borderline concentrations. Still others, although potentially harmful, are probably not present in sufficient concentrations to contribute to the hazard, and some may be hazardous only when they interact with other substances in the smoke.

Substances and classes of substances in cigarette smoke which have been judged to contribute to the hazard of cigarette smoking have been classified into three priority groups. Those compounds which are judged most likely to contribute to the health hazards of smoking are listed in table 1. Additional substances which probably contribute to the health hazards of smoking are listed in table 2. Those compounds which are suspected contributors to the health hazards of smoking in the concentrations in which they are present in tobacco smoke are listed in table 3. Many other constituents of tobacco smoke are considered to be toxic under some conditions but probably do not present a health hazard in the concentrations in which they are generally found in cigarette smoke; these are not listed. This listing is not presented as final, and may be subject to modification as more information becomes available.*

In 1966, the Public Health Service prepared a technical report on "tar" and nicotine (*60*). Tobacco "tar" is the name given to the aggregate of particulate matter in cigarette smoke after subtracting nicotine and moisture. In that report it was stated:

> "It is clear that the overall risk associated with cigarette smoking increases as the average number of cigarettes consumed per day increases. In the studies which have reported other measures of exposure such as pack-years, degree of inhalation, and maximum level of cigarette consumption, the same type of relationship holds."

Individuals may differ in their inherent susceptibility to diseases in which cigarette smoking plays a role and differ in their exposure to other factors which may increase the likelihood of these diseases. Within these groups of varying risk, the degree of exposure to cigarette smoke appears to be the most critical factor for the development of smoking related disease. Therefore, the general statement that the lower the dosage the lower the risk is the most useful guide available. It was also stated that:

> "It is possible for a cigarette to be altered in such a way that its 'tar' and nicotine content is reduced but certain other harmful effects, for example the effect of the gaseous phase, may be increased. Although this is a theoretical possibility,

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* Subsequent to the conference on which this report was based, several studies were published reporting the presence of N-nitrosamines in cigarette smoke. Since these substances are accepted as carcinogens in experimental animals, they represent another portion of the "tar" which probably contributes to the total health hazard (18, 24).

there is no evidence that this has occurred to any serious degree."

The consensus is that there is inadequate evidence to support a change in that view at the present time.

In addition, it was concluded that "the preponderance of scientific evidence strongly suggests that the lower the 'tar' and nicotine content of cigarette smoke, the less harmful would be the effect." Several studies reported since that time have added strong support to this position. The present review is an attempt to identify those constituents of the "tar" as well as those constituents considered part of the gas phase which are most likely to contribute to the health hazards from cigarette smoking.

TABLE 1.—*Compounds in cigarette smoke judged most likely to contribute to the health hazards of smoking.*

Compound	Concentration in cigarette smoke micrograms/cigarette	Primary phase classification G—gas P—particulate	References
Carbon Monoxide	5,240–21,400	G	(1, 10, 23, 26, 29, 34, 35, 37, 42, 46, 49, 61, 63)
Nicotine	200–2,400	P	(9)
[1] "Tar"	3,000–33,000	P	(9)

[1] "Tar" is defined as the total particulate matter collected by a Cambridge filter (CM-113) after subtracting moisture and nicotine and includes the class of compounds known as polycyclic aromatic hydrocarbons (PAH). PAH are generally accepted as being responsible for a substantial portion of the carcinogenic activity of the total "tar." Although "tar" from different cigarettes varies in its carcinogenic potential as measured by the bioassay methods in current use, it remains the most practical single "indicator" of total carcinogenic potential. Special mention should be made of Beta Naphthylamine which is a known human urinary bladder carcinogen for which there is no known safe level of exposure and which has been reported present in tobacco smoke in very low concentrations (16, 28, 30) (0.022 μgm./cigarette).

It is recognized that the substances in cigarette smoke may interact so that the combined pathological effects of several substances may be quite different from the sum of their effects produced in isolation. An example of this type of interaction might be the carcinogenic effects of tobacco "tar" as a result of the combined action of cancer initiating, cancer promoting, and cancer accelerating agents in producing the total effect. Such interactions theoretically could take place among substances within the gas phase, or substances within the particulate phase, or between constituents of the gas phase and constituents of the particulate phase. In the absence of data which identify the interactions of cigarette smoke components, judgments concerning the action or identification of harmful substances in cigarette smoke have, of necessity, been made pri-

TABLE 2.—*Compounds in cigarette smoke judged as probable contributors to the health hazards of smoking.*

