

MONOGRAPH

ADVANCING KNOWLEDGE ON REGULATING TOBACCO PRODUCTS

World Health Organization

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WHO wishes to express particular gratitude to the following contributing authors:

Mr Clive Bates
Dr Hatai Chitanondh
Dr Tapani Piha
Dr William Rickert
Dr Channing Robertson
Dr Donald Shopland
Mr Harald Siem
Mr David Sweanor
Ms Judy Wilkenfeld
Dr Derek Yach
Mr Mitchell Zeller

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INTRODUCTION

This monograph follows the presentations and discussions at the International Conference: Advancing knowledge on tobacco products, held in Oslo, Norway 9-11 February, 2000. At the conference it was recognized that a central goal of those assembled was to build scientific and epidemiological evidence for the effective and appropriate regulation of tobacco products. Tobacco products are not currently well-regulated; where good regulations do exist they are not well implemented.

Rather than a straightforward reproduction of individual papers, this monograph presents a synthesis of the issues raised, grouped as topics. The aim of this was to bring together the various points of scientific evidence, as well as opinion, with information on regulations already in place to line up with those proposed. This approach shows clearly the areas where detail is lacking and this should be viewed as an invitation to readers to contribute further to the topic.

Part 1 provides an epidemiological review of tobacco use as a cause of disease and death, looking at the global trends, at issues such as environmental tobacco smoke, and reviewing dose-response relationships.

Part 2 contains information on the technical aspects of tobacco products, establishing cigarettes as engineered products, reporting on the various new forms of nicotine-providing devices, and centrally, exploring both the history of the machine-testing process set up by the Federal Trade Commission (FTC) and the International Organization for Standardization (ISO), and the arguments against its continued use on public health grounds, considering, for example, the impact of compensating mechanisms in people's smoking behaviours and how those invalidate the tests. The issues of "low-tar" and "light and mild" branding of products, the role played by nicotine in smoking, and the related issues such as the marketing position developed on so-called "light cigarettes" are covered. This part also explores the issue of the other harmful ingredients in cigarettes and cigarette smoke beyond tar, nicotine and carbon monoxide, and raises points to substantiate the argument for careful research into the additives to tobacco and regulation of them.

Part 3 looks at the overall picture of current tobacco product regulation highlighting the areas which need reform. This includes details of the regulatory forms in use, and problems with their implementation, with proposals for key elements such as ingredient disclosure to be included in new regulatory frameworks. There is a summary of current international tobacco product regulation and a specific analysis of the proposed future directions in tobacco control in the European Union. This part also describes the status of international collaboration, WHO's role and the scientific resources available. Parallel examples in the pharmaceutical field are given, and an account of the tobacco industry's opposition to measures which recognize tobacco use as harmful to health.

The recommendations made at the conference are reproduced in full in Annex 1 and are also inserted at the relevant points throughout the text.

Science and policy

Research is needed to advance further progress.

- Global tobacco control research needs to be better supported. Within such a plan, emphasis should be given to research to support product regulation within developing countries. Existing research institutions should work together to implement such an approach. ...
- Develop better measures, including biomarkers, to assess the health impact of the use of “less harmful” tobacco products in order to drive future regulatory actions. ...

(Recommendations from the Oslo conference)

A science-based process is vital. At the Ninth International Conference of Drug Regulatory Authorities (ICDRA) in Berlin in April 1999, WHO Director-General Dr Gro Harlem Brundtland noted that cigarettes are "highly-engineered consumer products". She called upon international food and drug regulators to bring cigarettes and tobacco industry products under the same type of regulatory frameworks as other drugs, saying that “the time has come for concerted regulation of tobacco products”. She has also stressed the need to find the scientific evidence that could be used as the basis for regulating tobacco products; this was the core theme of the Oslo Conference. Tobacco product regulation is an area in which a wide range of strategies will be essential to address the complex and dynamic nature of the problem. Accordingly, regulatory approaches must be flexible, incremental and evolutionary (WHO, 1999).

Sweanor (2000) suggests that there needs to be an interaction between science and policy, with the caveat that it takes time to consider developments in science and adapt laws accordingly. The process of turning science into law can be accelerated by a constant interaction between those with scientific information and those determining policy directions. The WHO conference on the Regulation of Tobacco Products (Helsinki, 1999) concluded, *inter alia*, that “The regulatory process must be guided by the best available science and the effects tracked so as to maximize health benefits, minimize unintended consequences, and thereby to foster self-correction” (see Annex 2 for the full text of the conclusions).

Bates et al (1999) recommend the development of expert and regulatory capacity, saying that regulation of tobacco products is complex and requires expert advice and assessment of evidence. A knowledge and skill base needs to be built in areas such as tobacco content, toxicology etc, with funding provided for the development of toxicological, biochemical skills etc, and for an expert programme of research into product modification. Regulatory bodies should be given full authority to find out from the tobacco industry what they need to know to be able to carry out their roles properly.

It is now widely recognized that the FTC/ISO measurements of tar and nicotine content in cigarette smoke are seriously flawed and do not present an adequate basis for measurement, regulation and labelling of tobacco products. Bates et al. (1999) suggest

that the test should be kept only for archival continuity and replaced with other approaches for measuring toxicity (see section 4 on cigarette testing methods).

Current regulatory policies make it hard to market the least harmful forms of nicotine delivery (see Part Three on regulatory issues). Better information on the role of nicotine and its methods of delivery are needed to inform discussions on regulatory change. Sweanor (2000) suggests that there is also a need for far more information on novel products and the potential health impacts of those products (see section 12 on novel tobacco products). There needs to be an acceptable way of measuring progress toward reduced harm. This requires knowledge of the relative impact on the health of individuals of different products, as well as knowledge of the population effects.

There will be many hard choices to be made. With any novel product there is a risk of unintended consequences as well as potential health gains. There is also a real possibility that the actual impact of a particular product can only be assessed through post-marketing surveillance. All of this will require the continuing strong interaction of good science and determined pro-health and pro-consumer policy development (Sweanor, 2000).

What is missing, and so desperately needed, is an adequate scientific base to support the evaluation of recent changes in the marketing strategies of both tobacco companies and pharmaceutical companies. These new strategies may result in products bearing claims that expressly or implicitly promise to reduce the exposure to and harm from tobacco products (Zeller, 2000).

PART ONE

EPIDEMIOLOGY AND TOBACCO CONTROL

1. Tobacco as a cause of death and disease

Global trends in tobacco use and impact

Overall, the world has seen an approximate 1% average annual increase in adult per capita consumption of cigarettes over the last two decades. The most rapid declines in per capita consumption of cigarettes have been seen in countries like Canada and the United Kingdom where average annual declines of 1.8% and 1.6% respectively have been recorded since the early 1970s. These have not been matched by equivalent declines in smoking prevalence (WHO, 1997).

In contrast, and over the same time period, there have been dramatic average annual increases in per capita consumption of cigarettes in China (8%), Indonesia (6.8%), Syria

(5.5%) and Bangladesh (4.7%) (WHO 1997). In both China and Syria, the rates of smoking among women remain low. There is growing concern about the efforts of the tobacco industry to increase smoking rates among women in developing countries.

Globally, there are currently 1.2 billion smokers over the age of 15 years; over 300 million of these are in China. The average amount smoked per person varies considerably between countries at different levels of development. In general, per capita consumption and the proportion of the smokers who want to quit are lower in poorer countries in Asia and Africa than in advanced industrialized countries and transition economies. Many developing countries may be able to move more rapidly to full cessation than highly addicted populations.

The 40-year follow-up of male doctors in the United Kingdom of Great Britain and Northern Ireland (UK) and the two American Cancer Society prospective studies (CPS I & II) in the United States of America (US) provide among the most extensive evidence of the impact of tobacco on health. In the UK study for example, mortality rates from cancers of the upper respiratory tract, lung and esophagus among heavy smokers were at least 15 times those in non-smokers; and cancer of the pancreas and bladder were three times more common in heavy smokers (Doll et al., 1994). Many groups of diseases of the respiratory and circulatory systems were strongly related to tobacco use. Overall, positive associations were found with 24 causes of death. A negative association was found for Parkinson's disease.

Using actuarial survival methods, the clearest differences between smokers and non-smokers are in the proportions who die between 35 and 69 years of age, which vary from 20% in non-smokers, to 41% in all smokers, and to 50% in those who smoke 25 or more cigarettes a day. For cigarette smokers, the age by which half have died is eight years less than for non-smokers, while for heavy smokers it is 10 years less than for non-smokers. The CPS II study provides more detailed information comparing death rates in smokers and lifelong nonsmokers for men and women (Thun et al., 1997). While the strength of the relationship between lung cancer and tobacco is greater than that for heart disease, the latter is more common. In fact, in most developed countries and transition economies, heart disease accounts for most of the deaths from cigarettes.

Table 1 compares relative risks from CPS I and II (Lopez, 1999) highlighting the importance of age-specific values. Relative risks increased for most conditions over the period. This is particularly apparent for women and is related to increased exposure over time.

Table 1: Summary of estimated relative risks for current cigarette smokers, major disease categories causally related to cigarettes, males and females aged 35 years and older, CPS-I (1959-1965) and CPS-II (1982-1986), United States cohort study

<i>Underlying cause of death</i>	<i>Males</i>		<i>Females</i>	
	<i>CPS-I</i>	<i>CPS-II</i>	<i>CPS-I</i>	<i>CPS-II</i>
CHD, age < 35	1.83	1.94	1.4	1.78
CHD, age 35-64	2.25	2.81	1.81	3
Cerebrovascular lesions, age < 35	1.37	2.24	1.19	1.84
Cerebrovascular lesions, age 35-64	1.79	3.67	1.92	4.8
COPD	8.81	9.65	5.89	10.47
Cancer, lip, oral cavity and pharynx	6.33	27.48	1.96	5.59
Cancer, esophagus	3.62	7.6	1.96	10.25
Cancer, pancreas	2.34	2.14	1.39	2.33
Cancer, larynx	10	10.48	3.81	17.78
Cancer, lung	11.35	22.36	2.69	11.94

Source: United States Department of Health and Human Services, 1989

Recent Chinese and Indian studies confirm many of the findings from earlier US and UK studies (Liu et al., 1998; Niu et al., 1998). Importantly, results suggest that tobacco magnifies underlying risks. Thus, tobacco causes a significant proportion of tuberculosis deaths and a higher proportion of chronic respiratory conditions and a lower proportion of heart disease than in other studies. Indian prospective studies (Gupta & Mehta, 2000) have started to report their results. Importantly, overall death rates among smokers and all tobacco users are about twice those of non-users. The pattern of tobacco use is more complex in India than in the US or UK with a very wide variety of forms of tobacco being used.

Overall, the impact of tobacco on health is one of the best documented relationships in all of public health. As studies include more women and developing countries, the strength of the evidence grows.

Environmental tobacco smoke

Second-hand smoke is a real and significant threat to public health. Supported by two decades of evidence, the scientific community now agrees that there is no safe level of exposure to second-hand smoke.

Both smokers and nonsmokers can incur adverse health effects from the smoke of burning cigarettes. While smokers inhale mostly mainstream (MS) smoke, nonsmokers inhale mostly sidestream (SS) smoke, which is emitted into the surrounding air between puffs from the end of the smoldering cigarette. Sidestream smoke is the major source of environmental tobacco smoke (ETS).

ETS is the smoke that a person inhales from sources other than by directly smoking a cigarette. It is composed of the smoke that:

- is exhaled by the smoker (second-hand smoke);
- burns off the tip of the cigarette (sidestream smoke);
- seeps through the paper and filter of the lit cigarette (lateral-stream smoke).

Although sidestream and mainstream smoke have qualitatively similar chemical compositions, the respective quantities of individual smoke constituents can be quite different (US DHHS, 1987 and 1989). In studies of nonfilter cigarettes smoked by machines, the yield of carbon monoxide (CO) in undiluted sidestream smoke was 2.5 to 4.7 times more than that of mainstream smoke, whereas the corresponding SS/MS ratio for N-nitrosodimethylamine (NDMA), an animal carcinogen, was 0.2 times greater (US DHHS, 1989). In one compilation of toxic and tumorigenic agents in cigarette smoke, the SS/MS ratio ranged from 0.03 to 130 (Hoffman and Hecht, 1990). In another study, the concentration of the carcinogen 4-aminobiphenyl in undiluted sidestream smoke was 32 times more than that of mainstream smoke. The sidestream smoke from so-called "reduced-yield" cigarettes does not necessarily have reduced emissions of toxic and carcinogenic chemicals (Adams et al., 1987; Rando et al., 1992).

Whereas exposure to sidestream smoke depends on the distance from the burning cigarette and conditions of ventilation, the higher concentrations of certain toxic and carcinogenic chemicals in sidestream smoke result in measurable levels of these chemicals in nonsmokers exposed to ETS. For example, nonsmokers exposed to relatively high concentrations of sidestream smoke have detectable urinary levels of the metabolites of the tobacco-specific nitrosamine 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone (NNK) (Hecht et al., 1993). Young children exposed to ETS via smoking mothers have detectable levels of PAH-albumin adducts in their blood (Crawford et al., 1994).

Exposure to specific chemical agents in ETS can produce pathological effects in humans and in animal models. The carbon monoxide in sidestream smoke reduces the blood's ability to deliver oxygen to the heart, an effect that is especially important in patients with coronary heart disease (Sheps et al., 1990). Second-hand cigarette smoke activates blood platelets, which in turn play a role in development of atherosclerotic plaques in coronary heart disease (Glantz and Parmley, 1995).

Consensus exists that ETS causes lung cancer, stroke and ischaemic heart disease in adults; and a wide range of health problems in the unborn child and in children. The former includes low birthweight, while problems for the latter include acute respiratory infection, sudden infant death syndrome, asthma, middle ear infection and possibly certain learning defects.

Tobacco smoke is also an important source of indoor air pollution, contributing to a noxious environment, and causing eye irritation, sore throat, cough and headache.

Despite the evidence, this area is much disputed by the tobacco industry, which has funded its own research in Europe and Japan and set up "front groups" to dispute the evidence and maintain a sense that the issue is still controversial.

The impact of possible product modification on sidestream smoke is an issue to be considered.

Information on relative risks is useful for deciding which conditions are caused by tobacco. Peto, Murray and Lopez have used measures such as attributable risk or population-attributable risks to develop global estimates of the impact of tobacco (Doll et al., 1994; Murray & Lopez, 1997). In doing so they used causal relationships established in the classic (US and UK) studies and applied them with certain assumptions to smoking prevalence rates in all countries.

Two important areas of concern are mortality and lack of progress in reducing smoking prevalence. (1) Tobacco currently kills about 4 million people a year. This figure will increase to about 10 million a year by the late 2020s. By then over 70% of deaths will be in developing countries. (2) Callard's analysis (2000) of Canadian data suggests that the lack of progress in reducing smoking prevalence in the 1990s could be due to the remaining smokers being more addicted; and/or the impact of differently manufactured cigarettes. She highlights the fact that increased use of nicotine replacement therapy has not been associated with a decline in smoking prevalence. This could be due to imperfections in data collection systems. If real, these observations raise vital issues about the strength of the knowledge base with regard to both product modification and the use of nicotine replacement therapy.

2. Dose-response relationships

All countries need to introduce comprehensive tobacco control policies and strategies along the lines recommended by the World Health Organization.

... The emphases of policies should be to prevent initiation, increase the quit rate, and eliminate exposure to passive smoking. ... Product regulation needs to apply to all forms of tobacco and nicotine products. ...

(Recommendations from the Oslo conference)

Increased exposure, increased disease and death rates

The earliest prospective studies clearly demonstrated that a dose-response relationship existed for tobacco. Studies of US veterans showed that the mortality ratio increased with increased tobacco use and was related to the age at which smokers started to smoke (Hrubec & McLaughlin, 1997). These dose-response relationships have been shown to apply for most specific causes of death.

