2005).

So, Ranbaxy already had initial success in new drug discovery research. However, it had no experience in taking a product alone from pre-clinical development to launch. Therefore, when

MMV approached it for the development of arterolane, the company took it as a learning opportunity. As one respondent explained:

"If Ranbaxy had to develop a product then how to go? One of the ways was to collaborate with people who are already into drug development. So, it (MMV partnership) was supposed to be a training program for Ranbaxy."

A formal contract between MMV and Ranbaxy was signed in 2003. In line with its mission, MMV did not expect any return on investment, and the objective was to make the drug adequately available at affordable prices in malaria-endemic countries. The contract separated public and premium markets. The main focus was the former to which Ranbaxy agreed to supply the final product in adequate quantities at cost plus a small mark up. A premium market such as the US could be subjected to different pricing and from that MMV expected a milestone royalty payment. Until then Ranbaxy had restricted its R&D activities to few valuable disease areas such as cancer, central nervous system disorders or cardiovascular problems (Kumar & Satish, 2007).

Malaria was not on its research agenda as the company did not consider it a good return on investment. Joining hands with MMV meant that it could learn from MMV's supervision as well as gain reputation while not investing much money. As explained by another respondent as:

"Ranbaxy entered into the contract thinking it as a win-win situation. The company was involved in the development part like defining dosage and so on but MMV was the major financial partner. So, the project will give us a good name, and we will not put in money also."

In fact, throughout its development, Synriam (the brand name that was later given to the combination of arterolane and piperaquine) remained associated with Ranbaxy's respect factor. There was a consensus in the management that Synriam will have a good impact on company's reputation even more at the time when the company was going through quality issues with the US FDA and the WHO. This shows that working with PDPs developing country firms can not only learn and reduce risks but also gain legitimacy.

4.3.4. Project Reorganization after MMV-Partnership Ended

By 2005, the program had moved from pre-clinical to clinical studies. Also, following the WHO recommendations of using combination therapy for the treatment of malaria, piperaquine was identified as the partner drug. However, the results of the phase II trials of arterolane monotherapy were disappointing for MMV as it effect was aberrant and efficacy was low. First, arterolane showed decreased exposure, i.e., low plasma concentration in malaria patients compared to healthy volunteers (Saha et al., 2014; Valecha et al., 2010). It meant that malaria parasite had direct contact with the drug for a shorter time as it was quickly eliminated from the body. So, for effect to last longer subjects needed to take a higher dose of the drug than what was originally expected. Second, even at the high concentration (once daily dose of 200 mg for seven days), the recrudescence was between 28% and 37% (Valecha et al., 2010). This was much higher compared to artesunate monotherapy which has a cure rate of over 90% for a six-day treatment. These results did not fit MMV's target product profile. In March 2006, MMV expert committee recommended not to invest any further in the project, and MMV decided to pull out after having invested nearly US$ 28.8 million of which US$ 7 million was dedicated to on discovery activities, and rest was directed to pre-clinical toxicology, phase I and phase II trials and manufacturing.

By the time MMV parted ways, pre-clinical studies, phase II trial of the single agent (arterolane) and phase I of the combination consisting of arterolane and piperaquine (Synriam)[77] had been accomplished. So, the primary tasks that were left included phase II and phase III trials of the combination drug. As a part of the break-up, Ranbaxy also got the license to exploit the patent on arterolane. However, Ranbaxy had internal financial targets and was in no position to divert to the project and the management considered that the return on investment on an antimalarial drug was not going to be much. However, initial results indicated that combination product had no such issues that were observed in arterolane monotherapy and management decided to take the project further. One respondent pointed out:

"This was a new chemical entity (NCE) in the mid-stage of development, and there was a confidence that this could become a product."

[77] This combination product would be later branded and marketed as Synriam by Ranbaxy.

To move further, Ranbaxy reorganized project targets and restructured the finances. The initial idea of the MMV-Ranbaxy partnership was to develop a full range of products (pills, intravenous, rectal suppository) but the withdrawal of finances required Ranbaxy to rethink the strategy. It was decided that it might be possible to develop the basic product which would not require a lot of resources. Additional help came from the Department of Science and Technology, Government of India. It signed a public-private partnership with Ranbaxy under Drugs & Pharmaceutical Research Program and provided financial support through a loan of $1 million in 2007.[78]

Phase II trials were finished in 2008 (Valecha et al., 2012). In the same year, the Japanese firm, Daiichi Sankyo acquired Ranbaxy. It was evident that they overtook it for its generic business. The Japanese focused on the generic development with the argument that it is where that the strength of the company lies. In the reorganization, drug discovery division of Ranbaxy became the part of Daiichi Sankyo's portfolio, and Ranbaxy was limited to generic business only. Nevertheless, Synriam project remained with Ranbaxy. Indian government once again extended a grant-in-aid[79] of $2 million towards phase III trials and the development of a pediatric formulation with Ranbaxy's commitment to supply the final product to the public sector at a preferential price. Part one of the phase III trials were done in India as the government wanted most of the money to be spent in the country. Nevertheless, heat waves and the resulting drought caused a reduction in the cases of malaria. So, new collaborations were searched, and Ranbaxy identified several sites in Africa and Asia (Democratic Republic of Congo, Malawi, Mali, Ivory Coast, Senegal, Mozambique, Bangladesh, and Thailand) to complete the trial (Toure et al., 2016).

4.3.5. Bringing Synriam to Market

Arterolane component of Synriam was a new chemical entity, and Ranbaxy was the first company to bring the product to market which meant it had to generate its own safety and efficacy data. Going through stringent regulatory authorities (SRAs) such as the European

[78] http://dst.gov.in/sites/default/files/drugs%26pharma06-07.pdf

[79] http://dst.gov.in/sites/default/files/drugs-08-09.pdf

Medicines Agency or the US FDA was difficult and expensive, and Ranbaxy was already facing budget constraints post MMV exit from the project. One manager explained:

"We did not have that kind of budget or support. Till the time MMV was partnering we could have had done two trials but for Indian pharmaceutical to do two phase III with 1100 subjects was very difficult" So, we restricted to single phase III trial that included both Indian and African patients."

