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Comparisons of the Composition of Tobacco Smoke and the Smokes from Various Tobacco Substitutes*

by

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SUMMARY

By the late 1970s, eight technologies in the design of a "less hazardous" cigarette were classified as significant. The eight included: The tobacco blend, the filter tip, filter-tip additives, reconstituted tobacco sheet, paper additives, air dilution via paper porosity, expanded tobacco, and air dilution via filter-tip perforation. In addition to these eight cigarette-design technologies was another proposed technology which involved the incorporation of a substitute for some or all of the tobacco in the cigarette filler. Despite considerable research and development (R&D) effort on various tobacco substitutes that indicated the replacements in most instances fulfilled the definition of a "less hazardous" cigarette with regard to the chemical and biological properties of their mainstream smoke, tobacco substitute-containing cigarettes failed to attain consumer acceptability. As a result, several marketed products containing tobacco substitutes had an extremely brief tenure in the marketplace. Outlined herein is a summary of some detailed research conducted on the composition of the mainstream smokes from cigarettes containing either all-substitute filler or fillers comprising various substitute and tobacco mixtures as well as an all-tobacco cigarette. [Beitr. Tabakforsch. Int. 22 (2006) 258–289]

ZUSAMMENFASSUNG

In den späten 70er Jahren des vorigen Jahrhunderts wurden acht Technologien zur Entwicklung einer "weniger schädlichen Zigarette" als bedeutsam klassifiziert. Diese acht Technologien beinhalten: Tabakmischung, Filter, Zusatzstoffe im Filter, Tabakfolie, Zusatzstoffe im Zigarettenpapier, Ventilation durch Papierporosität, Blähtabak und Ventilation durch Filterperforation. Zusätzlich zu diesen acht Technologien zur Konstruktion von Zigaretten wurde eine weitere Technik vorgeschlagen, bei der ein Teil oder der gesamte Tabak der Zigarettenfüllung ersetzt wird. Trotz beträchtlicher Anstrengungen im Bereich der Forschung und Entwicklung verschiedener Tabakersatzstoffe, die in den meisten Fällen in Bezug auf ihre chemischen und biologischen Eigenschaften des Hauptstromrauchs der Definition einer „weniger schädlichen Zigarette" entsprachen, fanden Zigaretten mit Tabakersatzstoffen keine Akzeptanz beim Raucher. Aus diesem Grund waren Zigaretten mit Tabakersatzstoffen nur für sehr kurze Zeit auf dem Markt. Dieser Beitrag liefert eine Zusammenfassung detaillierter Forschung auf dem Gebiet der Zusammensetzung des Hauptstromrauchs von Zigaretten, die entweder vollständig einen Tabakersatzstoff als Füllmaterial enthalten oder deren Füllmaterial aus verschiedenen Ersatzstoffen und Tabakmischungen bestehen und von Zigaretten, die ausschließlich Tabak enthalten. [Beitr. Tabakforsch. Int. 22 (2006) 258–289]

RESUME

A la fin des années 1970, de nouvelles technologies de conception d'une cigarette « moins dangereuse » ont été considérées comme importantes. Au nombre de huit (8) elles impliquent: le mélange de tabac, le bout filtre, des additifs du bout filtres, le tabac reconstitué, des additifs du papier à cigarette, la ventilation d'air par la porosité du

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papier, le tabac expansé et la dilution d'air par la perforation du bout filtre. En plus de ces huit méthodes pour la conception de cigarettes, une autre technologie a été proposée comportant l'incorporation d'un substitut pour une partie ou la totalité du tabac de la cigarette. Malgré des efforts considérables de recherche et de développement de substituts de tabac, correspondant dans la plupart des cas à la définition d'une cigarette « moins dangereuse » en ce qui concerne les propriétés chimiques et biologiques de la fumée principale, les cigarettes contenant des substituts de tabac n'ont pas réussit à être acceptée par les fumeurs. En conséquence,, les produits contenant des substituts de tabac ont été disponibles sur le marché que pendant très peu de temps. Cette étude présente un résumé des recherches sur la composition de la fumée principale de cigarettes contenant un substitut complet de tabac, une cigarette comportant divers substituts et mélanges de tabac, et d'une cigarette faite de tabac normal. [Beitr. Tabakforsch. Int. 22 (2006) 258–289]

INTRODUCTION

Prior to the epidemiological and biological data reported in the early 1950s, relatively little had been done to define the chemical composition of tobacco and/or its smoke. However, a multitude of studies on the composition of tobacco and its smoke and the interrelationship between the two compositions was triggered by the publication of the results of statistical studies on the association between cigarette smoking and lung cancer in smokers in 1950 by WYNDER and GRAHAM (1) and DOLL and HILL (2) and by the presentation and publication in 1953 of the report by WYNDER *et al.* (3) on the production of carcinomas on mouse skin-painted with cigarette smoke condensate (CSC).

Prior to 1954, tobacco smoke was recognized as an extremely complex mixture but relatively little was known about its actual composition. In his report published in late 1954, KOSAK listed the components reported in tobacco smoke to that date (4). Of the approximately 80 entities catalogued by KOSAK (Table 1), the identities of some 33 (>40%) were questioned by KOSAK who did not "consider the evidence cited in the literature to be definitive proof" of their identities. Several of the components (α-, β-, and γ-socratine, obelin, lohitam, anodmin, lathraein, poikiline, and gudham) first reported by WENUSCH and SCHÖLLER (5) and listed under "Alkaloids" were subsequently demonstrated to be mixtures or a component listed elsewhere in Table 1. For example, KUFFNER *et al.* (6) demonstrated that obelin was a salt of ammonia, α- and β-socratine were mixtures of nicotyrine and 2,3'-bipyridine, and γ-socratine was *l*-nornicotine. Poikiline was subsequently identified as 4-amino-1-(3-pyridyl)-butanone.

The tremendous escalation in the number of identified tobacco smoke (and tobacco) components from 1954 to date was achieved by successive advances in analytical methodology, particularly those technologies concerned with the separation and identification of individual components in complex mixtures. In Figure 1 is shown the increase in the number of identified tobacco and tobacco smoke components from 1950 to 1995 (8).

Very few identified tobacco and smoke components have been added during the past decade. Also noted in Figure 1 are the approximate dates when the major analytical advances were implemented in the study of tobacco smoke composition.

Prior to 1950, the major part of the isolation and characterization of individual components from tobacco smoke involved so-called "classical" chemical techniques, i.e., the fractionation of tobacco extracts or cigarette smoke condensate (CSC) into neutral (aliphatic hydrocarbons, polycyclic aromatic hydrocarbons (PAHs), esters), acidic (acids and phenols), and basic fractions (amines, nicotine-related alkaloids), followed by repeated crystallization and/or distillation of these subfractions.

GREEN and RODGMAN (8) summarized the major advances after 1960 in analytical methodology that enabled the isolation and/or identification of literally hundreds of the components in tobacco and its smoke. One could readily discern the effect of the gradual advancement of the analytical methodology for the separation and identification of components in a complex mixture such as tobacco or tobacco smoke. In the years following the report by KOSAK (4), publications described the isolation and identification by classical chemical means of one or a few tobacco and/or smoke components, e.g., the identification of the terpenoid alcohol solanesol in flue-cured tobacco (9), the sugar ester from Oriental tobacco (10), the phenols eugenol and isoeugenol in the mainstream smoke (MSS) from Oriental tobacco (11), and maltol in the MSS from an additive-free German tobacco blend (12).

As time and the analytical methodology progressed, publications for some years described the isolation and identification of perhaps a dozen or more components. Many of the early studies dealt with MSS vapor-phase components or the non-polar components in the MSS particulate phase or a tobacco extract. The lack of knowledge about polar components in tobacco and the particulate phase of smoke was primarily due to the inability at that time to separate highly polar components of a complex mixture. This situation continued during two decades of intensive effort on cigarette MSS composition but was finally resolved and utilized by SCHUMACHER *et al.* (13) in the 1970s. Eventually, publications were issued in which the identities of literally hundreds of tobacco and/or smoke components were defined, e.g., of the over 800 MSS components identified by SCHUMACHER *et al.* (13), by NEWELL *et al.* (14), and by HECKMAN and BEST (15), many were highly polar components new to the tobacco smoke literature. Early studies on cigarette MSS led to the identification of a few PAHs (16) and aza-arenes (17) but subsequent studies in which new technologies were employed by United States Department of Agriculture (USDA) personnel resulted in the identification of hundreds of PAHs (18, 19) and aza-arenes (20).

As additional components were defined in studies of the compositions of tobacco and its smoke, periodic reviews of the enhanced compositions were published in the next two decades after that of KOSAK. These included the 1959 review by JOHNSTONE and PLIMMER (7), the 1963 monograph provided by PHILIP MORRIS INC. (21) to the 1964 Advisory Committee to the US Surgeon General, and the 1968 review by STEDMAN (22). In some instances, a review was limited

Table 1. Tobacco smoke components listed by KOSAK in 1954 (4)

Class/component	Class/component	Class/component
Hydrocarbons	*Ketones*	*Acids*
Hentriacontane (?) [a]	3-Pentanone	Formic acid
Acetylene	4-Heptanone	Acetic acid
"Unsaturated hydrocarbons"	17-Tritriacontanone (?)	Butyric acid
Azulene	2,3-Butanedione	Valeric acid
Phenanthrene (?)	"Higher" ketones (?)	Caproic acid
Anthracene (?)		C_7 and C_8 aliphatic acids (?)
Benzopyrene (?)		Succinic acid (?)
"Condensed aromatics" (?)		Fumaric acid (?)
		Citric acid (?)
		Benzoic acid (?)
		Phenolic acids (?)
Alcohols and phenols	*Alkaloids*	*Miscellaneous components*
Methanol	Nicotine	Levoglucosan [b]
Glycerol	Pyridyl ethyl ketone	"Phytosterol" (?)
Diethylene glycol	Myosmine	$C_{10}H_{14}O$ (a furan ?)
Ethylene glycol	Nicotyrine	"Resins" (?)
Phenol (?)	α-Socratine [c]	"Resin acids" (?)
Catechol (?)	β-Socratine [c]	
	γ-Socratine [c]	
	Obelin [c]	
	Lohitam [c]	
	Anodmin [c]	
	Lathraein [c]	
	Poikiline [c]	
	Gudham [c]	
Aldehydes	*Other N-containing components*	*Inorganic components*
Formaldehyde	Pyrrole (?)	Ammonia
Acetaldehyde	"Pyrroles" (?)	Carbon monoxide
Butyraldehyde	"*N*-Methyl-pyrrolidines" (?)	Carbon dioxide
Acrolein (?)	Pyridine	Hydrogen cyanide
Benzaldehyde	"Picoline" (?)	Hydrogen sulfide
2-Furaldehyde (?)	"Lutidine" (?)	Thiocyanic acid (?)
	"Collidine" (?)	Oxygen
	"Pyridine bases" (?)	Arsenic [d]
	Methylamine (?)	"Acetates" (?)
	"Chlorophyll degradation products" (?)	"Chlorides" (?)
	"Uric acids" (?)	"Cyanides" (?)
		"Nitrates" (?)

[a] The question mark indicates that Kosak did not consider the evidence in the literature to be definitive proof of the identity of the component.

[b] 1,6-Anhydro-β-D-glucopyranose.

[c] Subsequent study demonstrated this component was not a well-defined compound but an artifact, a mixture, or an ammonium salt (see discussion by JOHNSTONE and PLIMMER (7)).

[D] Probably present as As_2O_3.

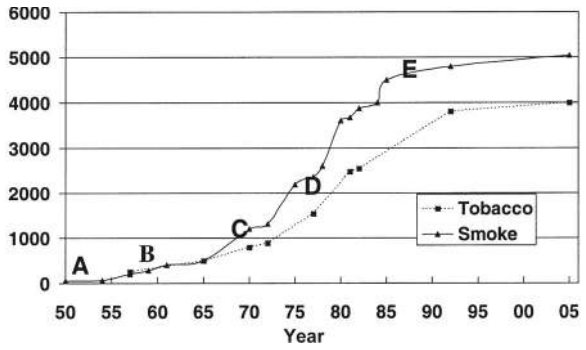


Figure 1. Number of identified tobacco and tobacco smoke components reported since 1954: Accumulative by year; A = prior to 1953: "classical" chemical techniques; B = 1953–1960: column chromatography; C = 1960–1970: gas chromatography; D = 1970 to mid-1970s: glass capillary gas chromatography coupled with mass spectrometry; E = mid-1970s to date: derivatives for HRGC, HPLC, mass spectrometry.

to tobacco smoke composition (23) or to the cataloguing of a specific class or type of component identified in tobacco smoke, e.g., summaries of PAHs (24), vapor-phase components (25), nitrogen-containing components (26, 27), or acids and phenols (28). Examination of such lists indicates they were generated by Tobacco Industry-related institutions (21, 23, 24, 25, 26), government agencies (18, 19, 20, 22), and academic/medical institutions (4, 16, 17, 27).