Reduced exposure, reduced disease and death rates

The benefits of quitting have also been extensively studied in prospective studies. The most important recent studies include the 26-year follow-up among US veterans and the

12- year follow-up among US nurses (Kawachi et al., 1997). Both studies provided clear evidence on the positive benefits of quitting. Importantly, in the US veterans study, male smokers had to quit for five years or more before an appreciable reduction in overall mortality was evident. In other studies, residual effects remained until 15 years after quitting. For some conditions, the benefits were more immediate. The excess risk of stroke for women is virtually eliminated two years after quitting.

Importantly, the authors of the eighth monograph of the National Cancer Institute (NCI) on smoking and health concluded that:

“ The residual risk produced by past smoking in former smokers is less among those who had smoked fewer cigarettes per day compared with those who had smoked two or more packs per day. However, the difference in death rates between continuing smokers and those who quit is greatest for those who have the greatest risk: heavy smokers. The more one smokes, the greater one’s risk of disease and, correspondingly, the more risk one can avoid by quitting”.

Issues for the future

Interventions aimed at shifting entire distributions of population characteristics such as blood pressure and cholesterol have been recognized as leading to better population outcomes than a sole focus on “high-risk” groups. Does this apply to the distribution of smokers? How would such a shift to lower categories of tobacco consumption be accomplished? Would such an approach reduce the likelihood of increasing the overall cessation rate in the population?

Trends in global mortality will only be marginally affected by strong preventive measures. However, death rates in current smokers would clearly be significantly reduced if two measures were successful: widespread use of effective means of treating tobacco dependence-especially if the cessation rate could be dramatically increased- and a substantial reduction in exposure to the harmful constituents of tobacco products. How will the public health impact of such approaches be measured? The illusory benefits of “light” cigarettes to health were proclaimed by many public health professionals before evidence of harm was available. That experience must be taken into account. Innovative thinking is needed to ensure that the pace of progress in tobacco control dramatically accelerates.

PART TWO

PRODUCT ISSUES

3. Background

The tobacco plant

Tobacco is the most widely grown commercial non-food crop in the world (Pedin, 1999). Today, approximately 80% of total world tobacco production is grown for use in cigarettes, estimated at 5.6 trillion pieces annually. (Chapman & Lazarus, 1992) China is by far the leading cigarette manufacturing country, followed by the US which is the largest exporter. An entire industry, from a diverse manufacturing sector to distribution and retail outlets, has grown to be a major economic force in many industrial and developing countries (Siem, 2000).

No other plant organism has been so well studied. Prior to 1971, there were approximately 9000 scientific publications on tobacco: between 1971 and 1989, another 60 000 papers were published, and from then until 1996, another 21 000 papers were added. The publications have expanded the knowledge on basic plant science, chemistry, physics, engineering and health science. The complex genetic make-up of the plant, environmental factors that promote or inhibit the expression of genes, and the numerous steps of human intervention all play a major role in shaping the final product. Approximately 4000 compounds have been identified in tobacco and 5000 in smoke (Siem, 2000). Bates, Jarvis and Connolly (1999) report that there are 600 tobacco additives allowed in the cigarettes in the UK, most of which were included in the manufacturing of cigarettes after 1970.

Tobacco products

Tobacco products currently on the market include cigarettes, tobacco for pipes, cigars, bidis, "roll-your-own" and smokeless tobacco (chewing tobacco). Overall, the large majority of the volume of tobacco product sales are in the form of manufactured cigarettes.

Cigarettes today are highly manufactured products, which can be manipulated to a very large degree. Cigarettes cannot be considered simply as a natural agricultural product. Cigarettes are produced by an industrial process which, through a number of steps in handling the tobacco and by the use of additives, is tailoring the product to satisfy the user (Siem, 2000). The product today is designed to meet consumers' tastes through various additives. It is designed, among its other characteristics, to fall within the maximum permissible yields of tar and nicotine set by authorities, and to take into consideration the aspects of combustion temperatures, pH, filters, sidestream smoke and ashes.

This view is supported by Professor Channing Robertson, presenting his expert report in court to the State of Minnesota (1998). This is the primary opinion given on the documents and materials presented by the defendants:

"...I have concluded that cigarettes are highly sophisticated devices designed and engineered to provide a means for the controlled delivery of nicotine for pharmacological effects. I have also concluded that this controlled nicotine delivery is accompanied by the delivery of the products of the combustion/pyrolysis process".

Zeller (2000) restates this emphatically: "The foundation for the regulation of conventional tobacco products is clear. The nicotine in these products is a drug. The products themselves are nothing more than devices for the delivery of this highly addictive drug. The marketplace for the continued use of tobacco products ... is based on creating and sustaining an addiction to nicotine".

The papers presented at the Oslo conference pool information on the way in which these "sophisticated devices" have been constructed, their context in the development of the industry, and on the additives used to enhance the delivery of nicotine whilst making the product distinctive and attractive to the smoker in taste and result. Information is given on what the products of "the combustion/pyrolysis process" are, and what their possible implications are for public health and the related need for further research and appropriate regulation. An important aspect of future regulation is the basis on which measurement of the "yield" of the cigarette is made (see section 4), given the limitations of the Federal Trade Commission test method. It will also be important to consider what drives consumer demand. One area which influences consumer behaviour is advertising. How tobacco products are promoted, including the use of terms such as "lights", "ultra-lights" or "mild" should be taken into account.

4. Cigarette testing methods

The Federal Trade Commission (FTC) test method

In the 1950s, following reports that cigarette smoke could cause cancer, cigarette companies began heavy promotion of various means of reducing substances from the tobacco that might be associated with ill health, coughing, and throat irritation. This led the United States Federal Trade Commission (FTC) to publish a series of guides designed to instruct industry on the advertising of tar numbers. In the mid-1960s, the FTC identified a standardized testing method for the measurement of tar and nicotine content in cigarette smoke (described below). In 1966, the FTC informed the cigarette industry that it would approve claims based on this standardized test and in 1967 it began operation of its own testing laboratory to determine tar and nicotine yields of cigarettes. It reported those results to Congress and to consumers.

In 1970, the FTC proposed to develop a formal regulation to guide the disclosure of tar and nicotine ratings in advertising. The rulemaking was suspended when most of the major cigarette manufacturers voluntarily agreed to include the FTC laboratory ratings in cigarette advertising. In 1981, the FTC published a standardized test for carbon monoxide and began testing and reporting those ratings. In that year, the 1981 Surgeon

General's Report concluded that, despite the slight reduction in lung cancer risk seen from the introduction of lower-tar cigarettes, "there is no safe cigarette and no safe level of consumption" (Department of Health and Human Services, 1981). In 1983, the Commission began to question the representativeness of its testing results and indicated that the results might significantly underestimate the level of tar, nicotine, and carbon monoxide smokers actually receive (Wilkenfeld et al., 2000).

Machine testing

In 1966 the United States Public Health Service issued the statement 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". This led to the recommendation that people who continued to smoke should smoke cigarettes yielding lower levels of tar and nicotine. In order to provide consumers with guidance to enable them to select cigarettes that would give them lower levels of tar and nicotine the FTC began to test cigarettes for tar and nicotine delivery.

The FTC recognized that this testing method would not necessarily provide consumers with precise dosing information. It was intended and assumed that such testing would provide consumers with guidance that would enable them to choose cigarettes that would expose them to lower levels of tar and nicotine. It was on this same assumption that the US Government encouraged consumers, who were unable to quit, to smoke cigarettes with lower tar and nicotine delivery ratings. A generally similar course with a similar cigarette testing procedure was followed in Europe and many other countries but the method was referred to as the "ISO method" after the International Organization for Standardization that had codified the method.

In the FTC and ISO methods, the cigarette was inserted into a port hole to a depth of approximately 5 mm. An automated syringe type of system was attached by tubing to the cigarette port, enabling a machine to draw a 2-second, 35-mL puff every 60 seconds. Machine puffing continued until a 23 mm cigarette butt length remained. For filtered cigarettes, puffing continued until the butt left was 3 mm longer than the filter plus the filter overwrap paper that connected the filter to the tobacco rod. The 35 ml puffs of smoke were drawn through a filter that trapped particulate material but did not trap gases such as carbon monoxide or any nicotine or other substances that were in a gas phase. The material in the filter is referred to as total particulate matter (TPM).

The quantity of nicotine in the TPM was identified as the nicotine yield of the cigarette and this value was provided to consumers as the nicotine rating. The TPM minus nicotine and water was identified to consumers as the tar yield of the cigarette. Many testing organizations and governments began to analyse the gas for carbon monoxide content as well and provided this information to consumers. A variety of other testing parameters were specified and controlled including the ambient air temperature and humidity, procedures for humidifying the cigarettes, and the nature of the cigarette holder ports. As described in a report to WHO (Thompson 2000) various details of the ISO method varied from country to country and were adjusted over time.

Cigarette yield values

The term 'yield', as applied to cigarettes, emphasizes the fact that published values for tobacco smoke constituents, such as 'tar' require the machine-smoking of cigarettes in order to produce (yield) the results. Thus a cigarette's 'yield' is defined to be the amount of substance (e.g. 'tar') which can be isolated from tobacco smoke under a fixed set of conditions. This should not be confused with the term 'delivery' which is defined to be the amount of a substance contained in tobacco smoke which is inhaled and absorbed by the smoker. Thus 'yield' is a fixed reproducible quantity while 'delivery' is highly variable and impossible to reproduce with smoking machines that are commonly used to test cigarettes. 'Content' refers to the amount of a substance that can be isolated from the cigarette filler (tobacco) before smoking. 'Yield', 'content', and 'delivery' are often used interchangeably and incorrectly contributing to the perception that "lower" refers to "tar contents" and "risk" (Rickert, 2000).

Cigarettes typically contain nicotine in the range of 10-15 mg. They yield approximately 10%-15% of their nicotine in the FTC/ISO test (i.e., about 1-2 mg), except in the case of extremely highly ventilated cigarettes, which may produce a yield of less than 2% of their nicotine in the machine test. Cigarettes do not contain tar. Tar is the conglomerate combustion product or TPM trapped in the filter minus the water and nicotine. How the cigarette is smoked can alter not only the tar yield (e.g. by taking more puffs than the machine) but the quantity and nature of the tar that is produced by the burning process (e.g., more intense puffs can produce higher temperatures in the cigarette and thereby alter the chemical process that produces tar. Similarly, cigarettes do not contain carbon monoxide (CO). Carbon monoxide is a gas combustion product in which both the yield and the quantity produced are influenced by how the cigarette is smoked.

Limitations of the FTC/ISO tests

None of the major smoking parameters adopted by the FTC and ISO for determining the tar and nicotine yield of cigarettes was based on scientific studies of human smoking behaviour. The parameters were similar to those which had been recommended by Ogg (1964) to provide a standardized means for cigarette developers to evaluate the effects of various changes in cigarette design and materials and was claimed to be based on observations of how people tended to smoke cigarettes in the 1930s (National Cancer Institute, 1996). The method may have been a reasonable test for comparing cigarettes from the perspective of cigarette designers and manufacturers but it was not intended, or validated, as an indicator of tar and nicotine exposure in humans. In fact, the 1988 Report of the US Surgeon General found that human cigarette smokers took their puffs at shorter intervals, took more puffs per cigarette, and took larger puffs than the machines. Pharmaceutical companies also routinely employ machine tests to expedite product development although such data are not allowed by medicine regulators to take the place of human exposure ("bioavailability" or "pharmacokinetic" testing) unless the methods have been well validated as predictors of human exposure. No such bioavailability data were provided by the tobacco companies or required for validation of the tests.

Furthermore, the FTC/ISO methods were developed to accommodate pre-1960s cigarette designs. These did not employ ventilation holes. These holes, which appeared in later cigarette designs, were never occluded by the cigarette smoking matching ports but were

easily blocked by the fingers and lips of human cigarette smokers. Many other cigarette design features further reduced the validity of the machine test as a measure of human smoke exposure. Such features included the addition of burn accelerants in the cigarette paper. These made the cigarette burn more rapidly between puffs and thereby reduced the amount of the tobacco consumed by the machine. Increasing the length of the filter overwrap was another means of preventing tobacco from being smoked by the machine even though it could be smoked by humans. Ingredients such as ammonia and other substances could also be used by cigarette manufacturers to increase the amount of nicotine that was passed, untrapped, through the filter as a gas, although gas phase nicotine could be absorbed by a human cigarette smoker.

As no human exposure data were required to validate the testing, there was little to deter tobacco companies from continuing to change the designs of their cigarettes so as to provide still lower tar and nicotine ratings, even as they advertised to cigarette smokers that they did not have to give up “taste” by switching to lower-yielding cigarettes. In fact, it is now clear from tobacco industry documents (Slade et al., 1995; Hurt & Robertson, 1998; Bates et al., 1999) that the companies embarked on a variety of deliberately targeted cigarette design changes. These had the explicit objective of enabling cigarette smokers to extract virtually whatever nicotine dose they sought from virtually any cigarette brand, regardless of how it was rated. The FTC and ISO methods appear to consumers to be government-endorsed systems of rating the tar and nicotine delivered by cigarettes, giving a meaningful reflection of relative tar and nicotine exposure across various cigarette brands. In reality this is not the case.

Shopland (2000) describes the internal tobacco industry studies which clearly show the major cigarette manufacturers to have known, since the mid-1960s, that the FTC test method was seriously flawed. Other industry documents show that the tobacco companies devised many ways to “cheat” the machines and the resulting FTC reports and UK “League Tables” presenting tar and nicotine ratings. A 63-page report of August 1994 for RJ Reynolds entitled “*FTC smoking method used for 'tar' and nicotine data*” provides extensive data documenting how tar and nicotine content varies across a wide range of different smoking parameters for several varieties of the company's *Winston* brand of cigarettes.

The one variable which did not appear significantly to affect tar and nicotine delivery was puff duration. Variations in puff frequency and puff volume, however, produced tar and nicotine levels between 50% and 150% higher than would have been predicted by the FTC method. In a comparison of cigarettes using what Reynolds termed “more realistic” smoking parameters (consisting of a 65 mL puff, of 2.0 seconds duration, and taken every 45 seconds), tar values for *Winston* cigarettes increased from 20.6 mg FTC tar to 35.7 mg; *Marlboro's* increased from 16.3 mg FTC tar to 30.1 mg, relative increases of 73% and 85%, respectively (Shopland, 2000).

People do not smoke like machines

The vast majority of smokers do not smoke their cigarettes in a manner consistent with current machine-based parameters. This is especially true for smokers of low and ultra-low tar and nicotine cigarettes. For individual smokers, puff volumes have been reported

to range from 21 mL to more than 60 mL, puff duration from 0.8 to 3.0 seconds, and puff frequency ranging from a puff every 18 seconds to one taken every minute or more (Shopland, 2000, Zancy & Stitzer 1996). As Bates et al. observed (1999), when the smoke is low in nicotine, people "compensate" (see section 9) or alter their smoking pattern, inhaling more deeply, taking more frequent and larger puffs, or blocking the ventilation holes in the filter. The result is that, when people smoke low-tar brands, their actual tar exposure (and hence risks to health) may be almost the same as for conventional cigarettes. The FTC test is therefore perpetuating what Bates et al. (1999) term "the fraud of low-tar cigarettes".

As British American Tobacco (BAT) acknowledged privately in 1978 (Creighton, 1987) "[T]here is now sufficient evidence to challenge the advice to change to a lower delivery brand, at least in the short term. In general, a majority of habitual smokers compensate for changed delivery, if they change to a lower-delivery brand than their usual brand. If they choose a lower-delivery brand which has a higher tar-to-nicotine ratio than their usual brand (which is often the case with lower-delivery products), the smokers will in fact increase the amounts of tar and gas phase they will take in, in order to take the same amount of nicotine. More realistic advice to smokers would be to choose a brand with a lower tar to nicotine ratio which gives them the satisfaction that they require in the lowest amount of smoke taken in."

