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Commentary: Can we facilitate the ethical approval of international observational studies?

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The paper by Claudot *et al*.[1] raises an important issue for today's epidemiological research: the disparity of norms and procedures for ethical review prevailing in different countries. Different standards may hamper the funding or the conduct of multicentric studies, or even prevent the publication of a paper reporting results of a study that has not received ethical approval in the forms required by a journal's country.

The problem is of particular concern for observational studies. These are generally considered to be less prone to ethical problems compared with intervention studies. Yet this very fact, combined with the variety of observational study designs, leaves considerable room for inconsistencies in the approach to ethical review. Does a study carried out on medical records to check a possible adverse effect (e.g. cancer) of a drug occurring years after its use require going back to the treated subjects to obtain their informed consent? Is this unnecessary, and the approval of an ethical review committee could be enough? Is even the latter not required, as for this type of study the clearance by a data protection authority is adequate? Or can it proceed without any *ad hoc* clearance if it is carried out by a cancer registry or, in general, by a legally authorized disease registry? Different answers to these questions are likely in different countries, and in some it may take a substantial time before the required ethical and/or legal clearances are obtained, delaying or even preventing the study to be carried out. For instance, in Italy, regulations have been recently issued that seriously impair individual record linkage of routine perinatal data, even if performed by the public institutions officially in charge of collecting and analysing such data.[2] Thus, basic indicators such as neonatal and infant mortality stratified by birthweight and gestational age are no longer available at national level.

Claudot *et al*.[1] suggest that different bodies may guarantee, despite their different names, the same level of protection to research subjects, and make a plea in favour of the recognition of such 'equivalence' across national boundaries. There are, in our view, two ways in which equivalence can in principle be documented. First, each review body, whatever its

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name, should be able to provide written documentation of its aims; procedures of selection of members; actual composition of the body, and degree of independence from the investigators and their institutions; and operating procedures for study review. A welcome consequence of this requirement would be increased publicity regarding the expertise and activities of these bodies, whose disparities in procedures, time to decision and type of decision reached for the same study have often been reported.[3] However, this measure finds a limit in the variable mix of scientific and ethical review functions that committees fulfil in many countries. Also, it would be of no use when a journal demands ethical clearance for a meta-analysis or a review paper while ethical committees in the paper author's country have no mandate to examine these types of studies.

A second approach lies in conforming and making reference to common guidelines. As of today, the only set of guidelines for epidemiological research available at worldwide level, are those prepared by the Committee for International Organizations of Medical Sciences (CIOMS).[4] These guidelines assert the nature of observational studies as distinct from intervention studies and make provisions for differential treatment of the various kinds of observational investigations (e.g. interview studies, studies using personal linkable records, studies using non-linkable records, etc.). Compliance with the twin CIOMS guidelines for biomedical research[5] is, for example, accepted as a sufficient requirement by the US Department of Health and Human Services (DHHS) – Office for Human Research Protection (OHRP)[6] for institutions conducting research on human subjects supported by US federal funds. This offers an indirect inroad towards obtaining the same kind of recognition for the CIOMS guidelines for epidemiological research.

Admittedly, the CIOMS guidelines for epidemiological research may need some refining to become more operational on aspects such as criteria for exemption from ethical review, and for waiving of informed consent for selected types of studies. This can be a worthwhile task for an international working group that, under the aegis of CIOMS and of the International Epidemiological Association, and provided with appropriate resources, should first document by means of available data or sampling surveys how observational studies are actually assessed in a number of different countries, gathering a 'table of equivalences and differences' of the guarantees offered; and second, identify the common ethical and legal background upon which the CIOMS guidelines, modified as necessary, may become accepted as a reference standard, formally endorsed by international and national authorities similarly to the European Union good clinical practice regulations for clinical trials on drugs.[7]

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