The company decided to register the product first in India where regulatory requirements are not as stringent as those of the US FDA or the EMA. This was regarded as the shortest path to bring the product to market. In 2011, Synriam was granted a market authorization for treatment against *falciparum* malaria in adults by the DCGI based on an interim analysis of Phase III data.

Indeed, this is not unusual. Novartis had first registered "Coartem" (artemether-lumefantrine) in Gabon in 1998. The product was subsequently approved by the Swissmedic in 1999 and received a WHO prequalification in 2004 (Hamed & Grueninger, 2012; WHO, 2011a). Similarly, Branciard (2012) notes that to shorten the delay in launch, Sanofi initially registered "Winthrop" (fixed-dose combination of artesunate-amodiaquine) in Morocco in 2007. The product was prequalified by the WHO in 2009.

Moreover, there was a question of trust among stakeholders as to why MMV had left the project. So, Ranbaxy created a *Universal Product Team* and engaged in active campaigning to create awareness regarding the Synriam through meetings, conferences, and workshops especially among the key opinion makers such as doctors and researchers. Earlier, Ranbaxy had also brought scientists leading the malaria research in India on board to conduct phase II and phase III clinical trials so that they have the first-hand experience regarding the safety and efficacy of the drug. The idea was to create a noise vis-à-vis the product before its launch. A strategy that Ranbaxy would later follow in the African market as well. In the words of one manager, the idea was *"to create the market before the launch"*.

The unique selling point was the low pill burden of Synriam. It was one tablet a day, three days regimen – an advantage over existing ACTs. The company also sponsored articles in newspapers to create awareness about malaria among the general population.

It was officially brought to the Indian market on 25 April 2012 to become the first NCE to be brought to market by an Indian company. Synriam was launched with a big fanfare by then the health minister of India and received widespread media attention. The reputational impact of this product is reflected by the following remark of Arun Sawhney then the CEO and Managing Director of Ranbaxy:

"This is a historic day for science and technology in India as well as for the pharmaceutical industry in the country. Today, India joins the elite and exclusive club of nations of the world that have demonstrated the capability of developing a new drug."[80]

4.3.6. Market Entry to Africa

Indian approval was given on the basis of an interim analysis of Phase III data and Ranbaxy waited for the completion of the trial before initiating the product registration process in Africa. In fact, since the beginning of product development, the target was the international market. Ranbaxy was well aware that the market was competitive. Countries in Sub-Saharan Africa had already included one or more ACTs as the first line of treatment against malaria in their national guidelines following the WHO recommendations. Further, several firms already had WHO prequalified ACT products. So, Ranbaxy faced institutional barriers. First, Synriam was a new product with a single phase III clinical trial. As such, it was not recommended by the WHO for the treatment of malaria, nor was it on the WHO List of Essential Medicines. Consequently, it was neither recommended by national malaria treatment guidelines in African countries nor was it on the respective national essential medicines list as they are guided by the WHO framework (Laing et al., 2003; Waning, Kyle, et al., 2010). Second, public sector procurement through donor-funding plays a crucial role in the uptake and distribution of antimalarial medicines. Synriam was not approved by an SRA or prequalified by the WHO. Therefore, it was not eligible for procurement by major international donors such as the Global Fund.

So, Ranbaxy intended to getting market authorization for Synriam in Sub-Saharan countries based on its approval in India and introduce it in the private market. Countries were selected

[80] Evaluate Group (2012)

on the basis several factors. First, the burden of malaria in the target country was to be high to ensure a larger market to compete. Second, the company also took the ease of registration into account. It meant choosing countries which did not require being on the national list of essential medicines or a prequalification by the WHO as essential criteria for antimalarial product registration. Most countries where the product was launched needed only a *certificate of pharmaceutical product (COPP)* from the government of India for market authorization. Third, in those countries, Ranbaxy already had an established business operations. This was for the reasons of legitimacy. As explained by one interview participant:

"Certain countries have a very good image about Indian companies. For example, Kenya. While there are others that are not so open about Indian companies."

Further, Ranbaxy planned to introduce Synriam in as many countries as possible to make its presence felt even if it could not tap all the market. This strategy was also guided by the motivation to generate safety and effectiveness data in real-world settings which could be useful in future for prequalification by the WHO or other regulatory authorities.

Moreover, there was also this consideration that if a country like Kenya approves the medicine, then certain other countries in the region would follow suit. In fact, countries like Kenya, Uganda, and Tanzania have a better regulatory system. So, the idea was that if awareness is created in these countries and product is approved then it would create noise in the region and subsequent registration in neighboring countries would be easy.

Marketing team got in contact with malaria experts in the region; lots of workshops were organized to create awareness. Buzz was created in every country registration was filed, and the product was launched. Phase III had shown excellent results, and this information was widely distributed by word of mouth and through experts. By 2015, the product had received marketing approval in 12 Sub-Saharan countries and was launched in 9 (Table 4.2).

However, WHO has still not made general recommendations regarding the use of Synriam due to insufficient data (WHO, 2015b). Further, the product has still not received a WHO prequalification or approval from an SRA. Therefore, its uptake is limited. Nevertheless, phase III trials for Synriam in pediatric subjects have been completed with positive results (Toure et al., 2017) and may prove valuable for future success.