Although nicotine-dependent cigarette smokers may strive to sustain the nicotine intake necessary to maintain their addiction and avoid withdrawal symptoms, cigarette smokers should not be blamed for obtaining higher levels of tar and nicotine than those advertised for their cigarette brands. With respect to food, drugs and alcoholic beverages, the labelled and advertised levels of constituents are generally predictive of maximum levels of exposure. Moreover, with respect to drug products at least, the labelling includes guidance to help ensure that consumers' exposure will correspond to the labelled level, particularly when the mode of administration might alter the actual exposure. In principle, cigarette smokers could be given guidance that would help them to achieve tar and nicotine intakes more consistent with those advertised, and most importantly, to avoid achieving tar and nicotine intakes higher than advertised. For example, the Addiction Research Foundation of Ontario, and a National Cancer Institute Monograph (Kozlowski, 1981; Kozlowski et al., 1996; Monograph conclusions), discussed the nature and means by which such information could be transmitted.

The tar and nicotine levels advertised for cigarettes do not denote maximum exposure levels and they have little predictive value as regards actual exposure levels. Furthermore, as discussed by Slade and Henningfield (1998), the cigarette companies provide no guidance to their customers on "smoking techniques". For example, they could show consumers the dose controlling mechanisms (such as blocking the holes or smoking past the point smoked by the machines) and how to avoid defeating them. Instead, the cigarette designs facilitate oversmoking with hidden ventilation holes and/or holes placed where smokers would naturally and readily block them. The cigarette companies themselves are therefore at least partially accountable for the level of compensatory smoking of cigarettes. This has been well documented even in reviews supported by the tobacco industry itself (e.g., Scherer, 2000).

FTC recognition of test limitations

In 1994, the National Cancer Institute, in response to a request from the US Congress and the Federal Trade Commission, sponsored a committee deliberation to determine the continued relevance and accuracy of the FTC testing method and its results. The NCI found: "The smoking of cigarettes with lower machine-measured yields has a small effect in reducing the risk of cancer caused by smoking, no effect on the risk of cardiovascular diseases, and an uncertain effect on the risk of pulmonary disease. A reduction in machine-measured tar yield from 15 mg tar does not reduce relative risk from 15 to 1".

The Committee also provided a list of suggestions for the modifications of the testing methodology.

In September 1997, the FTC proposed revisions to the FTC test, suggesting that tar, nicotine, and carbon monoxide yields obtained under two different smoking conditions should be measured and that the resulting ranges should be disclosed in advertising. They acknowledged that changes in cigarette design and increased knowledge about human smoking behaviour had highlighted the limitations of the existing test method. They also suggested that the system must be accompanied by public education to make smokers aware that individual exposure depends on how the cigarette is smoked, and that any benefits of switching to lower-yield cigarettes are small compared with quitting. Finally, they recommended that the system should be re-examined at least every five years to evaluate whether the protocol was maintaining its utility to the smoker.

Bates et al. report (1999) that these proposals were strongly criticized by American scientists as not being sufficient to give consumers accurate information, nor to give correct parameters for ensuring future reductions in harm.

The FTC withdrew the proposed new methodology, acknowledging that the machine methods of testing tar, nicotine, and carbon monoxide yields were open to serious criticism and needed a substantial rethink lasting 18 months. In that period, the FTC plans to launch adverts "designed to alert consumers to the significant limitations in existing tar and nicotine numbers". The FTC method report will be transmitted early 2001.

In a press release of 24 November 1998, the FTC quotes the National Cancer Institute and US Food and Drug Administration as stating that "new data suggests that the limited health benefits, previously believed to be associated with lower tar and nicotine cigarettes, may not exist".

Proposed Canadian testing methods

In June 1998, the Minister of Health of Canada proposed tobacco regulations that mandate the testing of all tobacco products (whole tobacco, cigarette filler, as well as mainstream and sidestream smoke) for a list of toxic constituents (Health Canada, 1998). The testing methods require emissions to be determined under two different smoking regimens; as defined in ISO 3308:1991 (puff volume 35 mL, puff duration, 2 seconds; and puff interval, 60 seconds) and 'intense' where the puff volume has been increased to

55 mL, (designed to better replicate actual extreme smoking), the puff interval shortened to 30 seconds and the filter taped to block the effect of ventilation on smoke yields¹. The list is comprehensive and includes aromatic amines, such as 4 aminobiphenyl, miscellaneous organics including compounds such as 1,3-butadiene, 8 carbonyls including formaldehyde and acrolein, phenolics such as phenol and catechol, tobacco specific nitrosamines, and trace metals including arsenic and mercury. These were selected based on published properties (toxicity/carcinogenicity), and lists of toxic compounds such as those which have been compiled and published by the American Health Foundation (NCI, 1998; Hoffmann 1993). The listing would include all ingredients that are in the product, including in the tobacco, in the paper and tubes, in the filter, as well as any other component or ingredient.

Bioavailability

What matters, to public health professionals and consumers alike, with respect to toxins is actual human exposure. This is the reason that FTC and ISO values have been required to be provided to consumers. Human exposure levels are not measured by the FTC/ISO tests and are not even accurately predicted. For example, over an approximately 10-fold range in FTC cigarette ratings there was little or no significant difference in blood nicotine levels in several studies (Benowitz 1996). Nicotine exposure in humans can be readily assessed by testing the nicotine concentration in blood samples, or by testing saliva or urine for cotinine, which is a primary nicotine metabolite (Benowitz 1996, NCI Monograph 1984). Smoking cessation studies typically assess nicotine exposure by the simple method of assessing cotinine in saliva, whereas blood nicotine levels are typically required for approval of medications where it is assumed that the labelled dosage of the product corresponds to human exposure. Such studies are typically referred to as bioavailability studies or pharmacokinetic studies, although the term pharmacokinetic study implies that several samples were measured over time to determine the time course of blood exposure and the maximum blood exposure.

Medications are labelled in accordance with either their actual drug content (e.g., nicotine gum) or the bioavailability of their constituent drug as determined in human exposure studies (e.g., nicotine patch). The general concept is simple, namely the labelled dosage implies the highest amount that the consumer will generally receive, and the same can be said of food products that are labelled with respect content of salt, cholesterol or sugar, and alcoholic beverages that are labelled with respect to their percentage of alcohol. In addition, where there are factors that dramatically affect bioavailability, e.g., consumption of food, using nicotine gum while drinking acidic beverages, or inserting the nicotine nasal spray device too deeply into the nostril, consumers are given explicit guidance to improve the likelihood that their actual intake will correspond to the labelled amount.

Carbon monoxide yields from machine tests could also be compared to actual human exposure because carbon monoxide can be measure in expired air or as carboxyhemoglobin in blood (Benowitz, 1996). Carbon monoxide is a generally reliable

¹ Porter & Dunn (1998) have reported that, for ventilated brands, between 3.7% - 10.3% of cigarette butts discarded by Canadian smokers could have had the vents blocked completely for at least one puff, 13.8% - 20.4% of the butts had vents that could have been partially blocked and 75.9% showed no sign of vent blockage.

and valid indicator of total smoke exposure as well. Human tar exposure assessment is more complicated because there is a multitude of substances that compose the material referred to as tar, and many of these do not reach the blood stream but are deposited in the lung. Nonetheless, exposure to tar and various constituents can be estimated by a variety of techniques that would enable determination of the validity of machine tests (Djordjevik et al., 2000 and Benowitz, 1996).

Future issues

Shopland (2000) queries whether the known, highly varied, smoking patterns of "actual" smokers can ever be factored into any machine-based testing protocol and whether regulatory agencies should permit cigarette makers to continue to use existing test results in their marketing strategies, given the problems with the current system.

It may be argued that today's cigarettes on the whole are less toxic than the cigarettes of the early and mid-twentieth century (Blizzard & Dwyer 2001), however, there is no convincing evidence that the cigarettes rated as "light", which emerged on the market in the 1970s and remain up to the present, are significantly less likely to cause disease than their full-flavoured counterparts. In fact, even according to machine tests, a typical "light" cigarette contains only about 20% less tar and nicotine than the typical "regular" cigarette.

5. Tar and "low tar"



Bates et al. describe the concept of tar as "misleading" (1999). Tar is a collective name for thousands of chemicals that form the thick, sticky residue of tobacco smoke. Different products have markedly different compositions which are likely to cause different degrees of harm.

The 1994 RJ Reynolds report on the FTC test method shows quite clearly how cigarettes which yield the same amount of tar when machine smoked can differ substantially with respect to the makeup of the tar because of the different technologies used to produce different varieties of cigarettes. Data were presented for eight experimental cigarette designs, all with 25mg FTC tar. The ratio of tar to the level of other smoke constituents

was compared. Despite the uniformity in machine-generated tar in each cigarette, the ratio of tar to benzopyrene was 0.54 to 1.56, for HCN (hydrogen cyanide) the ratio ranged from 9.7 to 12.7, while the ratio of tar to nicotine was between 12.4 and 70. Absolute values for nicotine ranged from nearly zero per cigarette to over 2.0 mg (Shopland, 2000). There may also have been changes in tar composition over time in response to changing tobacco plant varieties and tobacco processing. The "tar" in potential product innovations such as *Eclipse* (see section 12) is of a very different nature, being predominantly glycerol. Shopland (2000) proposes investigation (short and long-term studies) of the need for research into differences in tar composition, and further, what other constituents should be measured.

Low-yield cigarettes and changes in disease risk among smokers

Governments are urged, individually or at a regional level, to...

- Discontinue harm reduction strategies based on naïve interpretation of tar and nicotine yield measurements. This means abandoning the strategy of seeking lower nominal tar yields and instead, finding approaches that genuinely reduce harm to nicotine users.

(Recommendations from the Oslo conference)

Bates et al. (1999) ask "Are low-tar cigarettes less harmful?" There is uncertainty over whether the reductions in tar content of cigarettes over the past few decades have resulted in reductions in mortality and morbidity. The two largest, long-duration studies by Withey et al. (1992) and Frost et al. (1995) of switching to low-tar cigarettes, both of which randomized smokers and followed them over a period of six months, suggest that switching offers no significant health benefits as smokers compensate for reduced nicotine delivery. The former observed complete nicotine compensation and in the latter it was close to complete. Both of these studies found it difficult to recruit and retain smokers for the study duration, illustrating smokers' resistance to shifting (Bates et al., 1999).

The issues include the following: self-selection of lighter smokers with lower risk of smoking attributable disease to these brands; qualitative changes over time in the carcinogenicity of tar; and favourable changes in the tar to nicotine ratio of cigarettes, which mean that a given nicotine intake carries with it a lower tar exposure. Furthermore, low-tar cigarettes may have been mistakenly used as alternatives to quitting, so their introduction may have caused- and be continuing to cause - a higher number of smoking attributable deaths, than would have occurred had they not been an available option. In addition, recent studies by Stellman, Muscat and Hoffmann (1997); Hoffmann, Djordjevic and Hoffmann (1997) and Thun et al., (1997), have indicated that smoking low- tar brands may be related to the increasing incidence of adenocarcinoma of the lung. The speculation is that the rise in TSNA levels in lower-yield cigarettes, coupled with the manner in which these products are smoked by the smoker, i.e. deeper inhalation and longer, more intense puff volumes, may explain the significant rise in adenocarcinoma of the lung which has been observed over the past 25 years (Shopland, 2000).

Public understanding of tar and nicotine values



Surveys in both the US and the UK have consistently shown that most smokers do not know the tar and nicotine values of their usual brand of cigarettes, although a greater percentage of low-tar cigarette smokers will know their tar value compared to most other smokers. In a 1994 study, only 39% of smokers smoking very low tar-yield cigarettes (1-5 mg FTC tar) could correctly state the tar value of their cigarette when first asked (Shopland, 2000). Proportionately fewer smokers of higher tar and nicotine brands could recall the tar value of their normal brand of cigarettes. When asked how many cigarettes could someone smoke without taking in more tar when switching from a 10 mg to a 1 mg tar cigarette, 44 % of those smoking 1-5 mg tar brands believed a person could smoke "about 10" of the 1-mg tar cigarettes, another 10 % said they did not know.

Bates et al. (1999) describe the research, by Evans and Joossens (1999) for the Health Education Authority in England, which assessed the attitude of smokers to low-tar cigarettes. Over 1000 smokers were surveyed. Just over one-third (34%) of that group reported smoking cigarettes described as "light", "mild", or "ultra-light" (collectively referred to here as "light"). The "light" cigarettes were more popular among women, smokers from non-manual social groups, and smokers aged 35 or over. Almost half (46%) of women smokers in non-manual social groups reported smoking "light" cigarettes.

One-third of smokers who currently smoked "light" cigarettes said that a main reason for switching to a light brand was concern for their health. Almost 3 out of 10 (28%) smokers also said that a main reason for switching was as a step towards quitting. Over one-quarter (28%) of smokers thought that "light" cigarettes were less harmful than regular cigarettes. More than one-third (36%) of smokers currently smoking "light" cigarettes thought them to be less harmful than regular brands (Evans and Joossens 1999).

Bates et al. also refer (1999) to the detailed measurements released by British Columbia's Ministry of Health in its 1998 "*Reports on cigarette additives and ingredients and smoke constituents*" of the major cigarette brands on sale in the province. Cigarettes were measured under different smoking conditions. For "light" cigarettes, the ministry concludes: "Many smokers think that "light" cigarettes are safer than regular cigarettes,

and that by smoking “light” cigarettes they will inhale fewer cancer-causing chemicals, or less nicotine. BC’s new smoking tests have shown how wrong this belief can be. The reports filed by the tobacco companies show that light cigarettes are likely to deliver as many (or more) poisons and toxins to smokers as regular cigarettes”.

In 1985, in a probability-based survey of smokers' opinions about the tar and nicotine content information reported on Canadian cigarette packets, 51% of those who responded stated that, in their opinion, the numbers represented the *maximum* which could be inhaled from their brand of cigarette (Rickert, Robinson & Lawless, 1988).

Rickert (2000), referring to a Canadian Government 1969 article which states that "a cigarette of relatively low tar and nicotine content, which is probably less hazardous, can be manufactured readily", suggests that the linkage of “tar” reduction with “hazard” reduction has played, and continues to play, a significant role in directing cigarette design and government policy. He states that the pre-eminence of today’s ‘low’ tar cigarettes can be attributed to governments which continue to set limits for the hazard ("tar"), such as the proposed European directive in the European Bulletin EU9944-22 November 1999 (see section 21) and tobacco companies which market the perception of hazard reduction (i.e. “low tar”).

Zeller sums up (2000) that the assumption is that a reduction in exposure to tobacco will lead to an overall reduction in harm to the user. He cautions that it is necessary to be sure that a reduction in exposure to tobacco, or to substances in tobacco smoke, translates into some meaningful benefit in terms of actually reducing harm. He suggests that the only way to be sure of this is if there is an adequate scientific base, first to demonstrate a reduction in exposure, and then, to establish the critical linkage that exposure reduction leads to a meaningful reduction in harm.

6. Nicotine

Research is needed to advance further progress ...

- Determine whether regulators should encourage the development of substantially less harmful nicotine delivery devices. ...
- In order to reduce the addictiveness of tobacco products, research is urgently needed to evaluate the benefits and/or hazards of reducing nicotine and other possible addictive constituents in tobacco products over time. Particular attention should be given in research to determining whether a threshold exists for addictiveness.

(Recommendations from the Oslo conference)

Zeller asks what he terms "one of the central questions" about nicotine, which is whether there is a threshold level of addiction to nicotine and, if so, should regulatory agencies around the world systematically drive down the nicotine content of tobacco products to non-addictive levels?

Bates et al. (1999) deal with this also, cautioning on the possible consequences of reducing the nicotine content of tobacco products or smoke:

- First, the reduction in the nicotine content of smoke (more precisely in the ratio of nicotine to toxins) may mean a higher intake of toxins if smokers inhale more smoke to achieve the nicotine dose they desire.
- Second, Y-1¹ high-nicotine tobacco leaves may allow a smoker to achieve the satisfactory dose of nicotine from less smoke, if this smoke, like the leaves, has a higher concentration of nicotine.