Compound	Concentration in cigarette smoke micrograms/cigarette	Primary phase classification G—gas P—particulate	References
Acrolein	45–140	G	(12, 20, 21, 27, 36, 43, 45)
Cresol (all isomers)	68–97	P	(20, 40)
Hydrocyanic Acid	100–400	G	(26, 38, 43, 45, 46, 49, 53)
Nitric Oxide	0–600	G	(1, 3, 15, 40, 42, 44, 57)
Nitrogen Dioxide	0–10	G	(1, 40, 44, 57)
Phenol	9–202	P	(7, 19, 20, 32, 50, 52)

marily on the basis of the action of the individual substances. Nevertheless, experimental evaluation of modified cigarette smoke should be designed to take into account the possibility of such interaction.

Until there is a better understanding of the relative importance of the interaction of the constituents of cigarette smoke in the development of the diseases associated with cigarette smoking, it will be difficult to assess the significance of the reduction or elimination of one or several of the constituents named in this report. However, it is reasonable to take the position that unless there is positive information to the contrary, cigarettes in which overall "tar" and nicotine levels have been reduced present to the smoker lower concentrations of the harmful substances in the particulate phase. If, at the same time, significant reductions are made in those gas phase constituents which also contribute to the hazards of smoking, the resulting product should be less hazardous to health.*

The consensus is that a progressive and simultaneous reduction of all substances considered likely to be involved in the health hazards of smoking should be encouraged as the most promising step available at the present time towards the development of a less hazardous cigarette. Primary emphasis should be given to the reduction of the three substances or classes of substances named in the first table, and as a second priority to the reduction of those substances or classes of substances in the second table before reducing

* An alternative point of view held by some is that smoking behavior is a response to the need to reach a certain nicotine level and that lowering the amount of nicotine available from a cigarette may result in an increase in the number of cigarettes smoked, the depth of inhalation, or the number of puffs in order to maintain an accustomed level. Such an increase in smoking might result in an increased inhalation of other hazardous substances in the smoke, thereby potentially negating the effect of reducing the amount available in each cigarette.

TABLE 3.—*Compounds in cigarette smoke judged as suspected contributors to the health hazards of smoking.*

Compound	Concentration in cigarette smoke micrograms/cigarette	Primary phase classification G—gas P—particulate	References
Acetaldehyde	180–1,440	G	(4, 21, 27, 36, 43, 45, 48, 49, 53, 59)
Acetone	88–650	G	(12, 21, 27, 36, 43, 45, 48, 49, 53)
Acetonitrile	140–200	G	(12, 43)
Acrylonitrile	10–15	G	(12, 43)
Ammonia	60–330	G	(2, 22, 40, 41, 43, 64)
Benzene	12–100	G	(11, 12, 25, 43, 45, 49, 53)
2,3–Butadione	43–200	G	(43, 46, 49, 53)
Butylamine	3	P	(31, 40, 41)
[1] Carbon Dioxide	23,100–78,300	G	(1, 10, 15, 23, 26, 29, 34, 35, 42, 46, 49, 63)
Crotononitrile	4	G	(43)
Dimethylamine	10–11	P	(31, 40, 41)
DDT	0–0.77	P	(17, 39, 54)
Endrin	0.06	P	(14)
Ethylamine	10–11	G	(22, 31, 40, 41)
Formaldehyde	20–41	G	(4, 36, 43, 48, 53)
Furfural	45–110	P	(4, 13, 36)
Hydrogen Sulphide	12–35	G	(10, 43, 51, 58)
Hydroquinone	83	P	(6, 7)
Methacrolein	9–11	G	(12, 43)
Methyl Alcohol	90–300	G	(12, 21, 43, 46, 49)
Methylamine	20–22	G	(22, 31, 40, 41)
Nickel compounds	0–0.58	P	(5, 8, 47, 55, 56)
Pyridine	25–218	P	(40, 62)

[1] CO_2 is included because of the hazard it may represent to those with CO_2 retention, such as those with advanced COPD.

those named in the third table. In addition to the epidemiological and pathological data gained from human studies, it is important to develop better bioassay systems to evaluate cigarettes modified by these general guidelines.

It should again be emphasized that, in addition to the variation in chemical properties of the cigarette being smoked, procedures within the control of the individual smoker such as how many cigarettes he smokes, how far down he smokes the cigarette, and how frequently and deeply he inhales are critical factors in determining how much of the harmful substances which can be produced by the burning cigarette is given the opportunity to injure him.

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