Table 4.2: Timeline of development, testing and regulatory approval of Synriam

Year	Achievement(s)
2002	Patent for Spiro and dispiro 1,2,4-trioxolane antimalarials filed with the USPTO (US6906205 B2)
2003	The agreement was signed between MMV and Ranbaxy for the development of a new antimalarial drug (then code-named OZ 277 and later arterolane). Pre-clinical and pharmaceutical development of arterolane was initiated
2004	First-in-human study with arterolane completed in the UK
2005	Proof of concept trial completed in Thailand; piperaquine identified as partner drug
2006	Phase II trial with arterolane conducted in Thailand, Tanzania and India and Phase I study of combination drug initiated
2007	MMV left the project; Collaboration between Ranbaxy and Department of Science and Technology, Government of India. Phase II trial of the combination initiated in India and Thailand
2008	Completed Phase II trial and received approval for Phase III trial
2009	Phase III trials in *Plasmodium falciparum* malaria initiated in India, Democratic Republic of Congo (DRC), Malawi, Mali, Ivory Coast, Senegal, Mozambique, Bangladesh, and Thailand
2011	Drug Controller General of India (DCGI) granted approval to India's first new drug, Synriam for the treatment of acute uncomplicated *P. falciparum* malaria
2012	Synriam, India's first new drug, an anti-malarial product was launched successfully.
2013	Synriam got DCGI approval for the treatment of adult patients with *P. vivax* malaria. DCGI approval was received for conducting phase III study in pediatric patients with *P. falciparum* malaria
2015	DCGI approval was received for the conduct of Phase III study in pediatric patients with uncomplicated *P. vivax* malaria
2013-2015	Synriam has received marketing approval in 12 African countries (Senegal, Guinea, Kenya, Nigeria, Uganda, Cameron, Mali, Ivory Coast, Malawi, Gabon, DRC, Mauritania) and launched in 9 countries (Senegal, Guinea, Kenya, Nigeria, Uganda, Cameron, Mali, Gabon, DRC).
2017	Phase III study in pediatric patients with *P. falciparum* malaria completed

Source: MMV, interviews and literature

4.4. Conclusion

This chapter highlights the role of PDPs as alternative approach to drug development motivated by social goals. These niche and new dimensions of innovation within the domain of economy and society are providing incentives to pharmaceutical firms from developing countries to enter drug development for some of the most neglected diseases. The case of Synriam reflects that firms find it valuable to enter into strategic alliances with PDPs for developing capabilities, accessing new markets and gaining legitimacy. This also provides credence to the argument of Benito et al. (2009) that firms use market entry modes in combination and mode adjustments are more common than previously thought. Ranbaxy was already undertaking local production in Africa and has a large export base when it entered in partnership with MMV. We can consider this alliance as a strategic addition to Ranbaxy's existing engagement with the African market which would have allowed it to enter a new disease with an entirely new and innovative product.

Furthermore, the case of Synriam is peculiar because the MMV-Ranbaxy partnership was broken before comprehensive clinical trials and shows the importance of regulations imposed by international organizations in shaping a firm's foreign market entry. Ranbaxy had to restructure the project and finances and take a renewed approach to market entry after MMV's withdrawal from the project. Consequently, going through an SRA route was not an option and the company decided to register the product with the Indian regulatory authority. This became a crucial factor to consider when Ranbaxy was launching the product in Sub-Saharan countries which account for 90% of the global malaria incidence. In the absence of WHO recommendation, it only chose those countries which had no such restrictions for market authorization. Moreover, lacking approval from an SRA and prequalification from the WHO limited the scope of Synriam to the private market only. The case indicates that institutional environment shaped by international organizations can play a crucial role in determining firm strategy. This is especially true in the context of AIDS, tuberculosis, malaria and neglected tropical diseases which have become the focus of global development agenda and emphasized by the Sustainable Development Goals.

The study also had a few limitations. First, it relies on a small set of interview participants. Nevertheless, the details provided were rich and the overlapping information triangulated across participants suggesting the validity of their responses. Further, the study derives from

the examination of a single product from a single PDP (MMV) whereas, the PDP world is much larger. Future research comparing product development across several PDPs would not only help to shed more light on firm strategy but can also be used to answer an important question regarding the extent to which PDPs can be regarded as common-based approach for producing pharmaceutical technologies.

5. General Conclusion

This thesis started the discourse by demonstrating that the existing literature on the foreign expansion of Indian pharmaceutical firms has taken a reductionist approach towards the African market by treating it as an intermediate step in the process of internationalization. We did not find a single study dealing with the subtleties of the pharmaceutical market in Africa and functioning of Indian firms therein. The thesis undertook a quest to examine the market entry and operation strategies of Indian firms in Africa under the analytical frame provided by the neo-institutional theory which focuses on firm behavior under the influence of external environment. Researchers have already established that strategic choices made by firms are shaped by their interaction with the external environment as firms adapt and adjust their strategies to ensure survival. So, the argument that institutions matter is neither new nor does it necessitate further debate, but instead our exploration was concerned with how institutions matter.

In this light, the thesis contributes through an empirical approach by illuminating the importance of institutions as important factors behind the internationalization of Indian pharmaceutical firms within the African context. It shows that generic facilitating policies like the adoption of a National Essential Medicines List and procurement of generic medicines by the Central Medical Stores in African countries created opportunities for Indian firms to engage in these markets. The thesis also elucidates the emergence and governance of donor-funded markets which not only rely on the supply of Indian generic products but have also played a crucial role in the legitimization and transformation of Indian firms from “pirates” to the “pharmacy of the developing world”. These markets are quite specific to pandemics like HIV, TB and malaria and increasingly to a growing number of neglected tropical diseases where global health agencies are intervening throughout the pharmaceutical value curve and also fixing the regulatory criteria for the acceptance and absorption of new products.