From examination of the many publications on tobacco and tobacco smoke composition after the early 1950s, it was obvious that many institutions as well as the Tobacco Industry members monitored and catalogued the tobacco and tobacco smoke components as they were identified and reported. As noted by RODGMAN (29), many component lists were promulgated by academic and governmental institutions from the early 1960s to date. However, such lists usually did not deal with the totality of components but only with those tobacco and/or tobacco smoke components asserted to adversely affect the health of the consumer.

From 1955 to the end of the 20th century, the identified components of tobacco and its smoke reported in the literature were diligently catalogued by research and development (R&D) personnel at R.J. Reynolds Tobacco Co. (RJRT) (30, 31). Presumably, R&D personnel at other Tobacco Industry members were similarly involved. As indicated in Figure 1, the number of components identified to date in tobacco smoke approaches 4800. However, from his examination of chromatographic and spectral data available in the early 1970s when the number of identified smoke components was slightly more than a 1000, WAKEHAM (32) suggested that the total number of smoke components may approach 100000.

After the report in 1957 by WYNDER *et al*. that the % tumor-bearing animals (% TBA) decreased as the dose of "tar" used in skin-painting was decreased (33) and the assertion by WYNDER (34) that reduction of the per cigarette "tar" yield would be beneficial to the smoker, various means to reduce the per cigarette "tar" yield were studied during the next decade and the successful ones were incorporated into commercial products. Also, in response to the various assertions on the adverse effect of certain tobacco smoke components on the smoker, numerous cigarette design technologies were investigated with the object of reducing such components. Among the many technologies studied, eight were considered effective and were incorporated in various combinations and to various degrees in cigarettes that were subsequently marketed. Their utilization by the Tobacco Industry and the "less hazardous" cigarette goals achieved were commended even by those investigators and government agencies considered avid opponents to cigarette smoking [see Table 6 in (29) or Table 15 in (35)]. Eventually, however, commendations pertinent to the successful reduction of per cigarette "tar" and specific toxicant yields disappeared because of the assertions that reduced smoking machine yields were not parallelled by reduced smoker yields because of smoker compensation, a factor subsequently included in the various discussions of cigarettes with reduced "tar" yields (36).

In the 1960s and early 1970s prior to the introduction of the Ames mutagenicity test, the three criteria to define a "less hazardous" cigarette [see p. iii in (37); p. 372 in (38); p. 503, 531 in (39)] were: 1) the per cigarette yield of a specific toxicant in MSS was lowered; 2) the ratio of the specific toxicant yield to MSS "tar" yield was lowered; and 3) the specific tumorigenicity of the MSS "tar", as measured in the mouse skin-painting bioassay, was lowered.

Significantly, the elimination of the first criterion as a complete definition per se of a "less hazardous" cigarette was related to the requirement in the third criterion that the skin-painting bioassay be specific tumorigenicity-oriented, i.e., the "tar" painting dose was fixed at 25 or 50 mg/day and not related to the cigarette "tar" yield. The requirement that all three criteria in the definition be met arose because personnel at various research institutions and governmental agencies wished to avoid the appearance of endorsing low-"tar" cigarettes.

Since the early 1950s, it might appear that the cigarette design efforts of the Tobacco Industry R&D personnel were primarily directed to meeting these criteria. However, the R&D personnel in general were troubled by the overall definition and viewed two of the criteria as seriously flawed. Criticisms of these criteria were not limited to Tobacco Industry scientists but were also expressed by health scientists and governmental authorities.

Various health scientists and personnel of governmental agencies expressed conflicting opinions on the first criterion. Some interpreted the experimental evidence of lower % tumor-bearing animals (TBA) in mice treated with reduced levels of "tar" (equivalent to reduced cigarette yield) as an indication that a lower-"tar" yield cigarette is "safer" or "less hazardous" than a higher-"tar" yield cigarette. Others held the view that the biological response resulted from a dose-response factor [see pp. 504–506 in (39)] and was not, per se, related to reduced health hazards in smokers.

The second criterion for a "less hazardous" cigarette is paradoxical. On the one hand, some of its proponents recommended the reduction of the levels of specific components in MSS supposedly responsible for the observed tumorigenicity of particulate matter to mouse skin (40). However, on the other hand, other proponents of this criterion admitted either an inability to explain the observed biological effect on the basis of the levels of these components in the particulate matter or they accepted the lack of an association between the observed biological effect and chemical composition (41, 42, 43).

The third criterion suffers from several problems: It ignores the findings that 1) inhalation studies with laboratory animals exposed to cigarette MSS have consistently given inconclusive (negative) results with regard to carcinoma induction, 2) mouse skin-painting bioassays with cigarette smoke particulate matter do not measure smoke components reported to be tumorigenic in other systems such as ingestion, e.g., *N*-nitrosamines (NNAs), and 3) skin-painting and Ames test data with cigarette MSSs produced under certain conditions are widely divergent. Recently, some departure from the third criterion has occurred with the increased usage of various cytotoxicity tests.

In the design of a "less hazardous" cigarette, many approaches have been investigated over the years (35). Table 2 summarizes the cigarette design technologies studied by Tobacco Industry and non-Industry investigators, a list eventually reduced to the eight technologies considered significant.

The eight technologies subsequently deemed significant and much commended even by health and governmental personnel over the years [see listing and references in Table 6 in (29) or Table 15 in (35)] include: The tobacco blend, the filter tip, filter-tip additives, reconstituted tobacco sheet, paper additives, air dilution via paper porosity, expanded tobacco, and air dilution via filter-tip perforation. Their significance was recognized in "less hazardous" cigarette design by the National Cancer Institute (NCI) and the US Surgeon General. The eight design technologies are used in concert and to different degrees, thus enabling the design of consumer acceptable cigarettes with MSS FTC "tar" yields ranging from 1 to 40 mg/cig and MSS nicotine yields ranging from 0.1 to 3.0 mg/cig.

TOBACCO SUBSTITUTES

One technology that commanded an inordinate amount of research effort in the late 1960s and early 1970s was the study of tobacco substitutes which essentially replaced the

Table 2. Alteration of cigarette mainstream smoke yield, composition, and biological activity: Methods studied

Cigarette design technology			
Tobacco selection	*Tobacco additives*	*Amount of tobacco*	*Tobacco treatment*
Type	Combustion modifiers	Cigarette dimensions	Curing
Stalk position	Casing materials and humectants	Tobacco weight	Grading
Nitrate content	Flavorants	RTS (non-paper process)	Fermentation
Nicotine content	Pesticides, agricultural chemicals	RTS (paper process)	Extraction
Other components		Homogenized leaf	Denicotinization
	Diluents (substitutes)	Stem inclusion	Ammoniation
Filtration	Cytrel®	Expanded laminae	Expansion (laminae and/or stems)
Efficiency/selectivity	NSM® (New Smoking Material)	Moisture content	
Material (cellulose acetate, paper)	Expanded grains (J10)		*Cigarette paper*
Material (charcoal)	Carbon/carbonized filler	*Blending*	Porosity (air dilution)
Additives	SSM® (Sutton Smoking Material)		Additives
	Other plants (lettuce, peanut hulls,	*Air dilution (perforated filter*	Coatings
Tobacco cut width	etc.)	*tips)*	

tobacco in the cigarette filler or acted as diluents of the tobacco in the filler. Prior to the intensive study of specifically designed tobacco smoke, a great number of substitutes were proposed and tested (44). Among them were various plant materials, e.g., lettuce (45), peanut hulls (46), cacao bean hulls (47)[a], kudzu leaves (48), papaya leaves (49), which were examined as possible substitutes or diluents for the tobacco in the cigarette filler. None proved to be successful, primarily because of lack of consumer acceptance.

Those substitutes that did contribute to significant changes in the chemical and biological properties of cigarette smoke included Cytrel® from Celanese, the New Smoking Material (NSM®) from the Imperial Group, expanded grains (J10) from RJRT (50), and the Sutton Smoking Material (SSM®) from the Sutton Research Corporation. The latter was studied in great detail at RJRT R&D.

Unfortunately, even though several of the substitutes fulfilled the chemical and biological properties required for a "less hazardous" cigarette, Cytrel®- and NSM®-containing products placed on the UK market in 1977 proved unacceptable to the consumer. They were classified as commercial failures and subsequently removed from the marketplace after a relatively short marketing period. Obviously, these products had a serious problem discussed by several investigators. Even those as zealous as WYNDER and HOFFMANN were aware of possible major problems, if not *the* major problem, in the design of a "less hazardous" cigarette, namely, consumer acceptance. When the low-"tar" cigarette had obviously become the choice of many smokers, WYNDER and HOFFMANN, after commending the Tobacco Industry for its emphasis on low-"tar" cigarette design and marketing, noted in 1979 (51):

> Development of a less harmful cigarette acceptable to the majority of the smokers needs to continue. We must be realists. A completely safe cigarette smoked by only 1% of the smoking public is of considerably less societal benefit than a cigarette with some adverse effects smoked by 90% of the public.

and again (52):

> It is important to appreciate that a virtually harmless cigarette smoked by only 1% of the population will have a lesser impact on the reduction of tobacco-related diseases than a somewhat more harmful cigarette smoked by 80% of the total smoking population. Research on the less harmful cigarette should therefore be directed toward developing a cigarette containing the lowest possible amount of harmful elements for all tobacco-related diseases, but one that has sufficient acceptability for the largest segment of smokers.

On several occasions, including his summary of the 1979 Banbury Conference on the "less hazardous" cigarette (53), GORI expressed a similar sentiment (54).

Following the introduction of consumer-acceptable filter-tipped and low-"tar" cigarettes, the Tobacco Industry considered the value of introducing tobacco substitutes into cigarettes. A proportion of the natural tobacco was replaced with material of lower biological activity, offering the prospect of reducing the toxicity of the cigarettes. Having abided by guidelines for the "less hazardous" cigarette testing of substitutes, the Tobacco Industry marketed the first two major tobacco substitutes: Cytrel® 361 and NSM® in 1977. Because of lack of consumer acceptability, both were a commercial failure, and were eventually withdrawn from the marketplace. A large-scale epidemiological study to examine the long-term impact on the health of smokers of these products was also abandoned because it failed to enlist an adequate sample of substitute cigarette smokers.

It was realized that a substitute, in addition to meeting the criteria for a "less hazardous" cigarette, should also meet certain criteria for consumer acceptance and/or Tobacco Industry usage. These criteria included: 1) Combustion properties such that its burn rate and its ash formation, appearance, and properties approximated those of tobacco; 2) Generation of MSS and SSS that did not possess any off-odor or off-taste; 3) Deliver a bland smoke amenable to flavor enhancement by suitable additives; 4) Substantially influence cigarette MSS composition, yield, and properties at modest levels (10–25%) of inclusion of the substitute in the filler; and 5) Introduce into MSS no "strangers" with uncertain or unknown biological properties. A smoke "stranger" was defined as a component identified in the substitute cigarette MSS that was not found in the all-tobacco cigarette MSS. This criterion was significant at RJRT.

[a] Cacao bean hulls as a smoking material was patented by a former Hershey Chocolate Co. employee [Hess, E.H.: Tobacco composition; U.S. Patent No. 3,429,316 (February 25, 1969)] and ultimately appeared in the marketed Free cigarette.