Nicotine is rapidly absorbed into the blood and quickly delivered to the brain, where it produces a range of effects on the smoker. This quick absorption and effect permits the smoker to control the nicotine level; however, nicotine is rapidly eliminated from the body, which means the smoker has to deliver regular doses to the blood in order to maintain the effect. Information from previously secret industry documents reveals that pH differences in the smoke may under-report the total amount of nicotine in some brands of cigarettes. Manufacturers possess the technology systematically to alter the pH of the smoke and thereby alter the amount of free-base nicotine available to the user. Because this form of nicotine is delivered to the smoker in the gas phase, it would go undetected using any of the current testing protocols (Shopland 2000).

Robertson (2000) in his expert testimony, noted that, "While it is apparent that the manufacturers of cigarettes view themselves as being in a business where nicotine is the primary product, their principal mission is to deliver it to humans. They are in the nicotine delivery business. Clearly this dictates that they develop technologies and strategies to control and manipulate nicotine release from the delivery device". He provides industry evidence of the way in which the delivery of nicotine is controlled via tobacco grades, curing, expansion and blending:

"Nicotine levels in the tobacco that ultimately finds its way into a manufactured cigarette are controlled, in part, by the grade of tobacco chosen, the position in the plant from which the tobacco leaf is removed, expansion of the tobacco and processes used to cure the tobacco."

Nicotine is recognized as being a "pharmacologically active substance".

He quotes industry sources:

"Since only 10% of the nicotine is transferred to the mainstream smoke, any increase in the efficiency of nicotine transfer would lead to a dramatic change in the nicotine level and provide our company with another means for controlling nicotine delivery."

"Nicotine is the primary pharmacological agent in cigarette smoke."

Robertson (2000) quotes industry sources again to show that the tobacco industry knows that greater nicotine transfer efficiencies can be obtained through filter design.

¹ Tobacco leaves specially developed to have a high nicotine content

"The choice of filter material and its construction will affect the composition of the smoke that passes through it."

Robertson (2000) notes how cigarette companies recognize the need for establishing nicotine dose levels to be delivered to the human body. "Associated with the design of any drug delivery device is knowledge of dose amounts. The cigarette industry has described its attempts to provide the applicable optimal dosage range of nicotine for its consumers".

"What we should really make and sell would be the proper dosage form of nicotine with as many other built-in attractions and gratifications as possible -- that is, an efficient nicotine delivery system with satisfactory flavor, mildness, convenience, cost, etc."

Robertson (2000) describes how nicotine delivery in cigarettes is controlled, listing the efforts to manipulate and control nicotine in cigarettes:

- tobacco grades, curing, expansion and blending
- ammoniation of tobacco
- tobacco additives
- reconstituted tobacco sheet
- control of the tar/nicotine ratio
- increased nicotine transfer efficiencies
- filter design.

Robertson (2000) also explains the use of free-base nicotine in cigarette delivery systems: "Nicotine, which is an alkaline substance, exists in two forms - the bound or salt form and the free-form. However, only in the free-form is it relatively volatile. In tobacco, it is present mainly in the salt form. When a cigarette is smoked, nicotine is released momentarily in the free-form. In this form, nicotine is more readily absorbed through the body tissue. With this understanding, considerable effort has been expended in shifting nicotine from the salt to the free-form in cigarette smoke. This is accomplished by altering the pH of the cigarette smoke, indeed, by raising it. This, in turn, occurs with the addition of ammonia, di-ammonium phosphate and/or urea. RJ Reynolds summarized the methods whereby smoke pH and the associated nicotine "kick" could be increased.

"It is for this reason that the FTC test for nicotine can be misleading since the critical measure is not the mass of nicotine that reaches the human body, but the form in which that nicotine exists. The higher the levels of free relative to bound nicotine, the more bioavailable is the nicotine for absorption."

"If the desired goal is defined to be increased nicotine yield in the delivered smoke, there appear to be only two alternatives: either increase the absolute yield of delivered nicotine, or increase the pH, which increases the "apparent" nicotine content without changing the absolute amount."

Wilkenfeld reports (2000) the findings of the FDA in 1996:¹

- “The addictive and other pharmacological effects of nicotine are so widely known and accepted that it is foreseeable to a reasonable manufacturer that cigarettes and smokeless tobacco will cause addiction to nicotine and other significant pharmacological effects and will be used by consumers for pharmacological purposes, including sustaining their addiction to nicotine.
- Consumers use cigarettes and smokeless tobacco predominantly for pharmacological purposes. ...
- Manufacturers of cigarettes and smokeless tobacco know that nicotine in their products causes pharmacological effects in consumers... and that consumers use their products primarily to obtain the pharmacological effects of nicotine.
- Manufacturers of cigarettes and smokeless tobacco design their products to provide consumers with a pharmacologically active dose of nicotine.
- An inevitable consequence of the design of cigarettes and smokeless tobacco to provide consumers with a pharmacologically active dose of nicotine is to keep consumers using cigarettes and smokeless tobacco by sustaining their addiction to nicotine.”

Tar/nicotine

Governments are urged, individually or at a regional level, to...

- Give urgent priority to studying the implications for harm reduction of reducing levels of nicotine and other possible addictive constituents in tobacco products over time. ...

(Recommendations from the Oslo conference)

There is an assumption that a reduction in exposure to tobacco will lead to an overall reduction in harm to the smoker. Zeller (2000) notes that pharmaceutical companies are interested in using nicotine replacement products ("clean nicotine"), such as patches, to reduce a smoker's daily consumption of tobacco because of the theory that nicotine replacement products can help smokers smoke less rather than quitting altogether. "Dirty" nicotine from conventional tobacco products is perceived as being more harmful to health, because of its link with tar, and the very serious chronic diseases associated with tobacco use.

Robertson (2000) describes the tobacco industry's control of the tar/nicotine ratio thus: "Considerable effort has been directed towards controlling nicotine in cigarettes by manipulating the tar/nicotine ratio, namely to reduce it by reducing levels of tar and/or increasing the levels of nicotine in cigarette smoke".

Rickert (2000) describes how, in 1973, the call for tar reduction was modified by Michael Russell who suggested that, since nicotine is less harmful than tar and of importance to many smokers, tar and carbon monoxide should be reduced to a greater extent than

¹ See 61 Fed. Reg. at 44630.

nicotine (Russell et al., 1973 and Russell 1980). Thus the focus was shifted from tar reduction to a reduction in the tar/nicotine ratio; a policy which has strong proponents within today's tobacco control community. This approach may present a solution to the difficult problem of how to deal with both nicotine addiction and tobacco smoke toxicity at the same time (Robinson, Young & Rickert, 1984).

7. What should be measured?

Governments are urged, individually or at a regional level, to...

- Develop better measurements of the constituents and impact of tobacco products with the aim of substantially reducing their toxicity.

(Recommendations from the Oslo conference)

Shopland (2000) observes that, although research on the differences between low-yield cigarettes and other cigarettes has primarily concentrated on measuring tar, nicotine and carbon monoxide, cigarette smoke is actually composed of some 4000 different constituents, 60 of which are known carcinogens. Few published reports have provided detailed information on other smoke constituents across brands or how various cigarette brands differ with respect to the biological activity of the smoke generated across the spectrum of machine-measured tar and nicotine yields (see section 10 on additives).

Tobacco-specific nitrosamines (TSNA)

Table 2 shows a comparison of FTC- derived values for BaP and NNK against the actual intake from 133 smokers of medium- and low-yield cigarettes. Compared to FTC expected values, both groups were potentially exposed to nearly double the amount of the two carcinogens. According to the authors of the study, published in the Journal of the National Cancer Institute, "...a smoker who uses the FTC ratings to choose a brand of cigarettes with lower amounts of carcinogenic agents will not achieve the reduction anticipated".

Serious concern has been raised about the fact that lower-yield cigarettes contain TSNA levels that are inconsistent with their stated FTC tar values. In the US cigarette market, levels of benzo(a)pyrene (BaP) have declined steadily since 1960, but the levels of the lung carcinogen 4-(methyl nitrosamino)-1-(3-pyridyl)-1-butanone (NNK) has increased more than 50% since the 1970s when many "low-tar" products were being introduced (Shopland 2000).

**Table 2:
Mainstream smoke concentrations of two carcinogens delivered to smokers of low- and medium-nicotine yield cigarettes compared to levels measured via FTC method**

Component	Measurement	Low yield cigarette (≤0.8 mg/cig)	Medium yield cigarette (0.9-1.2 mg/cig)
BaP, ng/cigarette	Observed delivery	17.9 (15.3-20.9)	21.4 (19.2-23.7)
	FTC protocol	10.0 (8.2-12.3)	14.0 (10.1-19.4)
	Measured:FTC	1.8	1.6
NNK, ng/cigarette	Observed delivery	186.5 (158.3.-219.7)	250.9 (222.7-282.7)
	FTC protocol	112.9 (96.6-132.0)	146.2 (132.5-161.3)
	Measured:FTC	1.7	1.7

Source: Djordjevic et al., 2000

Star Tobacco Company claims to have a technology that eliminates all TSNAs. This company has lobbied the United States Congress for preferential regulatory treatment for its technology, and has also mounted a public relations campaign to call attention to its process (Zeller, 2000).

Shopland (2000) reports that a number of US epidemiological studies have found a decrease in mortality among smokers who switched from higher- to lower-yield products and among smokers of filtered versus non-filtered cigarettes. In the American Cancer Society's Cancer Prevention Study I (CPS I), which followed one million men and women for 12 years (1960 to 1972), smokers who switched to a lower-yield cigarette experienced a 15%-20% decline in their lung cancer risk compared to smokers who continued to consume higher tar and nicotine cigarettes. Other studies have found similar results. A decline in risk has not been consistently observed for other diseases, such as coronary heart disease or chronic lung disease.

Conversely, when the American Cancer Society reported six-year follow-up data (1982 to 1988) from their more contemporary prospective study (CPS II) of 1.2 million men and women, the relative risks for all the major smoking-related diseases had increased compared to the risks in CPS I participants. Lung cancer risks among male CPS II smokers had doubled while among CPS II women it increased over four-fold. Risks for heart disease, stroke, chronic obstructive lung disease, and cancers other than lung, were all greater among CPS II participants compared to the risks observed among CPS I participants. Given the substantial decline in machine-measured tar content of cigarettes over the time period covered by the two studies (sales-weighted tar levels declined by approximately 60 % between 1960 and 1986), it might have been predicted that relative risks might have declined, not increased, especially among males.

However, the addictiveness of nicotine means that smokers compensate for the reduced nicotine levels, and alter their smoking pattern to get their desired levels of nicotine. They can do this by inhaling more deeply, or by taking more frequent and larger puffs, or by

blocking the ventilation holes in the filter (see section 9 on compensatory smoking behaviour, below).

Bates et al. (1999) assert that modern cigarettes are designed to facilitate the discrepancy between people's smoking behaviour and the machine tests. One example is that, in some tests, the ventilation holes are not blocked by the machines although consumers can block them easily and even inadvertently (Slade, Henningfield, 1998).

Features designed to reduce cigarette toxicity are all based on the concept that "less is better". The perception has been that the modifications decreased harm. While there is evidence that some smokers may derive some limited health benefit by switching to a lower-yield product, these benefits are small compared to quitting entirely. It is now clear that switching from an FTC-measured 15 mg tar cigarette to a 5 mg tar cigarette will not reduce a smoker's disease risk by two-thirds.

In relation to this, Bates et al. (1999) note that the low-tar rating of cigarettes results largely from the filter and the way this performs when tested in a smoking machine - rather than from any inherent change to the tobacco. The filter is designed to retain more tar and nicotine than in higher-tar cigarettes. It may also have ventilation holes at the side, to allow air to be drawn in to mix with the smoke, thereby giving a lower reading when measured by a machine.

Many filter materials have been patented for use with cigarettes including compounds of aluminum, foams and sponges, resins, cellulose, charcoal, various types of paper, cotton, and other natural fibers such as wool, silk, flax and corn silk. Of these, only cellulose acetate, charcoal granules and combinations of them have had significant commercial success (Hoffmann & Hoffmann, 1997).

Since 1950, the proportion of filter cigarettes sold in North America has increased from less than 1% to over 97%. This is mainly due to studies in the early 1950s which linked lung cancer risk to "tar" exposure. Filters which reduced "tar" were thought to reduce lung cancer risk as well (Doll & Hill, 1950). Subsequent studies have demonstrated that this may be true for smokers of plain versus filter cigarettes (Rimington, 1981; Tang et al., 1995) but may not apply to smokers of 'high tar' versus 'low tar' cigarettes (Stellman et al., 1997).

Variations in cigarette construction, variations in the tobacco blend, number and type of additives) and manufacturing technologies (expanded tobacco, reconstituted tobacco sheets, perforated filter tips, filter tip additives, etc.) have been used together and to different degrees to attain specific tar yields ranging from 0.1 to over 40 mg. According to the 1994 RJ Reynolds report ("*FTC smoking method used for 'tar' and nicotine data*") the consumer smoking a 15-mg tar cigarette is inhaling tar entirely different in composition from the tar in the mainstream smoke of a cigarette whose tar yield is 20 mg or 7 mg" (Shopland, 2000).

In March 1999, ASH and the Imperial Cancer Research Fund released a survey of 57 patents related to the reduction of cigarette toxicity. These included features designed to

remove tar, carbon monoxide, polynuclear aromatic hydrocarbons, hydrogen cyanide, nitrosamines, oxides of nitrogen, carbonyls and other toxic constituents found in tobacco smoke. The report suggest that few, if any, of the innovations have had commercial applications because of legal implications, cost, the lack of regulatory standards and the impact of "low-tar" cigarettes (Rickert, 2000).

The Canadian Federal Government, in its publication "*Tobacco control: a blueprint to protect the health of Canadians*", has recognized that, for those who cannot or will not quit smoking, "...product modification may have some public health potential". In addition, the Government has also recognized that "If smokers would not buy these products, product modification initiatives would fail". As Wynder and Hoffmann comment (1979) "A completely "safe" cigarette that is smoked by only 1% of the smoking public has less preventive value than a cigarette with some adverse effects that is smoked by 90% of that public". Thus 'harm reduction' is part of the Canadian Government's policy regarding tobacco usage. However, "The federal government's policy objective with respect to tobacco continues to be to reduce tobacco consumption among Canadians and the resultant adverse health effects, to the extent possible".

The evidence suggests that there may be a role for technology in risk reduction at the user level (Rimington,1981; Tang et al., 1995). However, it is impossible to predict the net effect of "beneficial" modifications with respect to society as a whole. Harm reduction, at the population level, will not occur if the potential benefit of "reduced risk" products is negated through increased usage or a decrease in quit rates. The only truly "safe" cigarette is one that remains in the package (Rickert, 2000).

9. Compensatory smoking behaviour

Expert witness Robertson in the Minnesota trial in the US (1998), drawing on extensive tobacco industry documentation said, on the issues of compensation: "The delivery of any cigarette will depend on the way in which it is smoked. The term compensation is used to describe the tendency for a smoker to obtain a similar delivery, intake and uptake of smoke constituents on a daily basis, from a variety of products with differing standard (machine-smoked) deliveries". He quotes from an industry source:

"Smokers have been found to be unsatisfied by nicotine-low or -free cigarettes and will modify their smoking patterns in order to regulate their nicotine intake".

Smokers do not smoke cigarettes in a manner comparable to the FTC method; smokers significantly alter their smoking patterns, especially when smoking low-tar, low-nicotine products. Compensatory changes in smoking behaviour can take the form of larger puff volumes, more frequent puffs, inhaling more deeply, blocking filter vents, or smoking more cigarettes per day. Shopland (2000), reporting on this issue, comments that many smokers switching from higher to lower-yield products will adopt several of these behaviours simultaneously. Existing industry research suggests that, for the majority of smokers, these changes become part of their normal smoking pattern and are thus maintained for as long as they continue to smoke a lower-yield cigarette.