Further, the empirical investigation of the Francophone West African market through the case of Mali demonstrated that the general architecture of the pharmaceutical supply chain consists of four different market segments government-funded public market, donor-funded public market, formal private market and informal market. These segments differ in their construction, organization, regulation, functioning, and size. Moreover, the donor-funded market mimics the highly regulated market of developed countries with high entry barriers such as stringent requirements for medicine quality. As such, not all firms have capabilities to operate in this market. Based on this differentiation, this thesis reveals that the operation strategy of Indian firms is guided by the institutional characteristics of the segment in which they intend to operate. Indian firms are using only export with market seeking motivations to cater the Francophone West African market, but the organization of export varies from one segment to the other as they deal with different market actors, quality regulations, and distributional channels. In the case of the formal private market, export can further be supported by on-site representatives and promotion activities which may be outsourced to a third party.

Furthermore, the simultaneous pursuance of multiple market segments and the adaptation of export and product strategy to meet segment-specific requirements results in a combination of modes or "mode package". In such mode packages, mode adjustments are not uncommon, and new modes can be added and subtracted from the existing packages as we found in the case of Ajanta Pharma. Similarly, in the case of Synriam, Ranbaxy's alliance with MMV was a strategic step that added to its existing engagement with the African market. These findings provide further credence to the propositions of researchers like Benito et al. (2009) and Petersen and Welch (2002) that international business operations of firms are better explained by looking at entry modes as combinations.

This thesis also demonstrates that the underlying institutional structure may also create barriers to entry for Indian firms. This is evident in the case of Francophone West Africa as well as in the case of Synriam. In Francophone West African countries private market is controlled by a handful of importers (Mali is an exception) who handle their business from France. While this helps them to consolidate the Francophone market, it leaves little strategic option and room for negotiation for Indian firms to operate in the formal private market of these countries. Similarly, Ranbaxy's Synriam though approved in India lacks approval and recommendation from the WHO. Thus, even if Ranbaxy had a long presence and well-developed business networks in Sub-Saharan Africa, it could only launch its product in selected countries where

WHO recommendation was not required for obtaining market authorization, and even then, it could sell the product only in the formal private segment.

While this thesis adds valuable contributions to the internationalization literature, it is not without limitations. The primary approach of this thesis has focused on investing the impact of external institutional environment on firm strategy. As such, it did not take into account firm-specific factors that may influence entry-mode choices. It has two aspects. First, it is well established that the interaction between firms and their external environment is dynamic and causal pathway goes in both directions (Dunning & Lundan, 2008; Fligstein, 1996; North, 1990). Firms not only comply and conform to external environment but they also take active measures to shape institutions to benefit from favorable business conditions at home as well as in host countries (Hellman, Jones, & Kaufmann, 2000). Lobbying by industry groups, bribes, gifts and other corrupt practices are not uncommon business practices. Managers can use interpersonal relationships with politicians and government officials to frame friendly policies and combat environmental uncertainty by gaining access to scarce information and resources.

Second, strategies of a firm also depend upon its resources (Barney, 1991; Barney, Ketchen, & Wright, 2011; Peng, 2001). While this thesis accounts for the fact that policy measures employed by the Indian government were crucial for sector-wide capability building of the Indian pharmaceutical industry and finds evidence that not all firms are capable of operating in all market segments, especially, donor-funded markets; it does not go into deeper exploration examining interfirm differences in market entry strategy stemming from differences in firm-specific capabilities.

Next, the thesis analyzed the case of a single country – Mali, as such its findings cannot be automatically extended in its entirety to countries beyond Francophone West Africa. This is because even though the general architecture of the pharmaceutical market in Sub-Saharan Africa consists of four different market segments, their organization, regulatory norms and market-size among other can significantly vary. Furthermore, several Indian firms have shown their commitment to the African market, especially in Commonwealth countries by undertaking greenfield investments and acquisitions. This would require examining a broader set of entry mode choices rather than just exports.

A next logical step would be to take a synergistic framework consisting of both institutional and resource-based views as already suggested by several researchers (He et al., 2013; Meyer

et al., 2009) to get a comprehensive picture of firm strategy. This analytical frame would allow taking into account not only the dynamic interaction between the firm and its environment but also firm-specific capabilities. Future studies embedded within the context of multiple African countries, focusing on selected Indian firms of different sizes and at different stages of internationalization, would allow identifying and comparing their strategies across different African countries and market segments due to the differences in institutional environment. Such studies would also allow for an understanding of the extent to which firm-specific resource endowments determine strategic choices and can be directed to investigate the action of Indian firms in shaping the institutional environment to strengthen and support their business operations by exploring their interactions with home and host country governments and international organizations

Next, there are also issues concerning the quality of medicines and patient safety which this thesis did not explore even though they are associated with the operations of Indian firms in Africa. Beyond doubt, the supply of generics at competitive prices by Indian firms has been crucial in increasing access to medicines in Sub-Saharan Africa. This is reflected from the fact that nearly a third of pharmaceutical products registered in Mali are of Indian origin. Similarly, donor-funded markets for HIV and malaria primarily depend on the supply from Indian manufacturers. In fact, data suggests that African countries import nearly 70% of their pharmaceutical need sourced mainly from Indian and Chinese manufacturers (KPMG, 2015), and this import dependency is expected to continue and grow in volume as well as value (BMI, 2015). Nonetheless, countries like India and China are not only a source of affordable medicines but have also emerged as the global hub of substandard and falsified medicines.

High import dependency of African countries from a diverse group of firms combined with human, financial and technical resource constraints, legal loopholes, and corrupt practices makes the regulation of pharmaceutical supply chain a formidable task. These factors not only jeopardize medicine quality in the formal sector but also contribute towards nourishing the informal market which is a prime source of poor quality medicines and as such a significant public health threat. Future studies comparing institutional frameworks governing the circulation of medicines across several African countries can be the first step to identify the regulatory gaps which facilitate informal pharmaceutical trade.