Table 3. Pyrones identified in mainstream smoke from Sutton Smoking Material (SSM®) (55)

Pyrone	CAS No.	Estimated % of SSM® CSC	Tobacco MSS
2*H*-Pyran-2-one, 3-hydroxy-		+	
4*H*-Pyran-4-one, 3,5-dihydroxy-	488-18-6	27–30	59
4*H*-Pyran-4-one, 3,5-dihydroxy-2,6-dimethyl-		+	55
4*H*-Pyran-4-one, 3,5-hydroxy-2-methyl-	1073-96-7	+	55
4*H*-Pyran-4-one, 3-hydroxy-	496-63-9	4–7	55
4*H*-Pyran-4-one, 3-hydroxy-2-methyl- [a]	118-71-8	+	12, 55
4*H*-Pyran-4-one, 2-hydroxymethyl-3,5,6-trihydroxy-		4–6	55 (0) [b]
4*H*-Pyran-2-carboxylic acid, 5-hydroxy-4-oxo- [c]		3–5	55 (0)
4*H*-Pyran-2-carboxylic acid, 5-hydroxy-4-oxo-, (1-methylethyl) ester [d]		+	55 (0)

[a] Maltol
[b] (0) indicates none detected in all-tobacco smoke
[c] Comenic acid, isopropyl ester
[d] Comenic acid

Detailed examination of the composition of the MSS from the various tobacco substitutes provided some interesting results. In most instances, the MSS components in the tobacco substitute smoke were also present in tobacco MSS but the per cigarette MSS yields from the substitute usually varied considerably from those in tobacco MSS. In most instances, the substitute MSS component yields were less than those in tobacco MSS.

The mainstream CSC from cigarettes fabricated from SSM® was found by GREEN *et al.* (55) to be uniquely different from the mainstream CSC from an all-tobacco cigarette. The preparation and composition of various versions of SSM® and the final version used in the study of the chemical and biological properties of its MSS are described by RODGMAN *et al.* (56). Not only was the complexity of the SSM® CSC much less than that of tobacco CSC but also a large percentage (~50%) of the SSM® CSC comprised one class of compounds, the pyrones. Some of the pyrones identified and their percentage of SSM® CSC are summarized in Table 3. The structures of several other pyrones present in trace amounts in the SSM® CSC were proposed.

In the late 1960s when the SSM® CSC study was conducted, no pyrones had been reported in tobacco smoke. Thus, they were considered as "strangers" in the MSS. However, the "stranger" problem subsequently disappeared. In 1970, ELMENHORST (57) reported the isolation and identification of 2-hydroxy-3-methyl-4*H*-pyran-4-one from all-tobacco cigarette smoke. In 1971, GREEN and SCHUMACHER (58) reported the identification of four pyrones [3-hydroxy-4*H*-pyran-4-one, 3,5-dihydroxy-2-methyl-4*H*-pyran-4-one, 3,5-dihydroxy-2,6-dimethyl-4*H*-pyran-4-one, and 3-hydroxy-2-methyl-4*H*-pyran-4-one (maltol)] in tobacco smoke. The presence in MSS of the latter compound, maltol, was later confirmed by ELMENHORST (12). In 1974, HECKMAN (59) reported the identification of 3,5-dihydroxy-4*H*-pyran-4-one in burley tobacco smoke. ELMENHORST and NICOLAUS in the late 1970s also identified several dihydropyran-4-ones in tobacco smoke (60).

The wealth of spectral data (UV, IR, NMR, GC, MS) collected during numerous studies on the composition of tobacco and tobacco smoke and used in the characterization of a great number of their components was extremely useful in identifying many components in the MSS from cigarettes containing various tobacco substitutes. The reverse of this was also true. Because the MSS from tobacco substitute cigarettes contained higher levels of many components present in trace amounts in the MSS from all-tobacco cigarettes, the more definitive spectral data generated from them permitted identification of tobacco smoke components, the structures of which were previously suspected but not proven. The previously described case involving the pyrones is an excellent example of the latter situation.

During the next decade, the properties of the smoke chemistry of several of the above mentioned tobacco substitutes were studied in detail, not only on a chemical basis but also from a biological point of view. The results of the chemical composition studies are outlined in Table 4. In a detailed study of the composition of SSM® MSS, GREEN *et al.* (55) identified over 130 components in the MSS from an all-SSM® cigarette. More than 175 components were identified by GREEN *et al.* (61) in the MSS from cigarettes containing Cytrel(I308)®. Because the purpose of this study on Cytrel(I308)® by GREEN *et al.* (61) and their previous one on SSM® (55) was to determine whether any "strangers" were present in the substitute MSS, quantitation of the identified components was limited. Thus, in Table 4, only a few components identified in these two studies are indicated as being more (>) or less (<) in the substitute cigarette MSS than in the all-tobacco cigarette MSS. Contrary to the assertion by Celanese R&D personnel that all components in Cytrel® MSS were tobacco MSS components, GREEN *et al.* (61) identified several MSS components in their Cytrel(I308)® study that were not components in the MSS from all-tobacco cigarettes. The "strangers" included a series of Tergitol® ethers (I–IV) and nonane-related products generated during the smoking process by the degradation of Tergitol® ether III, an additive to the particular Cytrel(I308)® formulation provided at that time (see Figure 2). The Tergitol® ether III was omitted from a subsequent formulation, Cytrel(I324)® (62). Again, contrary to a Celanese R&D personnel assertion, several other components not reported in the MSS from an all-tobacco cigarette at that time were identified in Cytrel(I324) MSS. They included several 2(5*H*)-furanones and a dihydro-2(5*H*)-furanone. The precursor in Cytrel® of these compounds in its MSS was postulated to be the carboxymethylcellulose, an ingredient in the various formula-

Table 4. Chemical composition of mainstream smoke from cigarettes containing various tobacco substitutes

		Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
CAS No.	Component	SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
208-96-8	Acenaphthylene	<u[b]	u[c]	—	—	—	—	—	—	—	—	—	—	<z	z[c]
75-07-0	Acetaldehyde	<u	u	<v	v[c]	<w	w[c]	>x	x[c]	—	—	<t	t[c]	<z	z
60-35-5	Acetamide	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
64-19-7	Acetic acid	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
13831-30-6	Acetic acid, (acetyloxy)-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
141-78-6	Acetic acid, ethyl ester	u	u	v	v	—	—	—	—	—	—	—	—	—	—
79-14-1	Acetic acid, hydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
79-20-9	Acetic acid, methyl ester	u	u	—	—	—	—	—	—	—	—	—	—	—	—
108-21-4	Acetic acid, 1-methylethyl ester	—	—	v	v	—	—	—	—	—	—	—	—	—	—
75-05-8	Acetonitrile	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
926-64-7	Acetonitrile, (dimethylamino)-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
7429-90-5	Aluminum	—	—	—	—	—	—	—	—	<y	y[c]	—	—	—	—
7664-41-7	Ammonia	—	—	—	—	>w	w	—	—	—	—	—	—	z	z
120-12-7	Anthracene	—	—	v	v	—	—	—	—	<y	y	—	—	<z	z
613-31-0	Anthracene, 9, 10-dihydro-	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
779-02-2	Anthracene, 9-methyl-	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-36-0	Antimony	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-37-1	Argon	u	u	—	—	—	—	—	—	—	—	—	—	—	—
7440-38-2	Arsenic	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-39-3	Barium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
205-99-2	Benz[*e*]acephenanthrylene	<u	u	<v	v	—	—	—	—	<y	y	—	—	—	—
100-52-7	Benzaldehyde	u	u	—	—	—	—	x	x	—	—	—	—	<z	z
90-02-8	Benzaldehyde, 2-hydroxy-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
121-33-5	Benzaldehyde, 4-hydroxy-3-methoxy-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
56-55-3	Benz[*a*]anthracene	<u	u	v	v	—	—	—	—	—	—	—>t	t	—	—
62-53-3	Benzenamine	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
95-53-4	Benzenamine, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
122-39-4	Benzenamine, *N*-phenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
71-43-2	Benzene	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
100-42-5	Benzene, ethenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
100-41-4	Benzene, ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-88-3	Benzene, methyl-	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
95-47-6	Benzene, 1,2-dimethyl-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
108-38-3	Benzene, 1,3-dimethyl-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
106-42-3	Benzene, 1,4-dimethyl-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
108-67-8	Benzene, 1,3,5-trimethyl-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
103-82-2	Benzeneacetic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
140-29-4	Benzeneacetonitrile	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
	1,2-Benzenedicarboxylic acid, dialkyl ester [4 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
84-66-2	1,2-Benzenedicarboxylic acid, diethyl ester	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
117-84-0	1,2-Benzenedicarboxylic acid, dioctyl ester	u	u	—	—	—	—	—	—	—	—	—	—	—	—
120-809	1,2-Benzenediol	u	u	v	v	—	—	—	—	—	—	—	—	<z	z
2785-75-3	1,2-Benzenediol, 3,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
2785-78-6	1,2-Benzenediol, 3,6-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1124-39-6	1,2-Benzenediol, 4-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
488-17-5	1,2-Benzenediol, 3-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
452-86-8	1,2-Benzenediol, 4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
108-46-3	1,3-Benzenediol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
123-31-9	1,4-Benzenediol	u	u	v	v	—	—	—	—	—	—	—	—	z	z
608-43-5	1,4-Benzenediol, 2,3-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
615-90-7	1,4-Benzenediol, 2,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
95-71-6	1,4-Benzenediol, methyl-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
60-12-8	Benzeneethanol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
100-51-6	Benzenemethanol	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
617-94-7	Benzenemethanol, dimethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
645-59-0	Benzenepropanenitrile	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
501-52-0	Benzenepropanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
56832-73-6	Benzofluoranthene	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
207-08-9	Benzo[*k*]fluoranthene	u	u	v	v	—	—	—	—	—	—	—	—	—	—
238-84-6	11*H*-Benzo[*a*]fluorene	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
243-17-4	11*H*-Benzo[*b*]fluorene	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
60026-12-2	5-Benzofuranol, 6,7-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	2(3*H*)-Benzofuranone	u	u	—	—	—	—	—	—	—	—	—	—	—	—
16778-27-1	2(3*H*)-Benzofuranone, hexahydro-4,4,7a-trimethyl-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
65-85-0	Benzoic acid	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
100-47-0	Benzonitrile	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
529-19-1	Benzonitrile, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
104-85-8	Benzonitrile, 4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
191-24-2	Benzo[*ghi*]perylene	<u	u	—	—	—	—	—	—	—	—	—	—	—	—
195-19-7	Benzo[*c*]phenanthrene	<u	u	—	—	—	—	—	—	—	—	—	—	—	—
59-02-9	2*H*-1-Benzopyran-6-ol, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
119-84-6	2*H*-1-Benzopyranone, 3,4-dihydro-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
50-32-8	Benzo[*a*]pyrene	<u	u	<v	v	—	—	—	—	<y	y	>t	t	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM® [a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
192-97-2	Benzo[*e*]pyrene	<u	u	—	—	—	—	—	—	<y	y	—	—	—	—
95-21-6	Benzoxazole, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-41-7	Beryllium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
280-65-9	Bicyclo[3.3.1]nonane	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
92-52-4	1,1'-Biphenyl	u	u	—	—	—	—	<x	x	—	—	—	—	<z	z
28013-11-8	1,1'-Biphenyl, ar,ar'-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
643-93-6	1,1'-Biphenyl. 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
644-08-6	1,1'-Biphenyl, 4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
90-43-7	[1,1'-Biphenyl]-2-ol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
37275-48-2	Bipyridine	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
64859-47-8	Bipyridine, methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
581-50-0	2,3'-Bipyridine	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
38840-05-0	2,3'-Bipyridine, 4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
581-49-7	2,3'-Bipyridine, 1,2,3,6-tetrahydro-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-69-9	Bismuth	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7726-95-6	Bromine	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
590-18-1	1,2-Butadiene	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
106-99-0	1,3-Butadiene	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
78-79-5	1,3-Butadiene, 2-methyl-	u	u	v	v	<w	w	—	—	—	—	<t	t	<z	z
96-17-3	Butanal, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
590-86-3	Butanal, 3-methyl-	—	—	—	—	<w	w	—	—	—	—	—	—	<z	z
1113-57-1	Butanamide, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
109-73-9	1-Butanamine	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
13952-84-6	2-Butanamine	—	—	—	—	w	w	—	—	—	—	—	—	—	—
106-97-8	Butane	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
110-15-6	Butanedioic acid	u	u	—	—	—	—	—	—	—	—	—	—	—	—
431-03-8	2,3-Butanedione	u	u	v	v	<w	w	x	x	—	—	—	—	<z	z
109-74-0	Butanenitrile	—	—	—	—	<w	w	—	—	—	—	—	—	<z	z
107-92-6	Butanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
116-53-0	Butanoic acid, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
503-74-2	Butanoic acid, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
71-36-3	1-Butanol	u	u	v	v	—	—	—	—	—	—	—	—	—	—
78-93-3	2-Butanone	u	u	v	v	<w	w	<x	x	—	—	—	—	<z	z
10150-87-5	2-Butanone, 4-(acetyloxy)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
75-97-8	2-Butanone, 3,3-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
563-80-4	2-Butanone, 3-methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
4170-30-3	2-Butenal	—	—	v	v	<w	w	<x	x	—	—	—	—	>z	z
106-98-9	1-Butene	u	u	—	—	—	—	—	—	—	—	—	—	—	—