This has obvious public health implications: Bates et al. recommend (1999) that the ratio of specific carcinogens to nicotine should be reduced, to prevent the adverse effects of compensatory smoking which could erode the benefits of reduced carcinogenicity.

In evidence of this, Shopland (2000) reports that studies examining differences among smokers using various tar and nicotine yield cigarette brands, and using a variety of biomarkers for assessing such exposures - blood nicotine and cotinine, expired air CO, and tar deposition in the lung - have found few significant differences among smokers of low-yield cigarettes compared to smokers using higher tar and nicotine brands. Smokers adjust their smoking patterns to take in more nicotine than posted FTC values would suggest.

Rickert (2000) supports this, stating that smokers who are addicted to nicotine will extract whatever dose they require from their cigarette independent of the nominal (FTC) yield of their brand. This phenomenon both increases nicotine dosage from 'low' yielding brands and also decreases the dosage from 'high' yielding brands. Maximum oversmoking appears to occur when the machine measured levels of nicotine are about 0.4 mg. Little or no compensation occurs when standard nicotine yields fall in the range of from 1.1 to 1.4 mg (Kozlowski & Pillitteri, 1996). Although compensation may not be complete or permanent, it does have serious consequences particularly with respect to those who smoke 'low tar/nicotine' brands. This is due to the fact that the smoke matrix, which contains nicotine, also contains varying amounts of chemicals with known toxic and carcinogenic properties. Consequently, when compensation involves increasing the depth of inhalation, the peripheral lung is exposed to higher amounts of toxins and carcinogens (Hoffmann, Rivenson & Hecht, 1996).

Compensation does not necessarily mean that their nicotine intake will be stable across as nicotine yields vary because within upper and lower bounds apparently determined by noxious effects at high doses and withdrawal at insufficient dose, people can show considerable variation in nicotine intake. Furthermore, compensation can be facilitated or inhibited and total nicotine intake may be varied by a range of factors. For example, nicotine patches deliver nicotine gradually and with relatively little psychoactive effect. Therefore it is not surprising that cigarette smokers who are given patches will generally smoke somewhat less but their total nicotine intake will generally increase because their smoking is not proportionately decreased (Pickworth, Bunker and Henningfield, 1994). Similarly, cigarettes that vary widely in nicotine but were virtually identical in other sensory characteristics are not reliably smoked in such a manner so as to maintain stable nicotine intake (Griffiths, Henningfield, Bigelow, 1982). On the other hand, cigarettes in which air dilution reduces the concentration of nicotine and tar and reduces sensory cues tend to be smoked so as to extract much more nicotine and thereby result in similar blood levels as higher nicotine delivering cigarettes (Benowitz, 1996).

10. Additives

Research is needed to advance further progress. ...

- Determine whether countries should forbid addition of all new additives and explicitly address the possibility of reducing the use of additives that make tobacco products more attractive and/or taste better. ...

(Recommendations from the Oslo conference)

Additives may be natural or synthetic; they may include artificial tobacco substitutes, flavour extracts of tobacco and other plants, exogenous enzymes, powdered cocoa, and other synthetic flavouring substances. The number of additives used may vary, with anywhere from 30 to 150 different flavours being used for one brand (Manus, 1989). The tobacco industry claimed it had 1400 additives that could be put into cigarettes (Manus, 1989). A flavour may contain more than a hundred chemical ingredients (Chitanondh 2000).

Chitanondh (2000) suggests that the need for additives arose with the development of filters and "low-tar" products in response to consumer demand for a reduction in health risks. Filters, low tar and nicotine alter flavour – the smoke becomes drier, losing much of its body. Taste yield is reduced and the descriptive analytical profile of the smoke flavour changes. A repeatedly described taste deficiency is that of a “dry mouth feeling”. Frederick J. Triest, US tobacco industry flavour consultant said “regular smokers are accustomed to inhaling a certain amount of taste and body. With low tar, the only way manufacturers can give it to them is in flavours and fragrances”.

The European Union currently allows over 600 additives legally to be added to tobacco products. Bates et al., (1999) comment that little is known about the potential harmful effects of many additives when they are burned with tobacco or in conjunction with other additives. Siem (2000) notes: " Additives may be safe in food, but must be reconsidered when they go up in smoke".

In the UK, the “List of permitted additives to tobacco products” was first published in 1975 by the British Independent Scientific Committee on Smoking and Health. There are now some 600 in all. The list contains a number of known animal carcinogens considered potentially hazardous to human health. The FDA has its own list of food and drug additives: Generally Recognized as Safe (GRAS). The American cigarette producers adhere to the GRAS list for the defense of their flavour additives.

Additives- a trade secret

US health authorities have been concerned about the secrecy over cigarette ingredients for a decade. In July 1980 the-then Surgeon General Dr Julius Richmond wrote to the six major American firms asking for “a list of those substances which your firms use in the brands”. He received polite replies, but no specific information. His successors pursued Dr Richmond’s lead but the dialogue with the tobacco industry was complex, prolonged, and inconclusive. The best they could do was for Congress to enact the law in 1984 that

requires cigarette makers to submit a collective list of ingredients to the DHHS Secretary (see section 18).

Chitanondh (2000) describes how the tobacco industry, claiming increasingly low tar products, link each brand they create to some “ideal” safer cigarette, the formula for which is top secret. Robert Ruckeyser, public-affairs director for American Brands Inc. said “We really do consider flavour-enhancing to be a trade secret, and we prefer not to discuss that area at all”. Ernest Pepples, senior vice-president of B&W Tobacco said "It would be an extraordinary breach of our policy to discuss what we use or don't use" ... "The recipes (for flavouring) are carefully kept secrets". Art Bentlay, spokesman for US Tobacco said "due to the competitive nature of the tobacco industry, all information is proprietary and confidential".

Robertson (2000) states that "it is evident that the cigarette manufacturers were engaged in activities aimed at altering nicotine levels in cigarettes and thus in cigarette smoke", quoting industry sources as saying:

"The principle of this invention is to increase the smoke impact strength by raising the delivered nicotine in smoke and to reduce the inherent harshness of nicotine by adding a mono-carboxylic organic acid, preferably levulinic acid".

Increasing smoke delivery of nicotine has also been achieved using chemical additives such as nicotine maleate (Robertson, 2000).

Robertson (2000) notes that cigarettes possess attributes to mask the undesirable aspects of nicotine delivery, quoting industry sources:

"Nicotine is definitely an irritant in smoke and its taste must be blended out or modified by other constituents in the total particulate matter (TPM) to make the smoke acceptable".

In the case of nicotine, which has been described as tasting like “foul, rotten rubber”, flavourings must be added to the cigarette formulation to improve this undesirable feature.

Dangers of additives

Several additives are known to be dangerous to health. Ammonia is probably the most important additive. Research by James Pankow (1997), a chemist at Oregon Graduate Institute, showed that when the smoker lights up, nicotine is inhaled from tobacco and into the lungs by moist droplets within smoke. When ammonia is added, it allows more of the nicotine to appear in the free base form which is more available to the body. Pankow made his measurements by trapping the many chemicals of tobacco smoke on filters. He found that he could release the highly reactive, free-base form of nicotine by passing ammonia through those filters. Ammonia can make the nicotine in a cigarette up to 100 times more available to the smoker.

The intended purpose of additives needs to be fully understood (Bates et al., 1999). The tobacco industry has acknowledged that the addition of alkali such as ammonia to

increase smoke pH increases the availability of “free” or “unbound” nicotine and thereby increases the nicotine addictiveness for a given nicotine content. According to scientists from the tobacco companies:

“Since the unbound nicotine is very much more active physiologically, and much faster acting than bound nicotine, the smoke at high pH seems to be strong in nicotine” (Woods & Harlee, 1973).

“Methods which may be used to increase smoke pH and/or nicotine “kick” include: (1) increasing the amount of strong burley in the blend, (2) reduction in the casing sugar used on the burley and/or blend, (3) use of alkaline additives, usually ammonia compounds, to the blends, (4) addition of nicotine to the blend, (5) removal of acids from the blend, (6) special filter systems to remove acids from or add alkaline materials to the smoke, and (7) use of high air dilution filter systems. Methods 1–3 in combination represent the Philip Morris approach” (Teague, 1973).

“AT [ammonia technology] is the key to competing in smoke quality with PM [Philip Morris] worldwide. All US manufacturers . . . use some form of AT on some cigarette products.” (Johnson, 1989)

The addition of ammonia may be harmful, but it could conceivably be beneficial. Bates et al. (1999) note the apparent lack of any published assessment of the public health implications of the addition of ammonia to cigarettes, but point out that, if smokers can achieve the same “satisfaction” with less nicotine because more of the nicotine in the smoke is in its free form, and therefore more bioavailable, it may be that ammonia reduces the smoke intake and harm. Insofar as some additives have been used to increase the apparent impact and addictiveness of cigarettes, it may also be possible to reduce the addictiveness of cigarettes without eliminating the nicotine by either prohibiting certain additives or requiring them (Henningfield et al., 1998). Thus, regulation of additives will be an important issue for research and potential future regulatory attention.

Dangerous additives

Bates et al., (1999) note that some additives, although not directly toxic in themselves, may nevertheless increase tobacco-related harm by making cigarettes more palatable, attractive, or addictive to consumers. If the purpose is to facilitate extra smoking or to increase the addictiveness of the product, it hardly matters whether the additive itself is toxic or benign.

Chitanondh (2000) describes the known carcinogenic or otherwise dangerous additives currently known to be present in cigarettes:

Acetaldehyde is a volatile aldehyde and may be cytotoxic or genotoxic. Additives dl-Alanine, l-leucine and l-phenylalanine are amino acids which are known to give rise to aminoheterocyclic compounds during heating (Sugimura, 1988). One of them induces liver cancer in nonhuman primates (Adamson et al., 1990). These compounds are powerful genotoxic agents and several are experimental carcinogens.

Ammonia (see above)

Angelica root extract : two oils, angelica and bergamot contain furocoumarins, angelicin and 5-methoxypsoralin. Both furocoumarins can be photoactivated to DNA-damaging reactants (Papadopoulo & Averbeck, 1985). In conjunction with solar-simulated radiation, 5-methoxypsoralin has been judged by a working group of the International Agency for Research on Cancer (IARC, 1986) to be an experimental carcinogen and there was limited evidence for angelicin.

Benzyl acetate is used as a flavouring agent. It occurs naturally in plants such as apples, jasmine, and ylang-ylang. In 1988, the US National Toxicology Program reported that, for male and female mice, there was some evidence of carcinogenicity in that benzyl acetate caused increased incidence of liver and forestomach tumours.

Ethyl 2 Furoate was a possible chemical warfare agent in the 1930s. Ethyl furoid is a chemical in a family of “notorious liver toxins”. Little is known about ethyl furoid except that it causes liver damage when tested on animals. Eugenol itself is suspected of being a carcinogen. Another additive, freon, is a chlorofluorocarbon (CFC) which damages the ozone layer. The additives furfuraldehyde, glyoxal, and 2-hexenal are volatile aldehydes and therefore likely to be present in cigarette smoke. These may be cytotoxic or genotoxic.

Humectants are added to make aged tobacco workable and keep cigarettes fresh. The major ones are glycerol and glycol. According to the 1979 Surgeon General’s Report, it is suspected that glycols may influence the smoker’s risk of bladder cancer. Burning of triethylene glycol produces 1.4 dioxane, another harmful substance. Some industry sources say the triethylene glycol has been replaced with diethylene glycol, a humectant which is not known to be harmful (Cummings, 1983) The burning product of glycerol is acrolein which suppresses the action of microscopic cilia that force irritants from the lungs. As a result, the smoker’s risk of chronic obstructive lung disease is increased and the lungs are open to attack by toxins and carcinogens. Mintz, (1983) reported that 35 million pounds of glycerol was added each year just to keep cigarettes moist. Cigarette smokers are at increased risk of leukemia (Hoffmann, Brunnemann & Hoffmann, 1990). One of the leukemogenic agents in cigarette smoke is benzene) (IARC, 1982). Since many tobacco additives are known to give rise to benzene during burning (Higman, Higman & Chortyk, 1974), the effect of flavour additives on the smoke yield of benzene should be investigated.

Although cocoa powder makes a healthy drink, smoke from cocoa burned in cigarettes could be hazardous. In the mid 1970s Dr Gori of the NCI found that condensate of tar produced by cigarettes flavoured only with cocoa produced more tumours when painted on the skin of mice than did tars from unflavoured cigarettes.

Practically all licorice extract produced in the US goes into tobacco. It adds flavour, help keep tobacco moist, and improves the burning quality. Licorice root extract contains up to 25% glycyrrhizin, a compound which, when burned, is a precursor for cancer-causing polycyclic aromatic hydrocarbons.

Menthol is an inducer of enzymes and thus may accelerate the metabolic activation of tobacco carcinogen. Methoprene is a pesticide used to kill insects on stored tobacco.

Methyl salicylate, when given orally or topically to Syrian golden hamsters and rats, is teratogenic (Overman & White, 1983). Orange-peel oil promotes tumours in mice. Sclareol can react with other chemicals to produce convulsions.

A standard recipe for flavouring 100 pounds of tobacco calls for 14 pounds of sugar. When burned with tobacco sugar increases tar yield. Sugar is a precursor of carcinogenic polynuclear aromatic hydrocarbons. Certain forms of sugar, particularly caramel and invert sugar, produce catechol when heated. This is ‘the major known co-carcinogenic in tobacco smoke’, according to Dietrich Hoffman, associate director of the American Health Foundation.

Issues for the future

The example of ammonia highlights the problem in regulating additives merely according to the toxicity of the additive itself, rather than based on an assessment of whether the purpose of the additive, when used as intended, is in the public interest. Ammonia is one of many additives that could be challenged on public interest grounds. Others include additives that make smoke more palatable, burn enhancers that keep cigarettes smouldering, and compounds that may dilate the bronchial passages. Bates et al, (1999) conclude that regulators should know which additives are in which brands and only permit them in brands where it could be proved that they would facilitate a public health gain.

As Bates et al. observe (1999), the current regulatory framework for tobacco additives is inadequate. Ammonia technology is at least 25 years old, yet there has so far been no regulatory control on its use. In the past quarter century it is likely that there have been numerous innovations in the field of tobacco additives - all with minimal regulatory scrutiny of their intended purpose.

11. The "need" for novel products

Research is needed to advance further progress ...

- Expand behavioural research on how “cigarettes affect smokers” and how the population (of smokers and nonsmokers) responds to claims about new products and to new packaging rules. ...

(Recommendations from the Oslo conference)

Thus far, this monograph has focused largely on problems with the design, testing, and regulation, of cigarettes and how changes in design, testing and regulation might contribute to public health. Medications such as nicotine replacement products that are approved for medical indications such as smoking cessation and withdrawal relief have also been discussed. This section looks at a third category of products which have been

referred to as “novel products” or alternate nicotine delivery systems (Slade, 2000 and Sweanor, 2000). In addition to the products named in this section many other products have been marketed or at least proposed by the tobacco industry and have been discussed in the Proposed and Final Tobacco Rule of the US Food and Drug Administration (FDA, 1995,1996) and elsewhere (Slade, 1993; 2000; Slade and Henningfield, 1998).

This third category is controversial in many respects including how novel products should be regulated. For example, they might be regulated as tobacco products if they contain tobacco and do not make health claims. They might be regulated as new drugs and/or drug delivery devices on the grounds that their form and/or function sets them apart from conventional tobacco products. They might be marketed as a new category of product that requires prior approval from a regulatory agency before they can be marketed but than are allowed to be marketed according to the conventions imposed on tobacco products rather than those imposed on drug products (FDA, 1996; Slade, 2000; Slade and Henningfield, 1998; Henningfield and Slade, 1998; Page, 1998). This monograph does not address how these products should be marketed or attempt comprehensively to address the issues raised by such products. It describes some of the products as a means of illustrating some of the prominent issues they raise.