Lastly, we focused on a single PDP – Medicines for Malaria Venture (MMV) – and its involvement into the development of a specific antimalarial product focusing on a single firm (Ranbaxy; Chapter 4). However, the PDP-world is much bigger and is populated by a diverse set of entities which differ in terms of target diseases and products (vaccines, diagnostics, and medicines). They have played a crucial role in bringing neglected tropical diseases (NTDs) on the global health agenda and their importance in shaping the NTD research and bringing new, quality-assured, affordable and patient-adapted pharmaceutical products has been recognized and highlighted by the 2016 "Report of the United Nations Secretary-General's High-Level Panel on Access to Medicines". Nevertheless, our grasp of their market shaping actions is still limited. Further research through multiple PDP-centered studies is needed to assess their roles as catalyzers of innovation and their ability to produce pharmaceutical technologies as a public good. Such studies would also augment our understanding of their market shaping behavior and impact on the strategy of pharmaceutical firms.

To conclude, this thesis is a small step towards understanding the richness and complexities of the African pharmaceutical market and provides evidence to show that market entry and operation strategies of Indian firms are influenced by their interaction with states, markets, and international organizations.

6. Appendix

6.1. Algorithm for outlier detection and price standardizing

The analysis of prices requires special attention with regard to atypical observations. One way of avoiding this problem is to report median prices that do not take standard deviation into account and that are therefore not distorted by outliers. Nevertheless, using this strategy, essentially an "emergency exit", does not allow for further in-depth analyses: even the computation of unbiased confidence intervals is not possible. The straightforward statistical solution is to perform a "manual" screening under the univariate framework where a cut-off point is established on the basis of the standard deviation (i.e., prices that fall beyond the cut-off point are considered outliers). However, this univariate procedure does not take into account the fact that prices are linked to specific characteristics (i.e., geographical, economical, political, manufacturer, and drug characteristics, among others) that may have an impact on their relative value; this is a crucial aspect to take into account when working with the market intelligence data on pharmaceutical products. One particular feature of this data is the price heterogeneity introduced by the differences between Incoterms which makes the detection of outliers a challenging exercise. It is not possible to tell whether prices are atypical because of a problem in the reporting mechanisms (i.e. typographic errors) or because of the presence of different Incoterms. At the same time, the estimation of the relative differences of prices due to Incoterms has to be made within a framework that controls for the presence of outliers.

Ignoring outliers in a traditional multivariate framework like the Ordinary Least Squares (OLS) may result in erroneous inference. The underlying idea in this method is always to try to get as close as possible to the true value (of prices explained by different factors) by reducing the magnitude of residuals, as measured by an aggregate prediction error which is the sum of squared residuals (SSR) in the case of OLS:

$$\hat{\theta}_{LS} = \underset{\theta}{\operatorname{argmin}} \sum_{i=1}^{n} r_i^2(\theta) \qquad (1)$$

The expression in (1) is the objective function of the OLS technique, nevertheless, this criterion tends to award an excessive importance to observations with very large residuals and, consequently, the estimated parameters will be biased in presence of outliers.

Vertical outliers: prices are very different with respect to the mean (outlying in the y-dimension), but similar in terms of the explanatory variables (not outlying the x-dimension). *The presence of this type of outlier affects the estimation of the intercept.*

Bad leverage points: prices are very different with respect to the mean, but they are also very different in terms of the explanatory variables. These points are outlying both the y- and x-dimensions. *Their presence affects the estimation of both the intercept and the slope (parameters).*

Good leverage points: prices are similar with respect to the mean (not outlying the y-dimension), but they differ in terms of their characteristics (outlying the x-dimension). *Although their presence may inflate the standard errors of the estimated coefficients, this type of outlier does not affect the linear regression.*

In order to simultaneously deal with the presence of outliers and the need to estimate the relative differences in prices due to Incoterms, we used the MS-estimator (Maronna and Yohai, 2000). This technique is based on the combination of two types of estimators, and respectively two objective functions that are less sensitive to extreme values.

Step 1: S-estimator for continuous variables: the objective of minimizing squared residuals and σ^2 in OLS is replaced by a function $\rho(\cdot)$that awards less importance to large residuals:

$$\frac{1}{n}\sum_{i=1}^{n}\rho\left(\frac{r_i(\theta)}{\hat{\sigma}^S}\right) = b \qquad \text{with} \qquad b = E[\rho(Z)] \qquad \text{and} \qquad Z \sim N(0,1) \tag{2}$$

Formally, the S-estimator consists in finding the vector of parameters $\hat{\theta}_S$ that minimizes $\hat{\sigma}^S$ and is denoted as follows:

$$\hat{\theta}_S = arg\min_{\theta} \hat{\sigma}^S(r_1(\theta), \dots, r_n(\theta)) \tag{3}$$

For $\rho(\cdot)$ the most commonly used is the Tuckey-Biweight function. The S-estimator is resistant to a contamination of up to 50% of outliers, but with low Gaussian efficiency. The coefficients estimated for the continuous variables in this step, are used as given in the next step that consists in estimating the coefficients for the dummy variables.

Step 2: M-estimator for dummy variables: this estimator is resistant to vertical outliers and allows increasing Gaussian efficiency. It consists of finding the vector of parameters $\hat{\theta}_M$ that minimizes the following expression:

$$\hat{\theta}_M = arg\min_{\theta} \sum_{i=1}^{n} \rho\left(\frac{r_i(\theta)}{\sigma}\right)$$

The function $\rho(\cdot)$ is the same used in the S-estimator. Steps 1 and 2 are iterated until convergence. In this technique the S-estimator guarantees a high breakdown point, while the M-estimator ensures the Gaussian efficiency. This estimator is particularly helpful in the fixed effects panel estimation (Bramati and Croux, 2007). For the *legacy* dataset in the GPRM this seems to be the most adapted technique for controlling the individual effects of drugs, countries, and years by specifying dummy variables. The implementation of this technique not only offers the possibility of estimating the relative differences of prices due to Incoterms in an outlier-free context, but also to identify the outliers and to compute comparable Ex Works prices.