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
624-64-6	2-Butene (E)	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
590-18-1	2-Butene (Z)	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
110-16-7	2-Butenedioc acid (*Z*)	u	u	—	—	—	—	—	—	—	—	—	—	—	—
3724-65-0	2-Butenoic acid	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
627-27-0	3-Buten-1-ol	—	—	—	—	—	—	—	—	—	—	—	—	z	z
56915-02-7	2-Buten-1-one, 1-(4-hydroxy-2,6,6-trimethyl-1-cyclohexen-1-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
78-94-4	3-Buten-2-one	—	—	—	—	<w	w	<x	x	—	—	—	—	<z	z
814-78-8	3-Buten-2-one, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1203-08-3	3-Buten-2-one, 4-(2,6,6-trimethyl-1,3-cyclohexadien-1-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-43-9	Cadmium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-70-2	Calcium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
124-38-9	Carbon dioxide	u	u	v	v	<w	w	x	x	—	—	<t	t	<z	z
630-08-0	Carbon monoxide	>u	u	<v	v	<w	w	—	—	—	—	<t	t	<z	z
7440-45-1	Cerium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7782-50-5	Chlorine	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
57-88-5	Cholest-5-en-3-ol (3β)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-47-3	Chromium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-47-3	Cobalt	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-50-8	Copper	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
106-34-3	2,5-Cyclohexadiene-1,4-dione, 1:1 compound with 1,4-benzenediol	—	—	v	v	—	—	—	—	—	—	—	—	—	—
527-61-7	2,5-Cyclohexadiene-1,4-dione, 2,6-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
527-17-3	2,5-Cyclohexadiene-1,4-dione, tetramethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	1,2-Cyclohexanedione, 4-methyl-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
89-78-1	Cyclohexanol, 5-methyl-2-(1-methylethyl)	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
591-48-0	Cyclohexene, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
138-86-3	Cyclohexene, 1-methyl-4-(1-methylethenyl)-	u	u	—	—	—	—	<x	x	—	—	—	—	<z	z
5502-88-5	Cyclohexene, 1-methyl-4-(1-methylethyl)-;	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
1125-21-9	2-Cyclohexene-1,4-dione, 2,6,6-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
930-68-7	2-Cyclohexen-1-one	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
5298-13-5	2-Cyclohexen-1-one, 4-(2-buteny-lidene)-3,5,5-trimethyl-, (*E,Z*)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
5492-79-5	2-Cyclohexen-1-one, 4-(2-buteny-lidene)-3,5,5-trimethyl-, (*Z,E*)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
34318-21-3	2-Cyclohexen-1-one, 4-(3-hydroxy-1-butenyl)-3,5,5-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1121-18-2	2-Cyclohexen-1-one, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
78-59-1	2-Cyclohexen-1-one, 3,5,5-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-20-9	1,3,5,7-Cyclooctatetraene	—	—	—	—	—	—	0	x	—	—	—	—	—	—
542-92-7	1,3-Cyclopentadiene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
26519-91-5	1,3-Cyclopentadiene, methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
28473-29-2	Cyclopentanedione	—	—	v	v	—	—	—	—	—	—	—	—	—	—
13494-07-0	1,2-Cyclopentanedione, 3,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
13494-08-1	1,2-Cyclopentanedione, 3-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
	1,2-Cyclopentanedione, 3-ethyl-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
71608-11-2	1,2-Cyclopentanedione, 3-ethyl-5-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
765-70-8	1,2-Cyclopentanedione, 3-methyl-	u	u	v	v	—	—	—	—	—	—	—	—	>z	z
120-92-3	Cyclopentanone	u	u	v	v	—	—	0	x	—	—	—	—	<z	z
1120-72-5	Cyclopentanone, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1757-42-2	Cyclopentanone, 3-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1120-62-3	Cyclopentene, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
2687-69-6	3-Cyclopentene-1,2-dione, 3,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	3-Cyclopentene-1,2-dione, 3-ethyl-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
28982-58-3	Cyclopentenone	v	v	v	v	—	—	—	—	—	—	—	—	—	—
930-30-3	2-Cyclopenten-1-one	—	—	v	v	—	—	<x	x	—	—	—	—	<z	z
80-72-8	2-Cyclopenten-1-one, 2,3-dihydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
72692-71-8	2-Cyclopenten-1-one, dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1121-05-7	2-Cyclopenten-1-one, 2,3-dimethyl-	—	—	v	v	—	—	<x	x	—	—	—	—	<z	z
23048-13-7	2-Cyclopenten-1-one, 2,4-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
30434-64-1	2-Cyclopenten-1-one, 3.4-dimethyl-	—	—	v	v	—	—	<x	x	—	—	—	—	<z	z
931-22-6	2-Cyclopenten-1-one, 3,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
2931-10-4	2-Cyclopenten-1-one, 2-ethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
5682-69-9	2-Cyclopenten-1-one, 3-ethyl-	—	—	v	v	—	—	x	x	—	—	—	—	<z	z
5682-72-4	2-Cyclopenten-1-one, 2-ethyl-3-methyl-	—	—	v	v	—	—	<x	x	—	—	—	—	—	—
41496-77-9	2-Cyclopenten-1-one, 3-ethyl-2-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
	2-Cyclopenten-1-one, 3-ethyl-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	2-Cyclopenten-1-one, 3-ethyl-5-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1120-73-6	2-Cyclopenten-1-one, 2-methyl-	—	—	v	v	—	—	<x	x	—	—	—	—	<z	z
2758-18-1	2-Cyclopenten-1-one, 3-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
61892-84-0	2-Cyclopenten-1-one, 2-(2-oxopropyl)-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
	2-Cyclopenten-1-one, phenyl-	—	—	v	v	—	—	<x	x	—	—	—	—	—	—
24105-07-5	2-Cyclopenten-1-one, 2-propyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
35953-18-5	2-Cyclopenten-1-one, 3-propyl-	—	—	—	—	—	—	x	x	—	—	—	—	—	—
	2-Cyclopenten-1-one, 2,3,5-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
66309-82-8	2-Cyclopenten-1-one, 2,4,5-trimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
7220-78-2	4,8,13-Cyclotetradecatriene-1,3-diol, 1,5,9-trimethyl-12-(1-methylethyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
124-18-5	Decane	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
334-48-5	Decanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
132-64-9	Dibenzofuran	u	u	—	—	—	—	—	—	—	—	—	—	—	—
37112-31-5	6,8-Dioxabicyclo[3.2.1]oct-2-en-4-one, (1S)-	u	u	—	—	—	—	—	—	—	—	—	—	>z	z
484-73-1	5*H*,10*H*-Dipyrrolo[1,2-*a*:1',2'-*d*]pyrazine-5,10-dione	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-97-0	Docosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1599-67-3	1-Docosene	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
112-41-4	1-Dodecene	—	—	v	v	—	—	—	—	—	—	—	—	z	z
112-95-8	Eicosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
474-62-4	Ergost-5-en-3-ol, (3β,24R)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
75-04-7	Ethanamine	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
74-84-0	Ethane	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
107-22-2	Ethanedial	u	u	v	v	—	—	—	—	—	—	—	—	—	—
144-62-7	Ethanedioic acid	u	u	—	—	—	—	—	—	—	—	—	—	—	—
107-21-1	1,2-Ethanediol	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
64-17-5	Ethanol	u	u	v	v	<w	w	—	—	—	—	—	—	—	—
1192-62-7	Ethanone, 1-(2-furanyl)-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
118-93-4	Ethanone, 1-(2-hydroxyphenyl)-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
121-71-1	Ethanone, 1-(3-hydroxyphenyl)-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
	Ethanone, 1-(3-hydroxy-2-methoxyphenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
498-02-2	Ethanone, 1-(4-hydroxy-3-methoxyphenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
26444-19-9	Ethanone, 1-(methylphenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
577-16-2	Ethanone, 1-(2-methylphenyl)-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
122-00-9	Ethanone, 1-(4-methylphenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
932-16-1	Ethanone, 1-(1-methyl-1*H*-pyrrol-2-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
98-86-2	Ethanone, 1-phenyl-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
1122-62-9	Ethanone, 1-(2-pyridinyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
350-03-8	Ethanone, 1-(3-pyridinyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1072-83-9	Ethanone, 1-(1*H*-pyrrol-2-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
121198-50-3	Ethanone, 1-(tetrahydrofuranyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
74-85-1	Ethene	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
74-86-2	Ethyne	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
206-44-0	Fluoranthene	<u	u	<v	v	—	—	—	—	<y	y	—	—	—	—
86-73-7	9*H*-Fluorene	<u	u	v	v	—	—	—	—	<y	y	—	—	<z	z
26914-17-0	9*H*-Fluorene, methyl- [4 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1730-37-6	9*H*-Fluorene, 1-methyl-	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
1430-97-3	9*H*-Fluorene, 2-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1556-99-6	9*H*-Fluorene, 4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
486-25-9	9*H*-Fluoren-9-one	u	u	—	—	—	—	—	—	—	—	—	—	—	—
7782-41-4	Fluorine	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
50-00-0	Formaldehyde	u	u	<v	v	—	—	—	—	—	—	<t	t	—	—
107-31-3	Formic acid, methyl ester	u	u	—	—	—	—	—	—	—	—	—	—	—	—
57-48-7	D-Fructose	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
110-00-9	Furan	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
625-86-5	Furan, 2,5-dimethyl-	u	u	—	—	<w	w	—	—	—	—	—	—	<z	z
27137-41-3	Furan, methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
5534-22-5	Furan, 2-methyl-	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
109-99-9	Furan, tetrahydro-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
2745-26-8	2-Furanacetic acid	u	u	—	—	—	—	—	—	—	—	—	—	—	—
98-01-1	2-Furancarboxaldehyde	u	u	v	v	—	—	<x	x	—	—	—	—	>z	z
	2-Furancarboxaldehyde, hydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
67-47-0	2-Furancarboxaldehyde, 5-hydroxymethyl-	u	u	—	—	—	—	—	—	—	—	—	—	>z	z
26895-04-5	2-Furancarboxaldehyde, methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
620-02-0	2-Furancarboxaldehyde, 5-methyl-	—	—	v	v	—	—	<x	x	—	—	—	—	<z	z
498-60-2	3-Furancarboxaldehyde	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
88-14-2	2-Furancarboxylic acid	u	u	—	—	—	—	—	—	—	—	—	—	—	—
71278-16-5	2-Furancarboxylic acid, 3-hydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
108-31-6	2,5-Furandione	u	u	—	—	—	—	—	—	—	—	—	—	—	—
766-39-2	2,5-Furandione, 3,4-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
3552-33-8	2,5-Furandione, 3-ethyl-4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
98-00-0	2-Furanmethanol	—	—	v	v	—	—	<x	x	—	—	—	—	>z	z
20825-71-2	2(3*H*)-Furanone	u	u	—	—	—	—	—	—	—	—	—	—	z	z
29393-32-6	2(3*H*)-Furanone, 5-acetyldihydro-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
96-48-0	2(3*H*)-Furanone, dihydro-	u	u	—	—	—	—	0	x	—	—	—	—	z	z
18465-71-9	2(3*H*)-Furanone, dihydro-3,4-dihydroxy-3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
19444-84-9	2(3*H*)-Furanone, dihydro-3-hydroxy-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
599-04-2	2(3*H*)-Furanone, dihydro-3-hydroxy-4,4-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
52126-90-6	2(3*H*)-Furanone, dihydro(hydroxy-methyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
36679-81-9	2(3*H*)-Furanone, dihydro-4-(hydroxymethyl)-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
	2(3*H*)-Furanone, dihydro-5-(hydroxymethyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1679-49-8	2(3*H*)-Furanone, dihydro-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
108-29-2	2(3*H*)-Furanone, dihydro-5-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
497-23-4	2(5*H*)-Furanone	u	u	—	—	—	—	—	—	—	—	—	—	>z	z
	2(5*H*)-Furanone, 5-butylidene-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1575-46-8	2(5*H*)-Furanone, 3,4-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
5584-69-0	2(5*H*)-Furanone, 3,5-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
10547-85-0	2(5*H*)-Furanone, 4,5-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
22122-36-7	2(5*H*)-Furanone, 3-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	>z	z
6124-79-4	2(5*H*)-Furanone, 4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
591-11-7	2(5*H*)-Furanone, 5-methyl-	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
108-28-1	2(5H)-Furanone, 5-methylene-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
33488-51-6	2(5*H*)-Furanone, 3,4,5-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-55-3	Gallium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-56-4	Germanium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
498-07-7	β-D-Glucopyranose, 1,6-anhydro-	u	u	v	v	—	—	—	—	—	—	—	—	z	z
26655-34-5	α-D-Glucose	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
50-99-7															
28905-12-6	β-D-Glucose	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
32449-92-6	D-Glucurono-3,6-lactone	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-94-7	Heneicosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1599-68-4	1-Heneicosene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
630-04-6	Hentriacontane	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
4981-99-1	Hentriacontane, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
593-49-7	Heptacosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
	Heptacosane, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
14167-66-9	Heptacosane, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-78-7	Heptadecane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
6765-39-5	1-Heptadecene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1604-28-0	3,5-Heptadien-2-one, 6-methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
111-14-8	Heptanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
106-35-4	3-Heptanone	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-83-8	4-Heptanone, 2,6-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
2009-74-7	3-Hepten-2-one, 6-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
630-01-3	Hexacosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
544-76-3	Hexadecane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
57-10-3	Hexadecanoic acid	u	u	—	—	—	—	—	—	—	—	0	t	—	—
629-73-2	1-Hexadecene,	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
504-96-1	1-Hexadecene, 3-methylene-7,11,15-trimethyl-	—	—	—	—	—	—	0	x	—	—	0	t	<z	z
150-86-7	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	Hexadiene, methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
10420-90-3	1,3-Hexadien-5-yne	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
110-54-3	Hexane	—	—	—	—	<w	w	—	—	—	—	—	—	<z	z
50-70-4	Hexane, hexahydroxy-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
124-04-9	Hexanedioic acid	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
142-62-1	Hexanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
591-78-6	2-Hexanone	—	—	—	—	—	—	—	—	—	—	—	—	z	z
5166-53-0	3-Hexen-2-one, 5-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
74-90-8	Hydrogen cyanide	<u	u	<v	v	<w	w	<x	x	—	—	0	t	—	—
7783-06-4	Hydrogen sulfide	—	—	—	—	>w	w	—	—	—	—	—	—	—	—
288-32-4	1*H*-Imidazole	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
95-13-6	1*H*-Indene	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
53563-67-0	1*H*-Indene, 2,3-dihydrodimethyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
27133-93-3	1*H*-Indene, 2,3-dihydromethyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
29348-63-8	1*H*-Indene, dimethyl- [3 isomers]	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
29036-25-7	1*H*-Indene, methyl- [3 isomers]	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
60826-61-1	1*H*-Indene, trimethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
56631-57-3	1*H*-Indenol	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1470-94-6	1*H*-Inden-5-ol, 2,3-dihydro-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
72692-86-5	1*H*-Inden-5-ol, 2,3-dihydromethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
83-33-0	1*H*-Inden-1-one, 2,3-dihydro-	u	u	v	v	—	—	<x	x	—	—	—	—	—	—
71278-03-0	1*H*-Inden-1-one, 2,3-dihydrodimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
71278-04-1	1*H*-Inden-1-one, 2,3-dihydroethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
65436-86-4	1*H*-Inden-1-one, 2,3-dihydromethyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
17496-14-9	1*H*-Inden-1-one, 2,3-dihydro-2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
6072-57-7	1*H*-Inden-1-one, 2,3-dihydro-3-methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
120-72-9	1*H*-Indole	—	—	—	—	—	—	0	x	—	—	0	t	<z	z
10604-59-8	1*H*-Indole, ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1484-19-1	1*H*-Indole, 3-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
27323-28-0	1*H*-Indole, methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
95-20-5	1*H*-Indole, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
83-34-1	1*H*-Indole, 3-methyl-	—	—	—	—	—	—	—	—	—	—	0	t	<z	z
6917-35-7	Inositol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7553-56-2	Iodine	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7439-89-6	Iron	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
87-41-2	1(3*H*)-Isobenzofuranone	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
119-65-3	Isoquinoline	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
29832-78-8	Isoquinoline, tetrahydro-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
10557-82-1	Isoxazole, 3,4,5-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7439-92-1	Lead	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7439-93-2	Lithium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7439-95-4	Magnesium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7439-96-5	Manganese	—	—	—	—	—	—	—	—	<y	y	—	—	—	—