Sweanor (2000) and Slade (2000) have defined novel tobacco products as products that differ in form and or function from conventional tobacco products but which satisfy some of the needs, including nicotine delivery, that smokers currently satisfy through smoking cigarettes. They have the potential to be of less risk than a continued use of conventional tobacco products. The potential consumer market for such products can be seen by looking at the current cigarette market, which BAT listed in 1998 as constituting roughly 1.15 billion smokers paying US \$300 billion per year for six trillion cigarettes. This market, which is equivalent in size to the entire global pharmaceutical market (Novotny et al.,1999), is also characterized by the fact that the products will eventually result in an extraordinary level of mortality among long-term users (Peto, 1994). A very large proportion of smokers are looking for ways to reduce harm, with close to 70% of smokers in some countries expressing the desire to quit, as reported by the US Department of Health and Human Services, (1996).

As more is learnt about the science and technology of nicotine and its delivery, and more about the other ‘benefits’ smokers derive from smoking, it is very likely that there will be a proliferation of new products. Among the scientific issues pushing this development will be a growing awareness of the role of tobacco use as a form of nicotine self-medication (Pomerleau, 1997). Other issues, such as consumer rights, the updating of food and drug laws and litigation over tobacco-caused harm will accelerate the movement to novel products (Sweanor, 1998).

12. Novel tobacco products

PREMIER

Premier was a nicotine delivering product that was of a similar general size and appearance to a conventional cigarette but was constructed of materials including aluminium, fiberglass, and plastic. It was operated by the combustion of a carbon heating

element which volatilized nicotine contained in its aluminium drug cartridge rather than by burning tobacco (Slade, 2000; Slade & Henningfield, 1998; Henningfield & Slade, 1998; Siem, 2000). Compared to conventional cigarettes, the product delivered similar levels of nicotine, higher levels of carbon monoxide, and reduced levels of many other toxins (RJ Reynolds, 1988; Woodson et al., 1993). Premier was patented as a drug delivery article that could be used to deliver a variety of pharmacologically active substances, and it was found to be effective in delivering cocaine (Cone and Henningfield, 1989; Foltin et al., 1990; Siem, 2000). It was test marketed in the US in 1998 and withdrawn after a period of poor sales and requests from many health organizations and governmental agencies that it be withdrawn from the market until it could be reviewed and approved according to the procedures for other drug and drug delivery products (Slade, 2000).

ECLIPSE

RJ Reynolds Tobacco company developed a product which evolved from many of the same patents and technologies used to develop Premier. It was test marketed in the US under the brand name of Eclipse in 1995 (Slade, 2000). It was more extensively marketed and advertised with strong claims of reduced toxin delivery in 2000. The product was also sold in Sweden as "Inside" and in Germany as "Hi.Q". Outwardly it resembles a typical cigarette, but internally consists of four sections. The first is the heating element which is similar to that of Premier. It consists of a carbon-based fuel element surrounded by fiberglass. However, in Eclipse, the carbon was sheathed by a thin layer of reconstituted tobacco paper. The next section is the primary nicotine reservoir and contains about 280mg of a paper-like material made from equal quantities of tobacco and glycerin. It is sheathed by aluminum foil laminated to paper to ensure that adequate heat will be held to volatilize the nicotine. The third section contains about 420 mg of reconstituted tobacco, which terminates in a short 10 mm vented cellulose acetate filter. Lighting the cigarette ignites the carbon tip, heating the air which is drawn through its holes and through the fiberglass packing material surrounding it. The fourth section has the appearance of a filter, however, in the US version it is rendered virtually nonfunctional as a filter by a hole of approximately 2 mm in diameter which runs laterally through its centre. The heated air then passes through the initial processed tobacco section producing an aerosol that is primarily glycerin and nicotine. This glycerin vapour then picks up flavour components and nicotine as it moves through the reconstituted tobacco (Rickert 2000).

Zeller (2000) reports that, according to RJ Reynolds, the main difference between Eclipse and conventional cigarettes is that most of the tobacco in Eclipse is heated rather than burned; that the company viewed Eclipse as a reduced risk product; and that these factors formed the basis for its marketing as a cigarette (rather than as a new drug) and advertising as a reduced risk product.

According to Rickert (2000), Eclipse has been tested under FTC-like smoking conditions in at least two laboratories. At RJ Reynolds, the aerosol from a regular Eclipse yielded 2.9 mg tar, (defined to be the total tobacco smoke particulate matter (less nicotine and water) retained by a filter designed to trap at least 99.9% of all particles having a diameter equal to or greater than 0.3 μm of a dioctyl phthalate aerosol at a linear air

velocity of 140 mm/s (ISO 3308:1991); 0.19 mg nicotine and 7.5 mg carbon monoxide. In independent testing conducted by Labstat, the values obtained were 3.4 mg tar, 0.15 mg nicotine, and 8.8 mg carbon monoxide. It is important to note that the tar or particulate matter (PM) produced by smoking Eclipse is quite different in composition than that produced by smoking a typical cigarette. Particulate matter from Eclipse is about 80% glycerol and water and 20% other substances (including nicotine). The reverse is true of the particulate matter trapped from the mainstream smoke from typical cigarettes (Rickert, 2000).

Eclipse performance under proposed Canadian cigarette testing methods

Under proposed Canadian cigarette testing methods (see section 4), differences in particulate matter composition were still pronounced with nicotine and other constituents contributing a little over 10% to the PM from Eclipse but close to 60% of the PM from traditional cigarettes. The temperature of the charcoal element and the body of Eclipse are highly dependent on smoking conditions; maximum surface temperature readings increasing by a factor of two when changing from FTC to intense smoking conditions (Slade, 2000). This results in relatively high yields of carbon monoxide. For example, under mandated "intense" Canadian smoking conditions, carbon monoxide yields of about 40 - 45 mg were reported for Eclipse, which is greater than the yields from six other typical American brands which were tested (Borgerding & Rickert, 1997).

Considering other toxic smoke constituents, Rickert & Kaiserman (1998), in their comparative study of the composition of the smoke from Eclipse, demonstrated that large reductions occur when tobacco is mainly heated rather than burnt. For example, yields of the suspected lung carcinogen, benzo[a]pyrene (Denissenko et al., 1996), were only 6% of the average for the four typical cigarette brands which were tested. Also, Eclipse produces negligible amounts of sidestream smoke since only about 25 mg of tobacco are burnt during the smoking process. Thus the total emissions (mainstream plus sidestream concentrations) of most constituents are considerably less than that of other commercially available cigarettes. Once again, taking benzo[a]pyrene as an example, total yields from Eclipse were less than 20 ng (nanogram) per cigarette or about one-third of that which was obtained from the next lowest "tar" brand (Rickert 2000).

Rickert (2000) reports that the biological activity of particulate matter from Eclipse prototypes has been investigated using a range of *in vitro* toxicological tests. These include sister chromatid exchange, chromosome aberration, neutral red cytotoxicity assay and the Ames bacterial mutagenicity assay. Based on the results, it has been concluded that the genotoxic and cytotoxic potential of Eclipse PM was significantly less than the Kentucky reference cigarettes 1R5F and 1R4F (Boombick et al., 1997 and Boombick et al. 1998). This may be related to the observation made by Smith et al. (1996), that smokers of Eclipse type cigarettes void urine which is significantly less mutagenic than urine voided by smokers of typical American cigarettes. Whether the mutagenicity would be less than that produced by all reduced "tar" cigarettes presently marketed is not clear because the Kentucky Reference cigarettes used by RJ Reynolds are substantially higher in the delivery of many toxins than from many commercially marketed cigarettes. The State of Massachusetts, therefore, compared Eclipse to some commercially available low-yielding cigarettes using smoking machines. The Massachusetts study found that

Eclipse delivered comparable levels of many toxins to the commercially available cigarettes (Labstat International Inc, 2000).

Still other investigators from the Roswell Park Cancer Institute, US, found that the use of the fiberglass packing material in Eclipse leads to the product's contamination with fiberglass pieces that can be inhaled into the mouth and possibly into the lungs (Pauly et al., 1998). Public statements and recent research by RJ Reynolds have attempted to downplay the toxicological significance by arguing that the contamination is not as extensive as implied by the Pauly et al. study and that the physical size of the fiberglass material may not readily be inhaled all the way into the deep airways of the lung. Nonetheless, this issue was not disclosed by RJ Reynolds, despite its claimed extensive testing, and RJ Reynold's response has not been to fix the apparent product defect but rather to downplay its significance. These facts highlight the need for regulatory oversight of such products.

ACCORD

Rickert (2000) describes the Philip Morris product, "Accord", which burns less tobacco by restricting combustion through the use of a series of puff-activated electric heating elements. Although described by Philip Morris as a "cigarette" and a "lighter" or "holder", the device employs a tubular tobacco-containing load, which according to the company cannot and should not be smoked as a cigarette. It also contains a microprocessor-controlled device about the size of a small cellular telephone which includes puff sensor, timers, and heating elements. The tobacco load is shorter than a typical cigarette and consists of two segments each measuring approximately 30 mm in length. The first is a densely packed tobacco rod surrounded by a tobacco sheet which is encased in cigarette paper and the second is a hollow tube which ends in a 5 mm cellulose acetate filter. It cannot be easily lit or kept burning. Each load delivers eight "puffs" provided by the puff-activated ignition of one of the eight heating elements. After eight such activations the device will not operate and a fresh load must be inserted. The tobacco does not burn in a self-sustaining manner but rather only for the time that the heating element is activated. Consequently the amount of tobacco consumed is only about 50% that of a conventional cigarette. In addition, the use of an electrical heater causes the tobacco in contact with the heater blade to burn at a temperature that is lower than that of a conventional cigarette. This, in turn, affects smoke chemistry and emissions (Terpstra et al., 1998).

A comparison of the yields from Accord with those from the Kentucky reference cigarette (1R4F) indicates that yields are generally lower when tested under the standard ISO puffing regimen. However, some increase in distillation products such as glycerol and some low temperature degradation products (water and formaldehyde) has been reported. A decrease in yields of carbon monoxide, polynuclear aromatic hydrocarbons, and TSNAs has also been reported (Terpstra et al., 1998). From a toxicological standpoint, TPM produced by electrically heated cigarette prototypes appear to have reduced biological activity when tested using Ames Salmonella test. Also, cytotoxicity, as measured by the neutral red uptake assay, has been reported to be consistently lower for the electrically heated cigarette prototypes for both tobacco smoke particulate and gas phases. Based on these, and other tests, Carchman (1998) has concluded that the lower

peak burning temperature in the electrically heated cigarette results in lower yields of most biologically active smoke components with a corresponding reduction in biological activities (Rickert 2000).

How the product would compare to products tested in accordance with the Massachusetts protocol (Labstat International Inc., 2000) is not clear as the primary source of information is limited to what Philip Morris has disseminated. It is not known if Accord delivers additional toxins of concern that may only be discovered in studies by independent researchers as occurred when the Roswell Park researchers discovered the fiberglass problem with Eclipse.

Shopland (2000) notes the "critical gap" in knowledge about the health consequences of smoking low-yield cigarettes, and questions whether the benefits of smoking such cigarettes are overstated. He asks "How will nontraditional products such as Eclipse, Accord, Premier, be tested for smoke constituents?" "Do these products permit more of the nicotine to appear in the gas phase of the smoke than more traditional products?" Additional questions have been posed by others (Shiffman, 1998; Slade and Henningfield, 1998; Henningfield and Slade, 1998) including the following: Should the products be regulated as cigarettes, drug devices or some new category of product? Should nontraditional tobacco-derived products be required to have prior approval from regulatory authorities prior to their marketing? Should claims of reduced yield be based on comparisons with test cigarettes selected by the companies or on the commercially available lowest yielding cigarettes? Should reduced risk claims be permitted at all in the absence of data that demonstrate harm reduction? Should special marketing constraints and surveillance be required to ensure that these products do not undermine prevention and cessation efforts and thereby adversely affect overall public health even if they did pose a risk reduction for those who did smoke them compared to regular cigarettes?

13. Novel filters: recent examples

The potential of filters to reduce cigarette emissions is still an area of active research and commercial application. Rickert (2000) describes how, in 1996, a special filter containing wheat and charcoal was added to Canada's popular Player's brand of cigarettes. The new brand, *Players Premier*, a tobacco-burning cigarette, was heavily marketed with advertisements claiming that smokers would get "full-flavoured taste with reduced irritation". Carbon ("charcoal") substances added to filters have also been discussed as a means of reducing certain categories of toxin emissions (Hoffman & Hoffman, 1997).

BIOFILTER

The potential of filters to reduce cigarette emissions is still an area of active research and commercial application. About the same time as *Premier* was developed, a hemoglobin/charcoal based filter was introduced by a company located in Athens, Greece and became a commercial success based claims of toxicity reduction. According to a "Golden Filter SA" advertisement, "this new Biological Filter absorbs, inactivates or neutralizes a number of chemically toxic compounds in cigarette smoke such as free radicals, nitrosamines, H₂O₂, NO_x, quinones, catechols, acetaldehydes, acrolein, benzene derivatives and other organic compounds".

Claims of toxicity compound reduction raise the interest of many groups including manufacturers, regulators, and the public health community. This occurs for a variety of reasons ranging from simple curiosity to the possibility of misleading advertising. In the case of the *Biological filter* ('Biofilter'), it was impossible to substantiate the claim due to a lack of publicly available data. However, it was possible to characterize this innovative filter using data acquired by the RJ Reynolds Tobacco Company as part of a study by Labstat International Inc in 1998 of several "light" and "ultra-light" brands (FTC tar of 8-11 mg per cigarette) (Rickert 2000).

Filter tests

This project involved a determination of yields of 33 constituents under standard FTC conditions¹ using the proposed Canadian test methods published by the Canadian Government². The values obtained were then divided by those determined for a reference cigarette, 1R4F (University of Kentucky) to facilitate comparisons. The results do not support the manufacturer's claim. For example, relative yields of hydroquinone were highest for the Biofilter. Relative catechol yields were similar to Brand C but exceeded those of Brand B by over 50%. Both Brands B and C were constructed with 'common' cellulose acetate filters. Some relative reduction was noted for various volatile organics such as benzene and toluene but yields still exceeded those of Brand A. Taking all test constituents into consideration, based on these results, the Biofilter does not appear to be more effective than the common cellulose acetate filter in toxic constituent reduction. However, it is unclear whether the difference between the company's claim and the experimental results are product-related, method-related, or both. If claims around cigarette deliveries are to be allowed, standardized test protocols are required to ensure that independent validation is possible (Rickert 2000).

14. Novel approaches to communicating cigarette yields and/or toxicity

A tar/colour scale

Colour and odour are among the most widely recognized properties of tobacco smoke particulates. Odour has been the subject of numerous investigations, but tobacco smoke colour has received little attention, at least in the quantitative sense. In 1982 a method was described for the detection of the number of standard puffs taken on a filter cigarette by a visual comparison of the "colour" of spent filters to a colour scale constructed from three commercial Pantone colours (Kozlowski et al., 1982). This approach was expanded through the direct measurement of tar colour in relation to tar yield which resulted in the construction of a tar/colour scale (Rickert, Robertson & Kaiserman, 1994). In more recent studies, a linear relationship has been found, between tar and the yields of more than 40 toxic constituents, which extends the usefulness of tar colour as a predictor of

¹. The testing was subject to the conditions prescribed by the FTC in the Federal Register, Volume 32, Number 147, page 11,178, dated August 1, 1967. With regard to the testing of carbon monoxide content, the conditions are specified in the Federal Register, Volume 45, Number 134, page 46,483, dated July 10, 1980.

² see: <http://www.hc-sc.gc.ca/ehp/ehd/tobacco/index.htm>.

potential exposure (Borgerding et al., 1999). From a smoker's standpoint, the colour can be used to warn of compensation, and reduce exposure on a personal level.