Empirical implementation of the MS-estimator

In order to estimate the model allowing outlier detection and price standardizing we have created the following variables:

1) Logarithm of unit prices
2) Geographic dimension: consists of 6 groups of countries according to the World Bank definition
    a. East Asia and Pacific
    b. Europe and central Asia
    c. Latin America and the Caribbean
    d. Middle East and North Africa
    e. South Asia
    f. Sub-Saharan Africa
4) Strength-specific drugs: dummy variables
5) Formulation type dummies: co-formulation/co-blister
6) Therapeutic class dummies
7) Dosage form dummies
8) Logarithm of the Total number of smallest units
9) Incoterm dummies
10) Year of transaction dummies
11) Manufacturer implanted in a developed/developing country dummy

3) Logarithm of the Gross National Income

per capita: specified as time-varying

continuous variable

The implementation of the MS-technique may be costly in terms of computational time, according to the number of explanatory variables specified. A part of the log (unit prices) which is our dependent variable, five variables are crucial in the estimation in order to calculate comparable Ex Works prices: Geographic groups, GNI per capita, Strength-specific drugs, year order, and Incoterms. This implies the specification of several dummy and continuous variables. A simple OLS stepwise regression not only confirmed the importance of these variables, but also suggested the introduction of the log (total number of smallest units), and the developed/developing country of manufacture dummy.

6.2. Calculation of ACT Procurement Volumes and Treatment Prices

Each transaction in the dataset was specific to a particular product and provided information on the name of ACT, manufacturer, strength, package description (for example, a box of 30 blisters of Artemether + Lumefantrine where each blister contains 6 tablets), total number of packages procured and price paid. Information regarding the package description and number of packages procured allowed us to calculate the total number of tablets in each transaction.

Further, an important feature of ACTs is their pre-packaging into blisters of treatment courses, where a treatment course is defined as number of tablets needed to treat a case of uncomplicated falciparum malaria of a specific age-group. Such packing increases the rational use of drugs and improves adherence to treatment. For the purpose of analysis, information about the number of tablets in a blister when matched with the strength (quantity of active ingredient) of the product allowed us to know the number of tablets in the treatment. Total number of smallest units (tablets) in each transaction was then divided by the units in a treatment course to calculate the quantity of treatments procured.

Quantity of treatments = (total number of tablets in a transaction)/(number of units in one treatment dose of the product)

For example, procurement of 1000 packages of 30*6 blister pack (a pack of 30 blisters of 6 tablets each) of AL (strength: 20 mg + 120 mg) equates to 180000 tablets and 30000 treatments targeted for patients between 5 kg to 14 kg. Similarly, procurement of 1000 packages of 25*3 blister pack of Artesunate + Amodiaquine (strength: 100 mg + 270 mg) equates to 75000 tablets and 25000 treatments targeted for patients greater than 18 kg and less than 36 kg.

Similarly, we used Ex works (EXW) prices in US dollars for analysis (no charges included, i.e. factory gate price). Price of one treatment was calculated by multiplying number of units in a treatment course of a given product with EXW unit prices.

Price per treatment (PPT) = (unit EXW prices in US$) x (number of tablets in one treatment dose)

6.3. Interview guide for fieldwork in Mali

Identity of the Respondent

Name: ……

Function/Position: ……

Organization/Institution/Enterprise: ……

Email: ……

Date: ……

Place: ……

Name of Interviewer: ……

Start Time: ……..

End Time: ……

Themes

□ Regulatory Framework	□ Quality Control
□ Circuit in the Public Sector	□ Circuit in the Private Sector
□ Informal Market	□ Indian Firms

A. Introduction

1) Pourriez-vous me l'expliquer brièvement comment la chaîne d'approvisionnement pharmaceutique au Mali fonctionne? *(Use probe questions to know the existence of different markets: Public – government and donor based; private – formal and informal)*
……
……

2) Pourriez-vous me parler du rôle que Joue votre organisation dans la chaîne d'approvisionnement et le contrôle qualité des médicaments antipaludiques ?
……
……

3) Pourriez-vous me parler de vous-même, de votre position et de votre rôle au sein de l'organisation ?
……
……

B. Cadre Réglementaire

Généralités

Nom de l'autorité de réglementation pharmaceutique :

……

4) L'autorité de Réglementation Pharmaceutique,

Fait partie du ministère de la santé ? □ Oui □ Non
Est un organisme semi-autonome ? □ Oui □ Non
Autre (précisez) :
……

5) Quelles sont les fonctions de l'autorité de réglementation pharmaceutique nationale ?
   - □ Autorisation de mise sur le marché/enregistrement
   - □ Octroi des licences d'exploitation
   - □ Inspection
   - □ Contrôle de la qualité du médicament
   - □ Essais cliniques
   - □ Pharmacovigilance
   - □ Autre (précisez):

……

……..…

Autorisation de Mise Sur le Marché (AMM)

6) Une autorisation de mise sur le marché est obligatoire pour tous les produits pharmaceutiques distribués ? □ Oui □ Non

7) Il existe un mécanisme de procédure accélérée, d'exception, de dispense d'AMM ? □ Oui □ Non (Can you buy a medicine without an AMM ?)
   - Si oui, préciser:
     ……
     ……

8) Il existe un mécanisme de reconnaissance des AMM attribuées par d'autres pays ? □ Oui □ Non

   - Si oui, préciser:
     ……
     ……

9) Les critères d'évaluation des demandes d'autorisation de mise sur le marché des produits pharmaceutiques sont strictement définis par la loi ? □ Oui □ Non

   - Si oui, donner la référence du texte :
     ……
     ……

10) Quels sont les médicaments indiens titulaires d'une AMM dans votre pays ? (Joindre la liste) (If list is unavailable then, can you give me some estimate ?)