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
69-65-8	D-Mannitol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
3458-28-4	D-Mannose	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7439-97-6	Mercury	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
74-89-5	Methanamine	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
124-40-3	Methanamine, *N*-methyl-	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
62-75-9	Methanamine, *N*-methyl-*N*-nitroso-	—	—	—	—	—	—	—	—	0	x	—	—	—	—
74-82-8	Methane	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
74-87-3	Methane, chloro-	u	u	—	—	0	w	—	—	—	—	—	—	—	—
67-56-1	Methanol	u	u	v	v	<w	w	<x	x	—	—	—	—	<z	z
7439-98-7	Molybdenum	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
91-20-3	Naphthalene	u	u	v	v	—	—	<x	x	—	—	—	—	<z	z
39292-53-0	Naphthalene, dihydromethyl- [4 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
4373-13-1	Naphthalene, 3,4-dihydro-1-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
28804-88-8	Naphthalene, dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
575-43-9	Naphthalene, 1,6-dimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
27138-19-8	Naphthalene, ethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
1321-94-4	Naphthalene, methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
90-12-0	Naphthalene, 1-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
91-57-6	Naphthalene, 2-methyl-	u	u	v	v	—	—	—	—	—	—	—	—	<z	z
28652-77-9	Naphthalene, trimethyl- [2 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
2245-38-7	Naphthalene, 1,6,7-trimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
20490-42-0	1,4-Naphthalenedione, 2,3,6-trimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
90-15-3	1-Naphthalenol	—	—	v	v	—	—	—	—	—	—	—	—	—	—
135-19-3	2-Naphthalenol	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1076-26-9	2-Naphthalenol, 1-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
7440-02-0	Nickel	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-03-1	Niobium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7727-37-9	Nitrogen	u	u	—	—	—	—	—	—	—	—	—	—	—	—
10102-43-9	Nitrogen oxide (NO)	<u	u	v	v	<w	w	—	—	—	—	—	—	—	—
	Nitrogen oxides (N_2O+NO+NO_2)	<u	u	—	—	—	—	—	—	—	—	<t	t	—	—
630-03-5	Nonacosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1560-75-4	Nonacosane, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
14167-67-0	Nonacosane, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-92-5	Nonadecane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
27400-77-7	Nonadecene	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
1937-54-8	6,8-Nonadien-2-one, 8-methyl-5-(1-methylethyl)-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
	Nonane, 4-acetyl-2,6,8-trimethyl-	—	—	v	0	—	—	—	—	—	—	—	—	—	—
55023-57-9	2,8-Nonanedione, 5-(1-methylethyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
	4-Nonanol, 2,6,8-trimethyl-	—	—	v	0	—	—	—	—	—	—	—	—	—	—
	4-Nonanone, 2,6,8-trimethyl-	—	—	v	0	—	—	—	—	—	—	—	—	—	—
60619-46-7	3-Nonene-2,8-dione, 5-(1-methylethyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
630-02-4	Octacosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1560-98-1	Octacosane, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
65820-58-8	Octacosane, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
593-45-3	Octadecane	—	—	v	v	—	—	—	—	—	—	—	—	—	—
506-21-8	9,12-Octadecadienoic acid	—	—	—	—	—	—	—	—	—	—	0	t	<z	z
57-11-4	Octadecanoic acid	—	—	—	—	—	—	—	—	—	—	0	t	<z	z
463-40-1	9,12,15-Octadecatrienoic acid	—	—	—	—	—	—	—	—	—	—	0	t	<z	z
112-88-9	1-Octadecene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
112-80-1	9-Octadecenoic acid	—	—	—	—	—	—	—	—	—	—	0	t	<z	z
78-70-6	1,6-Octadien-3-ol, 3,7,-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
123-96-6	2-Octanol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
29414-56-0	1,5,7-Octatrien-3-ol, 2,6-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7782-44-7	Oxygen	u	u	—	—	—	—	—	—	—	—	—	—	—	—
629-99-2	Pentacosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
629-62-9	Pentadecane	—	—	v	v	—	—	0	x	—	—	—	—	<z	z
1002-84-2	Pentadecanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
13360-61-7	1-Pentadecene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
2140-82-1	1-Pentadecene, 2,6,10,14-tetramethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
41050-31-1	Pentadiene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
504-60-9	1,3-Pentadiene	u	u	v	v	—	—	—	—	—	—	—	—	<z	z
626-97-1	Pentanamide	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
600-14-6	2,3-Pentanedione	u	u	v	v	—	—	x	x	—	—	—	—	<z	z
7493-58-5	2,3-Pentanedione, 4-methyl-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
110-59-8	Pentanenitrile	u	u	—	—	—	—	—	—	—	—	—	—	—	—
6339-13-5	Pentanenitrile, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
105-43-1	Pentanoic acid, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
123-76-2	Pentanoic acid, 4-oxo-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
107-87-9	2-Pentanone	—	—	v	v	<w	w	x	x	—	—	—	—	<z	z
96-22-0	3-Pentanone	u	u	—	—	—	—	—	—	—	—	—	—	<z	z
123-42-2	2-Pentanone, 4-hydroxy-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
565-69-5	3-Pentanone, 2-methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
623-36-9	2-Pentenal, 2-methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
763-29-1	1-Pentene, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	Z
626-98-2	2-Pentenoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	Z
1629-58-9	1-Penten-3-one	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
25044-01-3	1-Penten-3-one, 2-methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
625-33-2	3-Penten-2-one	—	—	—	—	—	—	<x	x	—	—	—	—	<z	Z
13891-87-7	4-Penten-2-one	—	—	—	—	—	—	0	x	—	—	—	—	—	—
198-55-0	Perylene	<u	u	—	—	—	—	—	—	<y	y	—	—	—	—
85-01-8	Phenanthrene	<u	u	—	—	—	—	—	—	<y	y	>t	t	<z	Z
20291-72-9	Phenanthrene, 1,2-dimethyl-	—	—	v	v	—	—	—	—	—	—			—	—
1576-67-6	Phenanthrene, 3,6-dimethyl-	—	—	—	—	—	—	—	—	<y	y			—	—
31711-53-2	Phenanthrene, methyl-	—	—	v	v	—	—	—	—	—	—			—	—
832-69-9	Phenanthrene, 1-methyl-	—	—	—	—	—	—	—	—	<y	y			—	—
2531-84-2	Phenanthrene, 2-methyl-	—	—	—	—	—	—	—	—	<y	y			—	—
832-71-3	Phenanthrene, 3-methyl-	—	—	—	—	—	—	—	—	<y	y			—	—
108-95-2	Phenol	<u	u	<v	v	—	—	<x	x	<y	y	<t	t	<z	Z
91-10-1	Phenol, 2,6-dimethoxy-	—	—	—	—	—	—	—	—	—	—	—	—	<z	Z
1300-71-6	Phenol, dimethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
526-75-0	Phenol, 2,3-dimethyl-	—	—	v	v	—	—	—	—	<y	y	—	—	<z	Z
105-67-9	Phenol, 2,4-dimethyl-	u	u	v	v	—	—	—	—	<y	y	—	—	<z	Z
95-87-4	Phenol, 2,5-dimethyl-	—	—	—	—	—	—	—	—	<y	y	—	—	<z	Z
1006-59-3	Phenol, 2,6-dimethyl-	—	—	v	v	—	—	—	—	<y	y	—	—	<z	z
95-65-8	Phenol, 3,4-dimethyl-	—	—	v	v	—	—	—	—	<y	y	—	—	<z	z
108-68-9	Phenol, 3,5-dimethyl-	—	—	v	v	—	—	—	—	<y	y	—	—	<z	z
18441-55-9	Phenol, 2,3-dimethyl- 6-ethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
695-84-1	Phenol, 2-ethenyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
2628-17-3	Phenol, 4-ethenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
73850-05-2	Phenol, ethenyl-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	Phenol, 2- ethenyl-6-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
25429-37-2	Phenol, ethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
90-00-6	Phenol, 2-ethyl-	—	—	v	v	—	—	—	—	<y	y	—	—	<z	z
620-17-7	Phenol, 3-ethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
123-07-9	Phenol, 4-ethyl-	—	—	—	—	—	—	—	—	<y	y	—	—	<z	z
30230-52-5	Phenol, ethyl-methyl-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
3855-26-3	Phenol, 2-ethyl-4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
1687-64-5	Phenol, 2-ethyl-6-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
6161-67-7	Phenol, 3-ethyl-4-methyl-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
1123-94-0	Phenol, 4-ethyl-3-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
90-05-1	Phenol, 2-methoxy-	—	—	—	—	—	—	—	—	<y	y	—	—	<z	z
150-76-5	Phenol, 4-methoxy-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
93-51-6	Phenol, 2-methoxy-4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
97-53-0	Phenol, 2-methoxy-4-(2-propenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1319-77-3	Phenol, methyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
95-48-7	Phenol, 2-methyl-	u	u	v	v	—	—	—	—	<y	y	<t	t	z	z
108-39-4	Phenol, 3-methyl-	u	u	v	v	—	—	—	—	<y	y	<t	t	<z	z
526-75-0	Phenol, 4-methyl-	—	—	—	—	—	—	—	—	<y	y	<t	t	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
88-69-7	Phenol, 2-(1-methylethyl)-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
4074-46-8	Phenol, 4-methyl-2-propyl-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
644-35-9	Phenol, 2-propyl-	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
527-35-5	Phenol, 2,3,5,6-tetramethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
526-85-2	Phenol, 2,3,4-trimethyl-	—	—	v	v	—	—	—	—	—[b]	—[b]	—	—	—	—
697-82-5	Phenol, 2,3,5-trimethyl-	—	—	v	v	—	—	—	—			—	—	<z	z
2416-94-6	Phenol, 2,3,6-trimethyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
496-78-6	Phenol, 2,4,5-trimethyl-	—	—	v	v	—	—	—	—	—[b]	—[b]	—	—	—	—
527-60-6	Phenol, 2,4,6-trimethyl-	—	—	v	v	—	—	—	—			—	—	—	—
7723-14-0	Phosphorus	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
1121-89-7	2,6-Piperidinedione	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
7440-09-7	Potassium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
463-49-0	Propadiene	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
123-38-6	Propanal	u	u	v	v	<w	w	>x	x	—	—	—	—	<z	z
78-84-2	Propanal, 2-methyl-	u	u	v	v	<w	w	x	x	—	—	—	—	<z	z
1187-58-2	Propanamide, *N*-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
107-10-8	1-Propanamine	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
78-81-9	1-Propanamine, 2-methyl-	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
75-31-0	2-Propanamine	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
74-98-6	Propane	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
75-28-5	Propane, 2-methyl-	u	u	—	—	<w	w	—	—	—	—	—	—	—	—
141-82-2	Propanedioic acid	u	u	—	—	—	—	—	—	—	—	—	—	—	—
57-55-6	1,2-Propanediol	—	—	—	—	—	—	—	—	—	—	—	—	z	z