The potential public health significance of this type of measuring device was recognized in 1994 by the NCI Expert Committee on the FTC test method (NCI, 1994). Four recommendations were made; the third stated "A simple graphic representation should be provided with each pack of cigarettes sold in the United States and in all advertisements. The representation should not imply a one-to-one relationship between measurements and disease risk". Both the science and the technology are now available to act on this recommendation (Rickert, 2000).

Two caveats to the successful application of this approach would include the possibility of tobacco companies changing the colour of the filter to brown, which would obscure any such system, and the possibility of new additives being introduced which are designed to result in a light coloured particle, despite being more toxic.

A relative exposure index

Comprehensive testing, as proposed by the Canadian Government (see section 4), generates a wealth of complex data. It would require that manufacturers report to the Government on over 50 different chemical compounds, in whole tobacco, mainstream smoke, and sidestream smoke with an extensive list of constituents for cigarettes, cigarette tobacco, pipe tobacco, cigars, smokeless tobacco, leaf tobacco, kreteks (clove cigarettes), and bidis (handmade Indian cigarettes). The requirements include sales data, data regarding toxic emissions, cigarette construction, and various lists of studies including those relating to toxicity, health effects, taste and flavour, cigarette modifications, tobacco product development, and ingredient lists.

It is therefore extremely important to develop and test unique approaches to communicating this range of information in a simple but meaningful way. In particular, it would be useful to be able to convey the toxicological significance of the data. One possibility suggested by Rickert and Kaiserman (1998), is a relative exposure index (REI) in which all chemical yields are expressed relative to acceptable short-term (e.g. 15 minute) exposures in an industrial context. This is the same approach taken by the RJ Reynolds Tobacco Company in the characterization of the smoke produced by *Premier* (RJ Reynolds, 1988). It has also been used, more recently, in support of Massachusetts regulations regarding tobacco products (Vorhees, Heiger-Bernays & McClean, 1997). If a relative exposure index were to be used, consideration would need to be given to how consumers would interpret such data.

This approach has an advantage in that constituents are weighted both by their toxicological significance and their concentration in tobacco smoke. In addition, the relative exposure index is almost independent of smoking conditions which is a severe limitation for current methods of expressing cigarette yields.

In 1999, Rickert and Kaiserman carried out a calculation of the relative exposure index for various types of tobacco products including *Eclipse*, typical flue-cured Virginia and

American type cigarettes as well as small cigars,¹. Yields from *Eclipse* were the lowest at 4.4. Typical American blended cigarettes came next at 39.1 followed by Virginia flue-cured at 50.4 (ISO test conditions) and 69.4 ("intense" smoking conditions)². The composition of cigar smoke resulted in the largest REI at 187. The results of the calculation appear to make sense - for example, Bombick, Putnam & Doolittle, (1998) reported that cigarette smoke condensate (CSC) from flue-cured tobacco exhibited greater cytotoxicity than CSC from cigarettes comprised of burley tobacco, as would have been predicted by the index. However, problems still remain: toxicological data is lacking for some constituents and there are no limit values for Class A carcinogens such as 4-aminobiphenyl. Also, once the computational issues have been solved, validation experiments with biological endpoints must be carried out before the index can be used in any way other than as a research tool.

Issues for the future

Rickert (2000) notes that, at present, there are very few standard methods for the assessment of either the chemical toxicity or biological activity of tobacco products³. A range of tests is needed to ensure that factors which result in a decreased response in one test system do not result in an increase in activity in systems with other endpoints. Any framework for assessment should judge progress compared to a benchmark of biological activities obtained by a statistically sound survey of the range of cigarettes available in the marketplace. Results which suggest a potential for a significant reduction in diseases related to or caused by tobacco use must be confirmed by valid epidemiological studies. In most instances, the choice of both test condition and method of analysis is left to the manufacturer or the laboratory selected to carry out the analysis. Thus, it is possible for claims to be made that may or may not be true depending upon what procedures are used in the evaluation. Bates et al. recommend (1999) that a new measure of total toxicity be introduced, that includes, for example, a measure of total nitrogen content, or Ames tests.

There seems to be general agreement that there is a need for a technically competent body to be at the disposal of authorities in reviewing and evaluating ingredients in cigarettes and smoke (Siem 2000).

¹ For a definition of "small cigars" see Smoking and Tobacco Control Monograph 9 entitled *Cigars: Health Effects and Trends* and published in 1998 by the National Institutes of Health, National Cancer Institute.

² The proposed Canadian test methods include two test conditions (see section 4).

³ "Biological activity" is to be interpreted in the broadest sense including mutagenicity, teratogenicity, carcinogenicity, cardiotoxicity, pulmonary toxicity, tobacco dependence and any other measure deemed useful in the assessment of potential health outcomes. This would include exposure studies in both natural and laboratory settings. In its broadest sense, it also includes pharmacological activity that involves a different set of measures such as nicotine dose both on an individual and a population basis.

PART THREE

REGULATORY ISSUES

Regulation of consumer products including medications, manufactured food products, beverages, household devices, and automobiles, share at least two common purposes: one is to facilitate fair commercial trade and marketing, the second is to protect people from undue risk of harm caused by the products. Product regulation can also contribute to the evolution of better products from the perspective of how well they serve and their risk of causing harm. It has become increasingly apparent that the regulation of tobacco products is severely deficient. It has fostered trade and marketing practices that would not be allowed for other products and led to the development of products that are harmful. Even though it is understood that tobacco products are inherently dangerous products, their adverse impact on public health is more extensive than it would be if product regulation were more effective. Moreover, public health efforts to control tobacco attributable disease are impeded by existing product regulation approaches. In the absence of more effective regulation, the global epidemic will continue to accelerate, fostered by unchecked marketing that contributes to the development of addiction in youth and the manufacture of dangerous products.

Several areas of deficiency in tobacco product regulation are evident. For example, cigarette smuggling is rampant. Tobacco companies have developed product marketing campaigns for imported cigarettes that bypass the collection of duties. Marketing campaigns are designed to foster, rather than mitigate, the development of youth use and addiction. Cigarette designs include techniques that lead consumers easily, if not inevitably, to obtain higher levels of toxin exposure than are labelled. Cigarette manufacture includes ingredients such as burn accelerants, toxins, and substances that become toxic when burned. These have not been proved by the manufacturers to be necessary for the use of their products, but they increase the risk of their use to users and nonusers alike. There is little or no significant relationship between ISO or FTC ratings of tar and nicotine levels and the actual exposure of consumers (Benowitz, 1996). Marketing claims that imply health benefits and reduced risk are routinely made in advertisements and even in many cigarette brands' names without any evidence that the products provide those benefits, compared to their counterpart brands which do not imply them. Many other deficiencies have been identified (WHO Helsinki Tobacco Conference, 1999; Slade & Henningfield, 1998; Joossens 1999).

Many areas of tobacco product regulation could be reformed so as to develop regulatory approaches that would be consistent with public health goals and thereby contribute to reducing tobacco attributable disease. Part three summarizes critical areas of focus for tobacco product regulatory reform.

Product regulation is one aspect of the overall drive to reduce the tobacco epidemic. The context is of a range of efforts to reduce tobacco consumption, such as regulating access; and limiting demand through restrictions on advertising, marketing, promotion, distribution, and through taxation. Governments need to have relevant, accurate and current scientific information about the toxic substances in tobacco products and tobacco

smoke. They need to assist smokers and non-smokers to make more informed decisions regarding the use of tobacco (Siem, 2000). Changes to the regulatory framework could reasonably prevent manufacturers from increasing the harm caused by tobacco. Further, such changes, on the basis of full information on composition and researched understanding of the health implications of this, could reasonably prevent harm to consumer health.

15. International collaboration

International collaboration

- Establish under WHO authority, an international expert group on tobacco and nicotine delivery devices. It needs to be well-financed and have access to the best technical expertise available. It would guide international policy development with respect to product regulation and could facilitate access to scientific information needed for tobacco regulation. Its first task would be to study the recommendations of the Oslo meeting and recent scientific reports on the topic and make recommendations for action to WHO. ...

(Recommendations from the Oslo conference)

There are well-known limitations to national action to control tobacco: advertising bans are thwarted by means of the Internet, satellite television and foreign magazines; smuggling allows for cheaper products without health warnings to find their way to the market; and limited access to information about health effects in some countries hampers national action. In all these examples there is a need for global action to complement national action: that is the rationale for the proposed Framework Convention on Tobacco Control (FCTC). The Director-General of WHO has described the FCTC as "a political process brought in to serve a public health cause", noting that. "... the key to success lies in expanding inclusiveness, ensuring transparency and clarifying the key purpose of the exercise". At the Ninth International Conference of Drug Regulatory Authorities (Berlin, April 1999), she encouraged governments to take action at home, then to translate national successes into international gains, via the protocols to the FCTC.

The first Working Group of the FCTC was held in Geneva in October 1999 and the second Working Group meeting was held in March 2000. The first Intergovernmental Negotiating Body (INB) was held in October 2000, and a second meeting is scheduled for April 2001.

In the Chair's text of a framework convention on tobacco control released in January 2001, by Ambassador Celso Amorim, Chair of the Intergovernmental Negotiating Body, and in the accompanying letter, it was proposed that one of the initial protocols developed would address the regulation of the contents of tobacco products, tobacco product disclosures, and packaging and labelling of tobacco products. Such a move clearly indicates the need for international action uniformly to address product regulation issues at country and regional levels.

The Internet is an important way to bridge the divide between countries and local communities which are subject to harsh forms of marketing and need support. Increasingly, advances in access to information technologies will be used to equalize access to information and the media on a global basis. This will significantly accelerate local, national and global action simultaneously (Yach, 2000).

WHO's role

WHO is aiming to accelerate actions aimed at effectively controlling tobacco use, for example through the United Nations Ad-Hoc Inter Agency Task Force under the leadership of WHO, founded by the United Nations Secretary-General and through collaboration with Bretton Woods institutions. Among several national and regional meetings exploring issues related to regulation of tobacco products, in October 1999 WHO organized a conference in Helsinki, Finland, on this topic. The Conference concluded, among other matters, that the present regulatory framework had not fostered the innovations in tobacco product development and marketing that could lessen the morbidity and mortality associated with the use of tobacco products (for the conclusions of the meeting, see Annex 2).

Creation of a scientific advisory committee on tobacco products regulation

A global team of experts facilitated by WHO has been gathered to help countries deal with industry arguments and development of tobacco product regulations. The Scientific Advisory Committee on Tobacco Product Regulation (SACTob) was established by WHO in March 2000, to facilitate access to scientific information and guide international policy development in the area of tobacco product regulation. The Committee will study the recommendations made from the Oslo Conference, together with recent scientific reports, and make recommendations for action to WHO. The Committee will catalogue existing regulations and the impact of these if known. It will evaluate and make recommendations on the most appropriate and effective regulatory frameworks for tobacco products.

All tobacco products are of concern to the Committee, as all are presently understood to be capable of causing and sustaining nicotine addiction and contributing to a variety of disease states and causes of death. Among tobacco products, commercially manufactured cigarettes are a priority concern by the SACTob because they are projected to account for the vast majority of global deaths attributable to tobacco for many decades to come in most countries of the world, especially in developing countries.

Primary sources of information and analysis for SACTob's work will include the published literature, data provided by regulatory agencies, tobacco industry documents, experts and other expert groups. SACTob will be able to commission new work where appropriate.

Because of the potential for conflict and bias and the history of attempting to undermine WHO health efforts with respect to tobacco (Kessler et al., 1996) information from tobacco industry representatives will be considered with great caution.

The SACTob has so far met on two occasions – October 2000 and January 2001. Early deliberations have focused on testing methods, so-called ‘light’ and ‘mild’ labelling concerns, and the development of a common regulatory framework of tobacco products.

Terms of reference of the WHO Scientific Advisory Committee on Tobacco Product Regulation

- Advise WHO on recommendations to governments on the most effective ways to achieve a coordinated regulatory framework for tobacco products.
- Collate and assess information on the impact of different regulatory frameworks existing within WHO member states. Evaluate how regulatory approaches developed for cigarettes could be adapted to cover all forms of tobacco.
- Examine the role and advise on the most appropriate regulation of additives to tobacco products.
- Since FTC/ISO methods currently in use are not intended to measure the biological or epidemiological impact of tobacco products, consider how new methods and protocols could be developed to measure the impact of tobacco products on an individual and population basis.
- Identify and advise WHO on encouraging appropriate agencies to support research to evaluate the benefits and/or hazards of harm reduction of tobacco products.
- Consider how best to develop better measures, including biomarkers, to assess the health impact to individuals and population wide on the use of “less toxic” tobacco products in order to drive future regulatory actions.
- Identify how the population responds to claims about new products and to new packaging rules.
- Determine whether, and if so, how, governments and international agencies could encourage the development of substantially less harmful tobacco products and other nicotine delivery devices.
- The committee should also, at the request of WHO, monitor and make recommendations on products for treating tobacco dependence, and novel nicotine delivery devices, whether or not these are based on tobacco products.

16. Policy development

All countries need to introduce comprehensive tobacco control policies and strategies along the lines recommended by the World Health Organization.

... Within the context of a comprehensive policy, product regulation should be given explicit and urgent attention in order to reduce the health impact of tobacco among users. ...

Recommendations from the Oslo conference

The introduction of novel tobacco products and other alternative nicotine delivery products need to be managed in such a way as to be a net gain for public health. This could require a combination of measures designed to prevent unnecessary harm with measures designed to maximize potential benefits (Sweanor, 2000).

Bates et al. (1999) suggest that an important prerequisite for developing more enlightened regulation is a comprehensive disclosure regime. Regulators need a detailed characterization of the product to specify regulations that would result in meaningful improvements. This detailed disclosure should be distinguished from the consumer information made available on packs. This would support efforts to establish a common international strategy on tobacco product modification as, once disclosure is established, there could be improved consumer information and a move to consumer regulation, based on the disclosed data.

Siem (2000), has reported on the wide differences between the measures countries have taken in their efforts to regulate tobacco as a product. Until recently, the most relevant legal instruments to this issue - those to regulate consumer products and foodstuffs - have only exceptionally been used. He suggests that “the way is now open” for States to legislate their rights to verify the content of tobacco and smoke, to inspect production sites, limit the amount of certain ingredients, and approve additives. They can also request the declaration of certain additives, the purpose for their use and a toxicological evaluation.

Raw (1997) proposed the establishment of a “nicotine regulatory authority” which would have oversight of all forms of nicotine delivery. It would be able to control testing, stipulate allowable levels of toxic constituents, as well as standards for licensing, labelling, packaging, sales, marketing, etc. Its goals would be to take a comprehensive view of the overall market in nicotine delivery devices and to establish a framework that would deliver maximum health advantages.

Linked to this, Bates et al. (1999) have recommended developing a common international strategy on the future of product modification. An element of this would be the regulation of all nicotine delivery products within a common framework. Such a framework could establish common approaches to testing whether new product developments were in the public interest. It could encourage the production and marketing, for nicotine addicts, of less harmful forms of nicotine and thus eventually make it possible to minimize harm. However, because of its addictiveness, Bates et al. (1999) urge great caution in developing regulatory restrictions on nicotine; restrictions may have “perverse

consequences” as smokers adjust their smoking to maintain blood nicotine levels. They may ingest more smoke to attain the nicotine they are seeking. Similar arguments apply to banning Y-1 high-nicotine tobacco and may plausibly apply to the enhanced bioavailability of nicotine created by the addition of ammonia (see section 10 on additives). Actual exposure of smokers to nicotine should be carefully and regularly monitored.

Sweanor (2000), suggests that, as the establishment of an entirely new system of regulating nicotine products is unlikely, an alternative could be a form of co-regulation. In such a system tobacco products and novel products could be regulated separately, but with the regulation of each taking into account the impact of the regulation of the other category of products. This could again be directed at attaining the greatest overall reduction in tobacco-related morbidity and mortality. Such a system would seek to eliminate the current situation where, through the current lack of regulation, the deadliest products are given the greatest marketplace advantages.