11) Quels sont les antipaludiques titulaires d'une AMM dans votre pays ? (Joindre la liste)

12) Quels sont les antipaludiques recommandés par le PNLP de votre pays ? (Joindre la liste)

13) quels sont les antipaludiques inscrits sur la liste essential des médicaments ? (Joindre la liste)

14) A l'importation, une autorisation de l'autorité de régulation du médicament est-elle exigée pour la libération des produits par les autorités douanières ? □ Oui □ Non

   - Si oui, pouvez-vous décrire le fonctionnement de cette procédure ?
     ……

15) Une réglementation Identifie-t-elle des ports d'entré« obligatoires pour le transit des produits pharmaceutiques? □ Oui □ Non

   - Si non, décrire les principaux circuits d'entrée des médicaments sur le territoire national :
     Vole empruntée :

     □ Air □ Terre

Zone géographique d'entrée :

……

16) Savez-vous s'il y a des bureaux d'entreprises indiennes au Mali ? Ou partenariats locaux ?
    ……

17) Avez-vous déjà été contacté par un représentant d'une firme indienne pour la promotion de leurs produits ?

……

C. Achats Et Distribution

a. Secteur Public

18) Selon vous quelle est la part du marché des médicaments détenu par les structures publiques (PPM) ? Chiffres? (What was the turnover of PPM in last three years?)

……

19) Selon vous quelle est la part du marché des médicaments antipaludiques détenus par les structures publiques ? (How many number of treatments of antimalarial drugs were procured or received by the PPM? Or An estimation of quantity quantity?) (How much of it was received from the program partners like PMI and Global Fund?

…….

20) Une autorité centrale unique est-elle chargée des achats de médicaments pour le secteur public ?

□ Oui □ Non

21) Quel type de médicaments sont achetés par le secteur public ? Sont-ils générique vs origine (spécialité) dans la nature ?

……

22) Donner la liste des différentes structures/organisation/partenaires (like international organizations) fournissant les médicaments (antipaludiques) au secteur public : *(In case of clarification: Do you import directly from the manufacturer or are you dependent on a third party or use a mix?) Also ask about donations (les dons) of medicines from China?*

……

23) Est-ce que vous achetez des médicaments d'origine indienne dans le secteur public/privé?

□ Oui □ Non

- Si oui (Directly from the manufacturer or using a different channel? Explain.)

  ……
- Si oui (What is the percentage of Indian medicine in the public market) Any Data? Has it increased over the years?

  ……

24) Quel type de médicaments indiens achetez-vous ?

……

25) Où les produits indiens, que vous achetez sont fabriqué ? (Pouvez-vous préciser?)

……

26) Le département du système d'approvisionnement public dispose-t-il d'un entrepôt central au niveau national ? □ Oui □ Non

27) Nombre des entrepôts publics aux niveaux : (Ask for organizational explaination of PPM)

□ National (_____)

□ Régional (_____)

□ District (_____)
□ Local (selon organisation du système) (_____)

28) Les structures de santé du secteur public sont tenues de s'approvisionner exclusivement auprès des systèmes nationaux d'approvisionnement ? □ Oui □ Non

Si non, ou en cas de rupture/indisponibilité, auprès de quels fournisseurs ces structures sont-elles également autorisées à s'approvisionner ?

□ Grossiste privé
□ Officine privée
□ Fabricant/Distributeur local
□ Fabricant/Distributeur International
□ Structures confessionnelle
□ Autre, Préciser

……

29) Existe-t-il un code des marchés publics qui s'applique aux procédures d'achat de médicaments ? □ Oui □ Non

30) Quel est le mode principal d'attribution de marché que vous utilisez pour les antipaludiques ?
…….

31) Etes-vous confronté à des problèmes de rupture de stock concernant les antipaludiques ? □ Oui □ Non

SI oui, cela concerne-t-il un (des) médicament(s) en particulier □ Oui □ Non

- Le(s)quel(s) :
……

SI oui, quelles en sont les causes principales, selon vous :

□ Rupture fabricant
□ Brusque augmentation des sorties
□ Défaut d'anticipation des besoins
□ Défaut de gestion de stocks

32) Avez-vous mis en place des procédures spécifiques pour faire face à une brusque augmentation des besoins en antipaludiques en cas d'épidémie ? □ Oui □ Non
Si oui, précisez :
……
33) Pouvez-vous nous indiquez quels antipaludiques vous avez distribués au cours de l'année écoulée ? (INName/ Nom Spécialité/ Laboratoire fabricant/ Nombre de traitement distribués)
……
34) Pouvez-vous nous indiquez quels antipaludiques sont disponibles actuellement dans le système public ?

D. Prestations médicales/pharmaceutiques et exemptions

35) Dans le cadre du paludisme, le coût des consultations est-il généralement à la charge du patient ?
□ Oui □ Non

- Si oui, une subvention du ticket modérateur / gratuité est prévue pour certaines catégories de population ? □ Oui □ Non
- Si oui, s'agit-t-il :
  Des patients les plus démunis? □ Oui □ Non
  Des enfants de moins de cinq ans ? □ Oui □ Non
  Des femmes enceintes ? □ Oui □ Non
  Autres, expliquer :

……

36) Dans le cadre du paludisme, le coût des médicaments est-il généralement à la charge du patient ?
□ Oui □ Non

- Si oui, une subvention du ticket modérateur / gratuité est prévue pour certaines catégories de population ? □ Oui □ Non
- Si oui, s'agit-t-il :
  Des patients les plus démunis? □ Oui □ Non
  Des enfants de moins de cinq ans ? □ Oui □ Non
  Des femmes enceintes ? □ Oui □ Non
  Autres, expliquer :

……

E. Marche Parallèle — Médicaments De Rue

37) Avez-vous connaissance de l'existence d'un réseau parallèle de vente de médicaments dans votre pays ? □ Oui □ Non

38) Selon vos informations, pouvez-vous estimer son Importance en volume ou en valeur par rapport au marché officiel ?
……

39) Que savez-vous de son organisation ?
……

40) A votre connaissance, ces réseaux revendent des médicaments :

- □ Achetés de façon officielle auprès des établissements pharmaceutiques publics □ Oui □ Non
- □ Achetés de façon officielle auprès des établissements pharmaceutiques privés □ Oui □ Non
- □ Détournés des circuits de distribution publics □ Oui □ Non
- □ Détournés des circuits de distribution privés □ Oui □ Non
- □ Rentrés illégalement sur le territoire □ Oui □ Non

Autres, préciser :
……

41) Que savez-vous des circuits d'entrée officieux de médicaments dans le pays ?
Route empruntée : □ Air □ Terre

Points d'entrée dans le pays :

……

42) Une partie des médicaments vendus hors des réseaux officiels sont falsifiés, que savez-vous de leur origine ?