126-30-7	1,3-Propanediol, 2,2-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
107-12-0	Propanenitrile	u	u	v	v	<w	w	—	—	—	—	—	—	<z	z
78-97-7	Propanenitrile, 2-hydroxy-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
78-82-0	Propanenitrile, 2-methyl-	u	u	—	—	<w	w	—	—	—	—	—	—	<z	z
	1,2,3-Propanetricarboxylic acid, 2-hydroxy-, monoethyl ester	u	u	—	—	—	—	—	—	—	—	—	—	—	—
56-81-5	1,2,3-Propanetriol	—	—	v	v			—	—	<y	y	—	—	<z	z
26446-35-5	1,2,3-Propanetriol, monoacetate	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
102-76-1	1,2,3-Propanetriol, triacetate	—	—	—	—	—	—	x	x	—	—	—	—	—	—
79-09-4	Propanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
79-31-2	Propanoic acid, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
71-23-8	1-Propanol	u	u	—	—	—	—	—	—	—	—	—	—	—	—
67-63-0	2-Propanol	—	—	v	v	—	—	—	—	—	—	—	—	—	—
93-55-0	1-Propanone, 1-phenyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
67-64-1	2-Propanone	<u	u	<v	v	<w	w	—	—	—	—	—	—	<z	z
592-20-1	2-Propanone, 1-(acetyloxy)-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	2-Propanone, 1-(2-tetrahydrofuranyl)-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
116-09-6	2-Propanone, 1-hydroxy-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
103-79-7	2-Propanone, 1-phenyl	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
107-02-8	2-Propenal	<u	u	<v	v	<w	w	<x	x	—	—	<t	t	>z	z
79-06-1	2-Propenamide	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
115-07-1	Propene	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
557-31-3	1-Propene, 3-ethoxy-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
107-13-1	2-Propenenitrile	u	u	—	—	—	—	—	—	—	—	—	—	—	—
74-99-7	Propyne	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
142-68-7	2*H*-Pyran, tetrahydro	u	u	v	v	—	—	—	—	—	—	—	—	—	—
70898-35-0	2*H*-Pyran-2-carboxaldehyde, 3,4-dihydro-6-hydroxy-3-oxo-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
	2*H*-Pyran-2-one, methoxy-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
	2*H*-Pyran-2-one, methyl-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
	2*H*-Pyran-2-one, 3-hydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
21722-33-8	2*H*-Pyran-2-one, 5,6-dihydro-4-(1-methylethyl)-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	2*H*-Pyran-2-one, tetrahydro-3,4-epoxy-5-hydroxy-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
28564-83-2	4*H*-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
488-18-6	4*H*-Pyran-4-one, 3,5-dihydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
1073-96-7	4*H*-Pyran-4-one, 3,5-dihydroxy-2-methyl-	u	u	—	—	—	—	—	—	—	—	—	—	>z	z
496-63-9	4*H*-Pyran-4-one, 3-hydroxy-	u	u	—	—	—	—	—	—	—	—	—	—	—	—
118-71-8	4*H*-Pyran-4-one, 3-hydroxy-2-methyl-	u	u	v	v	—	—	—	—	—	—	—	—	—	—
	4*H*-Pyran-4-one, 2-hydroxymethyl-3,5,6-trihydroxy-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
	4*H*-Pyran-4-one, 2-methyl-3,5,6-trihydroxy-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
	4*H*-Pyran-4-one-2-carboxylic acid, 5-hydroxy-	u	0	—	—	—	—	—	—	—	—	—	—	—	—
	4*H*-Pyran-4-one-2-carboxylic acid, 5-hydroxy-, (1-methylethyl) ester	u	0	—	—	—	—	—	—	—	—	—	—	—	—
18138-05-1	Pyrazine, 3,5-diethyl-2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
25704-73-8	Pyrazine, dimethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	—	—
5910-89-4	Pyrazine, 2,3-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-50-9	Pyrazine, 2,6-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
15707-34-3	Pyrazine, 2,3-dimethyl-5-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
13925-00-3	Pyrazine, ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	z	z
13925-03-6	Pyrazine, 2-ethyl-6-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
109-08-0	Pyrazine, methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1124-11-4	Pyrazine, tetramethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
14667-55-1	Pyrazine, trimethyl-	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
129-00-0	Pyrene	<u	u	<v	v	—	—	—	—	<y	y	—	—	—	—
23281-21-7	Pyrene, 1-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
3353-12-6	Pyrene, 4-methyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
110-86-1	Pyridine	—	—	—	—	—	—	0	x	—	—	—	—	<z	z
532-12-7	Pyridine, 3-(3,4-dihydro-2*H*-pyrrol-5-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
583-61-9	Pyridine, 2,3-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
589-93-5	Pyridine, 2,5-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-48-5	Pyridine, 2,6-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1121-55-7	Pyridine, 3-ethenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
100-71-0	Pyridine, 2-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
536-78-7	Pyridine, 3-ethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1124-35-2	Pyridine, 2-ethyl-4,6-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
27987-10-	Pyridine, ethylmethyl- [4 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1333-41-1	Pyridine, methyl-	—	—	—	—	—	—	0	x	—	—	—	—	—	—
109-06-8	Pyridine, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-99-6	Pyridine, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
108-89-4	Pyridine, 4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
18368-73-5	Pyridine, 3-methyl-2-nitro-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
54-11-5	Pyridine, 3-(1-methyl-2-pyrrolidinyl)-	0	u	0	v	—	—	0	x	0	y	0	t	<z	z
1008-88-4	Pyridine, 3-phenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
494-52-0	Pyridine, 3-(2-piperidinyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	Pyridine, propenyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
15376-62-2	Pyridine, 3-(1-propenyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
4673-31-8	Pyridine, 3-propyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
494-98-4	Pyridine, 3-(1*H*-pyrrol-2-yl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
100-54-9	3-Pyridinecarbonitrile	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
98-92-0	3-Pyridinecarboxamide	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	2-Pyridinol, 6-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
109-00-2	3-Pyridinol	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
626-64-2	4-Pyridinol	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
6052-73-9	2(1*H*)-Pyridinone, 5,6-dihydro-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
109-97-7	1*H*-Pyrrole	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
	1*H*-Pyrrole, 3-ethyl-1-phenyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
96-54-8	1*H*-Pyrrole, 1-methyl-	—	—	—	—	—	—	>x	x	—	—	—	—	<z	z
	1*H*-Pyrrole, 2-methyl-1-phenyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
	1*H*-Pyrrole, 3-methyl-1-phenyl-	—	—	v	v	—	—	—	—	—	—	—	—	—	—
635-90-5	1*H*-Pyrrole, 1-phenyl-	—	—	v	v	—	—	<x	x	—	—	—	—	—	—
1003-29-8	1*H*-Pyrrole-2-carboxaldehyde	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
1192-79-6	1*H*-Pyrrole-2-carboxaldehyde, 5-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
634-97-9	1*H*-Pyrrole-2-carboxylic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
20189-42-8	1*H*-Pyrrole-2,5-dione, 3-ethyl-4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
5979-94-2	Pyrrolidine, 1-acetyl-2-(3-pyridinyl)-,	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
930-55-2	Pyrrolidine, *N*-nitroso-	—	—	—	—	—	—	—	—	0	y	—	—	—	—
38840-03-8	1-Pyrrolidinecarboxaldehyde, 2-(3-pyridinyl)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
123-56-8	2,5-Pyrrolidinedione	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
15542-96-8	2,5-Pyrrolidinedione, 1,3-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1121-07-9	2,5-Pyrrolidinedione, 1-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
14498-44-3	2-Pyrrolidinepropanol, 1-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
2555-05-7	2-Pyrrolidinone, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
486-56-6	2-Pyrrolidinone, 1-methyl-5-(3-pyridinyl)-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
54036-77-0	2*H*-Pyrrol-2-one	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
4031-15-6	2*H*-Pyrrol-2-one, 1,5-dihydro-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
91-22-5	Quinoline	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
27601-00-9	Quinoline, methyl- [4 isomers]	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
	Quinoline, tetrahydro-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
5541-68-4	8-Quinolinol, 7-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
7440-17-7	Rubidium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-20-2	Scandium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7782-49-2	Selenium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-21-3	Silicon	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-22-4	Silver	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-23-5	Sodium	—	—	—	—	—	—	—	—	>y	y	—	—	—	—
83-46-5	Stigmast-5-en-3-ol, (3β)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
83-48-7	Stigmasta-5,22-dien-3-ol, (3β,22*E*)-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-24-6	Strontium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7704-34-9	Sulfur	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7446-09-5	Sulfur dioxide	—	—	—	—	<w	w	—	—	—	—	—	—	—	—
13494-80-9	Tellurium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
	Tergitol ether I[d]	—	—	v	0	—	—	—	—	—	—	—	—	—	—
	Tergitol ether II	—	—	v	0	—	—	—	—	—	—	—	—	—	—
	Tergitol ether III	—	—	v	0	—	—	—	—	—	—	—	—	—	—
	Tergitol ether IV	—	—	v	0	—	—	—	—	—	—	—	—	—	—
646-31-1	Tetracosane	—	—	v	v	—	—	—	—	—	—	—	—	—	—
10192-32-2	1-Tetracosene	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
629-59-4	Tetradecane	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
544-63-8	Tetradecanoic acid	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1120-36-1	1-Tetradecene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
7440-28-0	Thallium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
693-95-8	Thiazole, 4-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
126-33-0	Thiophene, tetrahydro-, 1,1-dioxide	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
98-03-3	2-Thiophenecarboxaldehyde	—	—	—	—	—	—	—	—	—	—	—	—	<z	z

Table 4 (*cont.*)

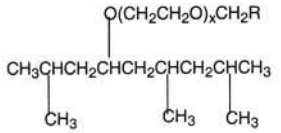
CAS No.	Component	Green *et al.* (55)		Green *et al.* (61)		Celanese Corp.						Gori (77, 78, 79)		Lloyd, Miller (64) and/or Green *et al.* (65, 66)	
						Vickroy *et al.* (70)		Mauldin (71)		Allen and Vickroy (72)					
		SSM®[a]	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	Cyt	Tob	1:1 J10:Tob	Tob
7440-29-1	Thorium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-31-5	Tin	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-32-6	Titanium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
630-05-7	Triacontane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
1560-72-1	Triacontane, 2-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
	Triacontane, 3-methyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
638-67-5	Tricosane	—	—	v	v	—	—	—	—	—	—	—	—	<z	z
18835-32-0	1-Tricosene	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
629-50-5	Tridecane	—	—	—	—	—	—	<x	x	—	—	—	—	<z	z
25377-82-6	Tridecene	—	—	—	—	—	—	0	x	—	—	—	—	<z	z
630-05-7	Tritriacontane	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
3796-70-1	5,9-Undecadien-2-one, 6,10-dimethyl-	—	—	—	—	—	—	—	—	—	—	—	—	<z	z
1120-21-4	Undecane	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
821-95-4	1-Undecene	—	—	—	—	—	—	—	—	—	—	—	—	>z	z
7440-61-1	Uranium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-62-2	Vanadium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7732-18-5	Water	u	u	v	v	—	—	—	—	<y	y	<t	t	—	—
7440-65-5	Yttrium	—	—	—	—	—	—	—	—	>y	y	—	—	—	—
7440-66-6	Zinc	—	—	—	—	—	—	—	—	<y	y	—	—	—	—
7440-67-7	Zirconium	—	—	—	—	—	—	—	—	<y	y	—	—	—	—

[a] Abbreviations: SSM® = Sutton Smoking Material; Cyt = Cytrel® Smoking Material; Tob = tobacco; J10 = expanded grain smoking material.

[b] The symbol < indicates lower yield in substitute MSS than that from an all-tobacco cigarette; > indicates a greater yield in substitute MSS than from an all-tobacco cigarette.

[c] The symbol *t* indicates that the component designated was reported by GORI (77, 78, 79) in the NCI "less hazardous" cigarette study of the MSSs from Cytrel® and tobacco cigarettes; *u* indicates that the component designated was identified by GREEN *et al.* (55) in the MSSs from SSM® and tobacco cigarettes; *v* indicates that the component designated was identified by GREEN *et al.* (61) in the MSSs from Cytrel® and tobacco cigarettes; *w*, *x*, and *y* indicate that the component designated was identified by Celanese personnel (70, 71, 72) in the MSSs from Cytrel® and tobacco cigarettes; *z* indicates that the component designated was identified by RJRT personnel (64,65,66) in the MSSs from J10, J10T, and tobacco cigarettes.

[d] The tergitol ethers possessed the following structures:



Tergitol ether I: R = CH_3, $x = 1$
Tergitol ether II: R = CH_3, $x = 2$
Tergitol ether III: R = CH_3, $x = 3$
Tergitol ether IV: R = H, $x = 1$.

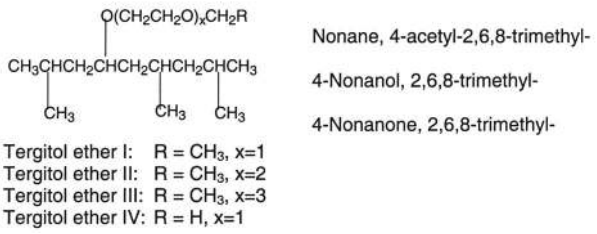


Figure 2. Components identified in mainstream smoke from Cytrel® cigarettes but not found in mainstream smoke from tobacco cigarettes

tions of Cytrel® [see BROWNE (63)]. However, a few years later, because of the availability of the many spectral data from the Cytrel®(I324) MSS study, the furanones and dihydrofuranone were identified in several different studies on the MSS composition from cigarettes containing tobacco (64, 65, 66) and/or various processed tobaccos (13, 67, 68, 69).

In three related studies, the research staff at Celanese, the originator of Cytrel®, conducted a detailed investigation of the MSS composition from the following: 1) all-Cytrel® cigarettes, 2) all-flue-cured tobacco cigarettes, and 3) cigarettes containing mixtures of Cytrel® and the flue-cured tobacco. VICKROY *et al.* (70) reported the identification of components in the MSS vapor phase from these sources whereas MAULDIN (71) and ALLEN and VICKROY (72) reported on the identification of components in the semi-volatile and particulate phases, respectively. Overall, more than 200 identified components were reported in the three studies (see Table 4), but no "stranger" was reported by Celanese personnel in the MSS from any Cytrel®-containing cigarette. Several components identified in the flue-cured tobacco MSS were not detected by Celanese personnel in the Cytrel® MSS, e.g., dimethylaminoacetonitrile (70, 71), cyclooctatetraene (71), cyclopentanone (71), 3-methylene-7,11,15-trimethyl-1-hexadecene (neophytadiene) (71), several indenes and indoles (71), *N*-methyl-*N*-nitrosomethanamine (NDMA) (72), pentenal and pentenone (71), pyridine (71) and several pyridine derivatives (71, 72), and *N*-nitrosopyrrolidine (NPYR) (72).

As summarized in Table 4, over 350 components were identified by LLOYD and MILLER (64) and GREEN *et al.* (65, 66) in the MSS from cigarettes containing a 50:50 blend of J10 and tobacco. Although J10 denoted expanded grains in Table 2, the particular expanded grain in much of the J10 research described hereafter was shredded popcorn.

In most instances, the per cigarette yields of MSS components from the J10:tobacco cigarettes were much lower than those from the all-tobacco cigarette. At first it appeared that the MSS from a J10:tobacco cigarette did indeed contain a "stranger" that interfered with the determination of phenol. However, in a study of the pyrolysis of J10, the "stranger" was isolated from the pyrolysate and identified as levoglucosenone (64). Subsequently, it was identified in the MSS from an all-tobacco cigarette (13). Examination of the Table 4 listing reveals that tobacco and the J10:tobacco blend gave essentially the same per cigarette yield of a few compounds, e.g., ammonia, 1,3-benzenediol, 2-hexanone. Examination also reveals a few cases where the MSS levels of a few components from the J10:tobacco cigarette exceeded the all-tobacco MSS yields, e.g., 2-butenoic acid, 2-furancarboxaldehyde and its 5-hydroxymethyl derivative, 2-furanmethanol (furfuryl alcohol).

Because J10, unlike SSM®, NSM® and Cytrel®, would not support combustion in a cigarette at the 100% level, a combustion-enhancing substance was required to sustain cigarette smolder between puffs. Thus, MSS composition studies on 100% J10 cigarettes were impossible. The problem was resolved by addition of a low level (2%) of nitrate to the J10. The nitrate-treated J10 is designated as J10T in Table 5. Comparison of the MSS compositions from 1:1 J10:tobacco cigarettes and 1:1 J10T:tobacco cigarettes indicated the nitrate had no significant effect on the MSS composition or its properties.

It is obvious that the number of MSS components from the various tobacco substitutes (J10, SSM®, NSM®, Cytrel®) is much less than the number in the MSS from all-tobacco cigarettes. The simplicity of the substitutes vs. the complexity of tobacco with its more than 3000 identified components is a rational explanation for the difference in the number of MSS components.

Because RJRT had prepared the experimental blend SEBIV from various tobaccos and the various cigarette prototypes used in the NCI "less hazardous" cigarette study on the

Table 5. Comparison of data from biological assays of mainstream smokes from J10-, J10T-, and SEBIV-containing cigarettes

Analyte	SEBIV	1:1 J10:SEBIV	1:1 J10T:SEBIV	J10T
	Carcinogenicity study (75)			
%Tumor-bearing animals, dose = 25 mg/day	36 54 [a]	21	22	7
18-Month survivors	38 46 [a]	38	46	37
Benzo[*a*]pyrene, ng/mg TPM	0.53 0.60 [b]	0.36	0.42	0.19
Phenol, µg/mg TPM	3.73 3.19 [b]	2.88	2.70	1.98
	Mutagenicity study (76)			
Ames test (TA98), rev/250 µg	330	210	215	90
Ames test (TA1538), rev/250 µg	560	450	310	105

[a] Biological data reported by GORI (79) for MSS from SEBIV.
[b] Analytical value reported by GORI (79) for MSS from SEBIV.

fourth set of experimental cigarettes, supplies of the same tobaccos were available (73). With them, a comparable SEBIV blend was prepared for use in the chemical and biological studies of the MSSs involving J10-, J10T-, and SEBIV-containing cigarettes. Biological studies (mouse skin-painting bioassays, Ames-type mutagenicity studies) were conducted on the mainstream CSCs from the following four cigarette samples: all-SEBIV, 1:1 J10:SEBIV, 1:1 J10T:SEBIV, and all-J10T.

The protocol used in the mouse skin-painting bioassay paralleled that described in the NCI "less hazardous" studies (74) except for one difference: A Borgwaldt 30-port smoking machine was used to circumvent the problems associated with the 360-port Process and Instruments Corporation smoking machine used throughout the NCI studies. An 18-month mouse skin-painting bioassay was conducted by Industrial Bio-Test Laboratories, Ltd. on the previously mentioned four cigarette samples. Only one CSC dose level was used, namely 25 mg/day, for each of the four samples (75). After 18 months, the %TBAs for the four samples were 36%, 21%, 22%, and 7%, respectively.

The mutagenicities of the four TPMs were examined in the early days of the Ames test (*Salmonella typhimurium*) when quantitation and determination of specific mutagenicity had not yet been defined (76). However, the mutagenicity findings paralleled those in the mouse skin-painting bioassay. The results of the bioassays of the J10 systems are shown in Table 5.

During the investigations from the late 1960s through the late 1970s of the composition of MSS from cigarettes containing individual tobacco substitutes or blends of various ratios of tobacco substitute to tobacco, considerable data were generated in various laboratories (61, 64, 65, 66, 70, 72, 77, 78) on the per cigarette yields of some of the components classified at that time as toxicants. The analytical data generated on several tobacco substitutes are summarized in Table 6. It is interesting to note that the MSS components determined quantitatively in industrial and governmental laboratories were eventually classified in the late 1990s as "HOFFMANN analytes" because of their frequent listing as harmful smoke components by HOFFMANN *et al.* [(36, 80), see also Table 2 in RODGMAN (29)]. In addition to the data compiled in Table 6, the per cigarette MSS yields were determined for several other components subsequently defined as "HOFFMANN analytes". Those included are listed in Table 7 with an indication of their per cigarette MSS level compared to that from an all-tobacco cigarette. Except for 2-propenamide and quinoline, all the "HOFFMANN analytes" listed in Table 7 in the MSS from an all-tobacco substitute cigarette or a tobacco:tobacco substitute mixture cigarette were reported at a lower per cigarette yield than the yield from an all-tobacco cigarette.

GORI, in his reports on the NCI Smoking and Health Program devoted to the search for a "less hazardous" cigarette, described the results of the biological studies (mouse skin-painting assay) conducted with the CSCs from several tobacco substitute cigarettes, namely, NSM® and Cytrel® (77, 78). Examination of the biological data in Table 6 indicates that NSM® CSC showed lower specific tumorigenicity to mouse skin than did the CSC from an all-tobacco cigarette. However, because of the variation described for the specific tumorigenicity of CSC from Cytrel®-containing cigarettes in the first bioassay results obtained in the NCI program (77), the study was repeated (78) with several different Cytrel® formulations. No improvement was observed. In the second NCI study, the Cytrel® CSCs again showed higher specific tumorigenicity than did the CSCs from the all-tobacco cigarettes. This increased specific tumorigenicity with Cytrel® CSCs was observed despite the fact that in both studies the per cigarette yields of benz[*a*]anthracene (B[*a*]A) and benzo[*a*]pyrene (B[*a*]P) in the Cytrel® CSCs were lower than those in the CSCs from the all-tobacco cigarettes. However, the ratio B[*a*]P:TPM was greater for the all-Cytrel® CSC than for the all-tobacco CSC.