……

43) quelles sont les autorités en charge de la surveillance/contrôle de ces circuits ?

……

44) Existe-t-il une cellule de lutte spécifique à cette question ? □ Oui □ Non
Si oui, préciser :

….....

45) Quelles sont les mesures de lutte contre les médicaments contrefaits mises en place ?

…….....……

46) Quels sont les résultats obtenus ?

…….....……

47) Des opérations de contrôle ont-elles donné lieu à des saisies de médicaments au cours des 5 dernières années ? □ Oui □ Non

48) Parmi ces saisies, avez-vous connaissance de la présence de médicaments antipaludiques ?
□ Oui □ Non

49) Quelles sont, selon vous, les principales raisons Incitant les patients à se fournir dans ces réseaux ?

- □ Proximité géographique
- □ Prix moins élevés
- □ Rapidité
- □ Absence d'ordonnance
- □ Discrétion
- □ Manque d'Information
- □ Autre, préciser :

…….....……

50) Les autorités de santé publiques diffusent elles des messages d'Information à ce sujet à destination des populations? □ Oui □ Non
NB: Si possible, collecter les supports diffusés aux populations (tract, compagne audio ou outres)

Avez-vous d'autres remarques à effectuer sur le sujet ?

…….....……

F. Conclusion

Voulez-vous ajouter quelque chose ?

…….....……

6.4. Interview Guide for fieldwork in India

Study number: [__|__]-[__|__|__]-[__|__|__]

Initials of interviewer [__|__] Date of interview (dd/mm/yyyy) [__|__]-[__|__]-[__|__]__|__]

Start time of interview (24 hrs.) [__|__]:[__|__] End time of interview (24 hrs.) [__|__]:[__|__]

1. Name: _____
2. Organization: _____
3. Position:
   _____
4. What are your responsibilities in this organization?

   …….....……
5. Do you supply (export) Medicines to the African market? (Yes/No)

   a. If yes, how many countries?
      …….....

   b. Any specific examples?
      …….....
6. When did you decide to Enter African market (domestic situation of that time)? Why that particular market?
   …….....……
7. Are you an exporter from the very beginning, or started it as a market expansion/diversification business model?
   …….....……
8. What decides your choice of export market (product, market knowledge, other factors)?
   …….....……

9. What is the organization of your export (sales is done by local firms, your subsidiary, open market, international organizations auction)? Any specific R&D for that market?
……

10. What are the areas where you have to bank on local knowledge/local expertise for successful exports in Sub-Saharan Africa?
……

    a. Also, suppose if you decide to launch a product 'A' into African market; do you need the help of a home or host country intermediary? For example, a *pre-wholesaler* or a product promotion agency?
    ……

11. What is the importance of Sub-Saharan (Africa) market for Indian pharmaceutical firms? OR Why Sub-Saharan market is important for Indian firms?
……

    a. Has this market changed over the years? (In what ways?)
    ……

    b. Do you think if such changes have an impact on actions taken by firms that are already active and on new entrants? Any example?
    ……

12. According to you, what are the major challenges faced by Indian firms in Sub-Saharan Africa?
……

    a. What are the measures taken by (your) firms to overcome these challenges?
    ……

13. Do you consider market as a Single African Market or distinguish it according to East and West Africa or likewise? (There are over 40 countries in Sub-Saharan Africa and they might have different regulations (for example of product registrations, quality) norms, languages, etc.)
……

    a. Even within the same country, do you see a single market with one set of regulations or different markets with different requirements? For example, government vs. private vs. medicines for programs such as malaria, HIV or TB?
    ……

        i. If so, how do you approach these markets?
        ……

b. What do you think about the demand of medicines by international organizations such as the UNICEF or the Global Fund?

…….....

14. Some Indian firms are setting up production units in African countries. Do you want to enter in this sector? If so, what determines the choice of destination?

…….....……

15. What are the challenges in starting a production unit Africa, and how these challenges vary across countries?

…….....……

16. How these challenges are different from setting up a production facility in India?

…….....……

6.5. Interview Guide for Synriam Case Study

Name of the participant:

Organization:

1. What are your roles and responsibilities in the organization?
2. How the research project that resulted in the discovery of arterolane (OZ277) was started?
3. What were your responsibilities in the project that led to the development of Synriam?
4. Who were the partners and their respective roles and obligations (Industry/academia)?
5. What were the arrangements between the partners regarding the division of labor, commitments, shared assets and benefit sharing?
6. Why MMV decided to select Ranbaxy and not any European or American firm? Also, why not any other Indian firm?
7. What was the importance of this project for Ranbaxy?
8. What were the major challenges faced during the project?
9. What were the sources of finance?
10. What were the returns that your organization was expecting out of this partnership?
11. What were the reasons that led MMV to quit the project? What was the impact of this break-up on MMV/other partners?
12. Why MMV gave the intellectual property rights to Ranbaxy when it left the project?
13. What was the learning experience for your organization through the Synriam collaboration?
14. What were the challenges faced by Ranbaxy? (Financial? Regulatory? Coordination?)
    - How did Ranbaxy overcome these challenges?
15. Why Ranbaxy chose particular countries to lunch Synriam?
    - Can you elaborate the specificities of the launch process?

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