Several years later, the biological effects of the MSSs from cigarettes with fillers containing different ratios of tobacco and Cytrel® were studied by Battelle personnel (COGGINS *et al.* (83) in an 18-month inhalation study with rats. On histopathological examination, the rats exposed to the MSSs from Cytrel®-containing cigarettes showed fewer changes than those exposed to the MSS from all-tobacco cigarettes even though the MSS exposure levels were essentially equivalent. The decrease in changes was roughly proportional to the level of Cytrel® in the Cytrel®-tobacco filler.

COGGINS *et al.* (83) also studied the tumorigenicity of the CSCs from Cytrel®-containing cigarettes in a 24-month mouse skin-painting study. As the percent Cytrel® in the cigarette fillers was increased from 0% (the all-tobacco cigarette) to 25%, 50%, and 100% (the all-Cytrel® cigarette), not only did the mainstream CSC yield per cigarette decrease but also its specific tumorigenicity decreased. From their assessment of the results of this study, COGGINS *et al.* (83) reported that the specific tumorigenicity of the CSC from the all-Cytrel® cigarette was about 50% less than that of the CSC from the all-tobacco cigarette. These skin-painting bioassay findings (83) differed significantly from those reported in the NCI study by GORI (77, 78) (see Table 6). A possible explanation is that the Cytrel® formulation used in the inhalation and skin-painting bioassays conducted by COGGINS *et al*. in the early 1980s (82, 83) differed from the formulations used in the two NCI skin-painting studies in the mid-1970s (77, 78). Several Cytrel® formulations available in the mid-1970s were described in 1979 by BROWNE (63).

CONCLUSION

Despite the fact that much R&D effort on tobacco substitutes indicated they fulfilled in most instances the definition of a "less hazardous" cigarette with regard to the chemical and biological properties of their MSSs, inclusion of tobacco substitutes such as NSM® and Cytrel® in marketed cigarettes was short-lived because their failure to attain consumer acceptability led to insignificant repeat sales.

ACKNOWLEDGMENTS

We greatly appreciate the meaningful discussions with F.W. Best, C.W. Miller, L.L. Vestal, and the late R.A.

Table 6. Per cigarette yields of various mainstream smoke components from cigarettes containing tobacco substitutes, substitute:tobacco mixtures, or tobacco

Substitute [a] (substitute:tobacco ratio)		TPM, mg	Nicotine, mg	CO, mg	Phenol, µg	Formal-dehyde, µg	Acetal-dehyde, µg	Acrolein, µg	HCN, µg	NO_x, µg	B[*e*]A [a], ng	B[*a*]P		Skin-painting tumorigenicity		
												ng	ng/mg TPM	12.5 mg	25 mg	50 mg
J10:tob (0:100)	(65,66)	314	187	162	117	142	1085	142	364	341	—	166	53	—	—	—
J10T:tob (50:50)	(65,66)	322	144	140	87	242	755	158	337	208	—	134	42	—	—	—
J10:tob (50:50)	(65,66)	281	123	122	81	251	770	158	311	189	—	101	36	—	—	—
SSM®:tob (0:100)	(81)	325	176	216	100	54	670	150	557	366	36	260	80	—	—	—
SSM®:tob (100:0)	(81)	217	0	178	<8	31	166	80	224	423	99	60	28	—	—	—
Cytrel(I308)®:tob (0:100) [b]	(61)	283	188	160	134	596	810	217	354	267	157	234	83	—	—	—
Cytrel(I308)®:tob (25:75) [b]	(61)	216	132	142	84	511	752	155	229	209	147	214	99	—	—	—
Cytrel(I308)®:tob (75:25) [b]	(61)	71	36	73	17	374	360	60	48	37	85	131	185	—	—	—
Cytrel(I308)®:tob (100:0) [b]	(61)	30	0	49	4	462	265	45	13	10	63	111	370	—	—	—
Cytrel(I324)®:tob (0:100) [c]	(62)	298	196	102	114	44	735	87	317	194	—	146	49	—	—	—
Cytrel(I324)®:tob (100:0) [c]	(62)	57	0	31	7	6	225	45	17	18	—	55	96	—	—	—
Cytrel(I324)®:tob (0:100) [d]	(62)	327	—	—	105	—	—	—	300	286	—	26	80	—	—	—
Cytrel(I324)®:tob (100:0) [d]	(62)	74	0	—	<5	—	—	—	9	79	—	15	203	—	—	—
Cytrel®:FC (0:100)	(70,72)	168	11	176	52	—	1436	—	280	93 [e]	—	20	119	—	—	—
Cytrel®:FC (10:90)	(70,72)	152	9	164	44	—	1214	—	256	98 [e]	—	20	132	—	—	—
Cytrel®:FC (20:80)	(70,72)	134	9	152	38	—	1022	—	248	90 [e]	—	13	97	—	—	—
Cytrel®:FC (50:50)	(70,72)	98	4	115	16	—	675	—	185	57 [e]	—	10	102	—	—	—
Cytrel®:FC (100:0)	(70,72)	36	0	60	<0.5	—	243	—	25	31 [e]	—	4	111	—	—	—
											B[*a*]A [f]					
Cytrel®:SEBII (0:100) [g]	(77)	328	179	198	125	31	985	101	354	386	305	233	71	—	47	48
Cytrel®:SEBII (50:50) [h]	(77)	204	76	210	55	30	756	109	214	192	273	239	117	—	46	42
Cytrel®:SEBII (100:0) [i]	(77)	98	0	204	9	41	627	226	74	16	357	201	206	—	66	66
Cytrel®:SEBIII (0:100) [j]	(78)	317	179	203	164	34	1173	109	338	440	448	323	102	27	46	—
Cytrel®:SEBIII (100:0) [k]	(78)	62	0	53	25	8	280	48	0	8	560	236	381	—	54	74
Cytrel®:SEBIII (100:0) [l]	(78)	63	0	65	11	9	276	49	0	18	315	214	342	—	42	70
Cytrel®:SEBIII (100:0) [m]	(78)	56	0	6	13	10	319	44	0	15	225	165	294	—	82	70
Cytrel®:SEBIII (50:50) [n]	(78)	187	90	161	93	25	703	66	78	175	312	181	97	—	51	39
Cytrel®:SEBIII (0:100) [p]	(79)	335	165	225	153	32	768	83	345	493	325	258	77	16	35	—
Cytrel®:SEBIII (100:0) [q]	(79)	69	0	53	37	7	206	11	0	6	329	160	232	17	34	—
Cytrel®:SEBIII (100:0) [r]	(79)	63	0	58	9	8	182	48	0	8	240	134	213	27	61	—
NSM®:SEBII (0:100) [g]	(77)	328	179	200	125	31	985	101	354	386	305	233	71	—	47	48

Table 6 (*cont.*)

Substitute [a] (substitute:tobacco ratio)		TPM, mg	Nicotine, mg	CO, mg	Phenol, µg	Formal-dehyde, µg	Acetal-dehyde, µg	Acrolein, µg	HCN, µg	NO_x, µg	B[*e*]A [a], ng	B[*a*]P		Skin-painting tumorigenicity		
												ng	ng/mg TPM	12.5 mg	25 mg	50 mg
NSM®:SEBII (50:50) [s]	(77)	160	66	136	50	18	592	70	84	171	331	286	179	—	48	55
NSM®:SEBII (100:0) [t]	(77)	70	0	62	8	8	346	59	0	11	76	55	78	—	6	9
NSM®:SEBIII (0:100) [h]	(78)	317	179	203	164	34	1173	109	338	440	448	323	102	27	46	—
NSM®:SEBIII (30:70) [u]	(78)	251	118	204	125	32	920	121	245	287	547	364	145	—	38	50

[a] Abbreviations: J10 = expanded grain substitute; J10T = nitrate-treated expanded grain substitute; SSM® = Sutton Smoking Material; NSM ® = New Smoking Material; B[*e*]A = benz[*e*]acephenanthrylene (benzo[*b*]fluoranthene); B[*a*]P = benzo[*a*]pyrene; B[*a*]A = benz[*a*]anthracene; FC = flue-cured tobacco.

[b] Each yield cited is the average of duplicate determinations.

[c] Analyses on Cytrel® I324 MSS performed by GREEN *et al.*

[d] Analyses on Cytrel® I324 MSS performed by Celanese personnel.

[e] Nitrogen oxide was determined as NO.

[f] In the National Cancer Institute studies (77,78,79), the MSS yield of B[*a*]A was determined, not the MSS yield of B[*e*]A.

[g] Each component yield cited is the average of quadruplicate determinations, see Samples 42-45 in (77).

[h] Each component yield cited is from a single determination, see Sample 64 in (77); also bioassay data are only reported on p. 152.

[i] Each component yield cited is from a single determination, see Sample 63 in (77).

[j] Each component yield cited is the average of quadruplicate determinations, see Samples 72-75 in (78).

[k] "Old formulation of Cytrel®, old dye"; each component yield cited is from a single determination, see Sample 97 in (78).

[l] "New formulation of Cytrel®, old dye"; each component yield cited is from a single determination, see Sample 99 in (78).

[l] "Old formulation of Cytrel®, no dye"; each component yield cited is from a single determination, see Sample 0 in (78).

[n] "Old formulation of Cytrel®, no dye"; each component yield cited is from a single determination, see Sample 01 in (78).

[p] Each component yield cited is from a single determination, see Sample A in (79); also bioassay data are only reported on p. 212.

[q] Each component yield cited is from a single determination, see Sample C in (79); also bioassay data are only reported on p. 212.

[r] Each component yield cited is from a single determination, see Sample D in (79); also bioassay data are only reported on p. 212.

[s] Each component yield cited is from a single determination, see Sample 47 in (77).

[t] Each component yield cited is from a single determination, see Sample 46 in (77).

[u] Each component yield cited is from a single determination, see Sample 93 in (78).

Table 7. Comparison of per cigarette yields of various mainstream smoke "Hoffmann analytes" from cigarettes containing tobacco substitutes, substitute:tobacco mixtures, or tobacco

Component [a]	Green *et al.* (55)	Green *et al.* (61)	Vickroy *et al.* (70, 71, 72)	Gori (77, 78, 79)	Lloyd, Miller (64); Green *et al.* (65, 66)
Acetamide	—	—	—	—	<
Arsenic	—	—	< [b]	—	—
Benzenamine, 2-methyl-	<	<	<	—	<
Benzene	—	—	<	—	<
Benzene, ethenyl-	—	—	<	—	<
Benzene, methyl-	—	—	<	—	<
1,2-Benzenediol	<	<	—	—	<
Benzo[*k*]fluoranthene	<	<	—	—	—
Beryllium	—	—	<	—	—
1,3-Butadiene	—	—	<	—	—
1,3-Butadiene, 2-methyl-	<	<	<	<	<
2-Butenal	—	—	<	—	<
Cadmium	—	—	<	—	—
Chromium (VI)	—	—	<	—	—
Cobalt	—	—	<	—	—
Furan	<	<	<	—	<
Lead	—	—	<	—	—
Methanamine, *N*-methyl-*N*-nitroso-	—	—	<	—	—
Nickel	—	—	<	—	—
2-Propanone	—	<	<	—	—
2-Propenamide	—	—	—	—	>
2-Propenenitrile	<	—	—	—	—
Pyrrolidine, *N*-nitroso	—	—	<	—	—
Quinoline	—	—	—	—	>

[a] The appropriate CAS No. for each analyte is listed in Table 4.
[b] The symbol < indicates the component was found at a lower per cigarette yield in the all-substitute MSS or the substitute:tobacco MSS than in the all-tobacco MSS; > indicates the component was found at a higher per cigarette yield in the all-substitute MSS or the substitute:tobacco MSS than in the all-tobacco MSS.

Heckman and M.P. Newell that contributed to the characterization of many MSS components. We also appreciate the extensive laboratory assistance of the highly skilled technicians A.L. Angel, M.A. Wagoner, and the late B.W. Woosley.

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