Significant elements in policy formulation

Before rules are written and legislation enacted, policy must be formulated.

Siem (2000) suggests that the following policy elements are important:

- *Evidence*
There is little debate about the evidence that tobacco is harmful to health.
- *Definitions*
One of the major obstacles to effective regulation of the product: raw materials, production, additives, packaging and end product, tobacco and smoke all need to be defined as to what shall be allowed, and what not.
- *Authority*
If there is a convincing purpose and political will, authority to regulate will be established. Health authorities in some states have the necessary basis to regulate the product tobacco. Some adjustments of present legislation are needed in others.
- *Practicality*
It must be possible to carry out the regulating measures effectively. Ways of inspecting production sites, imports and other shipments, and verification of the content and standards of samples appear to be feasible for tobacco when only a limited number of products are on the market. The issue might be more complicated in tobacco-producing countries which have many suppliers to the market.
- *Acceptance*
Surveys show that the majority of adults in the United States agree that the tobacco corporations should be regulated by the authorities. A total ban on nicotine or tobacco would not be accepted by smokers, and might lead to social unrest, black market trading of the product and smuggling. This might also happen if only “safe” cigarettes are available, if these cigarettes do not meet the smokers’ “needs”.
- *Enforcement*
Enforcement of tobacco product regulations should be feasible in countries which do not produce much tobacco. One central agency would be the most effective. In countries which have many producers and distributors, a decentralized system of

inspection and compliance control - similar to the enforcement of foodstuff regulations – would be the answer.

Problems with the existing regulatory structure

Tobacco products are excluded from consumer protection laws, such as food and drug legislation. Even the introduction of products such as “light” cigarettes (Warner, Slade Sweanor, 1997) has not attracted regulatory intervention. Novel products, regardless of the manufacturer, should be subject to the stringent regulations governing pharmaceutical products (see section 23 on the regulation of pharmaceuticals). The difference in regulation for different nicotine delivering devices (Food and Drug Law Supplement, 1998) has resulted in what Warner, Slade and Sweanor (1997) described as a “nicotine maintenance monopoly”. The deadliest products have the greatest regulatory advantages. This distorts markets in favour of continued high levels of mortality and morbidity (Novotny et al., 2000). Novel products, even those offering unequivocal health benefits compared to existing tobacco products, are often effectively banned from the marketplace due to burdensome regulatory standards.

Sweanor (2000), argues that the existing regulatory structures could cause significant problems as the novel products are introduced. All novel products might be seen as pharmaceutical products. They would then be required to meet safety and efficacy standards that might be unattainable. Getting the approval of drug regulatory bodies for products could involve such onerous conditions that the innovations are either not economically viable or are significantly constrained by marketing limitations. Existing regulation may keep potentially dangerous products off the market. The consequence may be that consumers have no option but to continue use of the current, considerably more toxic, products.

It is also possible that the existing regulatory structures would favour some forms of novel products in ways that have little to do with their health impact. For instance, a primarily tobacco-based novel product could be allowed on the market, as long as it met the existing exemptions for tobacco products provided in consumer protection laws. A less toxic product that is not as readily identified as a “tobacco product” would not be available to consumers. Such an outcome would direct product development efforts towards meeting regulatory loopholes rather than public health needs.

Existing regulatory structures are based on scientific information which is now out of date (see section 5). Bates et al. (1999) describe how “tar” has hitherto by general consent been agreed to be the major carcinogenic component of cigarette smoke. Reductions in cigarette tar levels were therefore seen as a form of product modification with the aim of reducing harm. It was also assumed that the tar yields printed on the box approximately represented the tar exposure to the smoker and that a 5mg-tar cigarette would deliver half the tar of a 10mg cigarette. Bates et al. (1999) point out that these assumptions are false, yet that they continue to inform policy on tobacco product regulation. The tar and nicotine levels are measured by machines using a test based on the FTC approach that was adopted by the ISO. The test does not measure what consumers ingest from their cigarettes because people do not smoke like machines. Bates et al. (1999) suggest that a better metric for health impact would be tar to nicotine ratio (see section 6).

17. Key elements of a regulatory framework for tobacco products

Governments are urged, individually or at a regional level, to take the following actions: ...

- Evaluate and implement the most effective ways to achieve a unified regulatory framework for nicotine delivery products, including tobacco products, products for treating tobacco dependence, and novel nicotine delivery devices, whether or not these are based on tobacco products. Key terms of reference are to
 - Maintain a primary focus on harm reduction
 - Develop better measurement of the constituents and impact of tobacco products with the aim of substantially reducing their toxicity
 - Promote international comparability
 - Implement a pre-market approval and post marketing surveillance system. ...

(Recommendations from the Oslo conference)

The regulatory bodies

Many ministries are involved in tackling tobacco use. One ministry governs taxation; another deals with smuggling, yet others with labour protection, consumer protection and environmental issues. However, most of the control falls with the Ministry of Health, in particular for the controls of content and yields of tobacco products. Piha (2000) has alluded to the potentially divisive aspect of this in the Finnish context, where negotiations with the tobacco industry at an early stage were conducted by both the Finance Ministry and the Ministry of Social Affairs and Health. The desired effect of multiple involvement is incremental; the engagement of several bodies should provide a firm supportive environment.

The central government, or the federal government, decides on the national legislation. In some countries, states and territories have the power to regulate as well. Often, the enforcement of the legislation is under the authority of local government. Local inspection of production sites and control of products for distribution is probably called for more in countries of tobacco production than in countries which have only a limited number of importers and producers (Siem, 2000).

In the United States, the regulation of tobacco products has so far been accomplished through a series of federal laws, by voluntary actions on the part of the industry and the ad hoc regulation of the advertising and marketing practices of the cigarette and smokeless tobacco industry by the FTC. The majority of government action consisted of providing information and education to the public. On August 23, 1996, the US Food and Drug Administration asserted jurisdiction over cigarettes and smokeless tobacco products as drug-delivery devices and enacted comprehensive regulations to reduce or

eliminate young people's use of these products (Wilkenfeld 2000). The action was subsequently declared invalid by the US Supreme Court.

Proposals for a comprehensive set of tobacco product regulations

Rickert asks (2000) "what are the elements that should be included in a comprehensive set of tobacco product regulations?"¹ A regulatory framework for tobacco products would ensure that all aspects of the product received scrutiny under reproducible and sensible test conditions. Reducing the harm caused by tobacco products goes beyond changing product characteristics. Other factors, such as rates of initiation and cessation, need to be considered. This means that there must be a monitoring programme to ensure that risk reduction at the level of the user is translated into harm reduction at the population level.

Even if data are available from the most comprehensive framework imaginable, Rickert questions (2000) who is responsible for the communication of that information and what form it should take. In particular, if a reduced risk product (as defined by some standard test protocol) is produced, would the tobacco companies be allowed to communicate this fact? Should tobacco companies be allowed to communicate 'beneficial' changes to their products and, if so, by what means?² The potential breadth and depth of information to be collected by the proposed Canadian reporting regulations is without precedent. However, Rickert (2000) suggests that it is the communication and not the information itself that will determine the public health impact of tobacco regulations in Canada and the rest of the world.

Bates et al. (1999) make the following recommendations for elements to be considered in future regulation of tobacco products.

- Abandon the existing approach (*and keep it only for archival continuity*)
- Establish a new basis for measurement, regulation, and labelling (*including some or all of the following: Upper limits, and progressive reductions, for concentrations of known carcinogens and other toxins in smoke; a new measure of total toxicity; and the ratio of specific carcinogens and other toxins to nicotine. Research should be commissioned to examine the pros and cons of setting an upper limit for nicotine yields.*)
- Regulate tobacco product additives (*One possible model for regulatory supervision could be drawn from the pharmaceutical sector - manufacturers wishing to add flavouring to nicotine gum have to undergo an arduous regulatory process.*)
- Require full disclosure by brand (*This information should be made public - the Tobacco Sales Amendment Act in British Columbia provides a precedent. Nicotine content, the proportion of nicotine in "free" form in smoke and a puff-by-puff pH profile should also be given by brand. Concentrations of known carcinogens and*

¹ This issue was addressed by the Canadian Expert Committee which met in Toronto in September 1998. The following statement comes from their report and provides one view of the scope of a regulatory framework. "In developing this framework, consideration should be given to measures for chemical toxicity, biological activity, exposure, smoking behaviours, and the results of both short and long term epidemiological health effect studies".

² Product manufacturers are typically permitted to make health claims only after thorough regulatory review and clinical data demonstrating safety and efficacy for the proposed claim.

other toxins in smoke and their ratio to nicotine should be disclosed by brand, and the tar/nicotine ratio should be specified for reasons of historical comparison. The percentage ventilation of cigarette filters should also be given by brand.)

- Remove misleading “low tar” or “lights” branding (*Consumer information on packets needs to be comprehensive and accurate. Implied health benefit claims and branding should be prohibited unless a genuine evidence-based health benefit, consistent with the implied health claim, can be established by the company to the satisfaction of an appropriate regulatory agency.*)
- Remove misleading tar yield numbers and strengthen warnings (*FTC/ISO tar and nicotine yield ratings are misleading and should be removed from the pack. A comprehensive list of warnings/messages should be included on packs or in package inserts.*)
- Monitor societal nicotine dependence (*Exposure to nicotine needs to be regularly monitored by cross-sectional and cohort population surveys, including cotinine measurement.*)
- Develop regulatory capacity (*Plans should be set in place to establish a European Union tobacco product modification expert committee, and to develop a fully skilled, Europe-wide, nicotine regulatory body that would have the authority to regulate all nicotine containing products. A properly funded programme of research into product modification should also be commissioned.*)
- Develop a common international strategy on the future of product modification (*establishing a common international strategy on tobacco product modification, involving other international agencies such as the World Health Organization in a three stage process.*)
- Review and update regulations (*Any future directive on these issues should be regularly reviewed and modified in the light of experience.*)

Future issues

Questions

Shopland (2000) queries whether in fact the routine testing of cigarettes for tar, nicotine and carbon monoxide serves a useful purpose, and whether it should be discontinued. If it is to continue, what research is needed prior to instituting major changes in the existing system?

Zeller (2000) asks "what scientific evidence is needed to evaluate what should be asked of tobacco manufacturers?" and poses a preliminary list of questions:

- How is exposure reduction measured?
- Are there biomarkers, on which experts can agree, to give the scientific comfort that meaningful exposure reduction has been achieved?
- What steps should be taken to agree on how to measure a reduction in exposure?
- What studies should companies and their researchers conduct to help establish the critical linkage between a reduction in exposure and a concomitant reduction in harm?
- Are there markers or surrogates for harm reduction?
- How will it be known when a meaningful reduction in harm has been achieved?

- What can be done to minimize the possibility that products marketed to reduce the exposure to and harm from tobacco instead reduce or eliminate any incentive a tobacco user might otherwise have had to quit?
- What can be done to minimize the chance that these products might create an incentive for nonsmokers, or quitters, to initiate tobacco use, thinking that tobacco is safe to consume in the form of these new products?
- What can be done to avoid the harm-reduction and exposure-reduction movement turning into a more scientifically sophisticated version of the endorsement of “light” and “low tar” cigarettes 30 years ago?

Zeller, 2000 notes that the FDA has funded a new expert committee convened by the Institute of Medicine in the United States, whose charge is to study these issues. It is to make recommendations to the FDA about an appropriate scientific and regulatory framework to address the complex questions related to appropriate regulation of tobacco products and cessation aids.

Points raised by the working groups

The working groups at the Oslo conference proposed various proactive global responses, among them:

- Global capacity within the public sector is currently inadequate to understand technical aspects of tobacco product regulation. Urgent attention should be given to developing expert capacity within the tobacco control community on technical issues relating to product design, manufacture and technology
- Clearing houses for global knowledge on tobacco products are needed. They should maximize the use of information technology and draw on existing centres of excellence.
- National expert reports should be used globally: for example the recent Royal College of Physicians (February 2000), the pending review conducted by the US Department of Health and Human Services for the FTC on low-tar policy and the Institutes of Medicine of the National Academy of Science (US) review conducted at the request of the Food and Drug Administration to establish a methodology for assessing tobacco products.
- Adequate funding is needed for all aspects of product regulation, including research and development, and institutional development especially for developing countries.
- A wider range of strategic partners should be involved in product regulation development and implementation. This could include any group that is willing to advance public health goals. As examples, such partners may include printers, pharmaceutical companies, large companies with workforces trying to quit, “ethical” corporations and consumer groups.

18. Ingredient disclosure

Governments are urged to ...

- require tobacco manufacturers to disclose the contents, purpose and effects of constituents in all their products at regular intervals ...

(Recommendations from the Oslo conference)

A new regulatory framework is required in which the manufacturer is obliged to demonstrate that no additional harm arises from tobacco product design decisions (Siem, 2000). Given the caution over consumer protection in so many other fields (e.g. pharmaceuticals, see section 23) it seems reasonable to prevent manufacturers from increasing the harm caused by tobacco use.

Bates et al. (1999) proposed that tobacco additives should be tested for their wider public health impact. There should be a full disclosure of ingredients, additives and smoke constituents by brand. For each additive that the tobacco companies wished to continue using the companies should submit evidence that its overall effect (including its intended purpose) is not adding to the health consequences of tobacco or any causing other damage. The burden of proof should be placed on the tobacco companies to make the case for continued use of each additive. The regulatory hurdles faced by a pharmaceutical company wishing to add flavourings to nicotine gum provide a starting point for development of a more robust regulatory framework for tobacco additives.

Proposed elements of tobacco product regulation

Bates, Jarvis & Connolly (1999) suggested that such a regulatory framework might have the following elements:

- *Disclosure* Manufacturers should be required to disclose all additives used in tobacco products, by brand, to a regulator.
- *Public information* Such information should not be confidential, but made available to the public through publications, the Internet or on request from the regulator.
- *Packaging* There may be some additives that should be listed as ingredients on tobacco product packaging. This is a separate decision to a requirement of disclosure and making the information public in other ways – the right approach will depend on assessment of the direct value of such information to consumers.
- *Disclosure of purpose* Tobacco companies should be required to disclose the purpose of an additive and any secondary consequences – whether intentional or unintended.
- *Conduct and disclosure of research* Tobacco companies should be required to undertake extensive toxicology and pharmacological testing of all additives.
- *Regulatory challenges* Regulators should have the power to challenge any of the existing 600 additives currently allowed (in some countries) and to have them removed until the manufacturer is able to show that no extra harm to the public arises as a direct or indirect result of the additives. If it is impossible to supply evidence, for example because of restrictions on animal testing, then under a precautionary approach the additive should be banned.

- *Focus on pharmacologically active additives* There should be an automatic challenge to any additive thought to have a direct or indirect pharmacological influence. New additives should be permitted only if the manufacturer can show that no extra harm or other net negative consequences arise from use of the additive.
- *Permit essential additives* Any regulatory framework should permit additives necessary for the manufacture and storage of tobacco products providing these are safe, but should challenge all additives that may influence smoking behaviour.

Current laws on ingredient disclosure

At present only two countries in the world - Canada and Thailand - have laws in force which require manufacturers of tobacco products to disclose the ingredients in each brand.

The United States has pursued a similar legislative path to Canada, but current legislation (due to industry lobbying) is less rigorous in its requirements. Massachusetts passed an ingredient disclosure law in 1996 which was then held up in the Federal Appeals court in 1997 after a suit by a group of cigarette companies. In other cases the law can only demand submission of a collective list of ingredients. The US has enacted the Comprehensive Smoking Education Act of 1984, amending the Federal Cigarette Labeling and Advertising Act and the Comprehensive Smokeless Tobacco Education Act of 1986. These require that cigarette and smokeless tobacco companies submit confidential lists of ingredients added to tobacco in the manufacture of these products. The lists are submitted annually to the Secretary of the United States Department of Health and Human Services. This official, by law, must treat these lists as confidential information. He or she may, however, report to any subcommittee or committee of the United States Congress on any ingredient which, in his or her judgement, poses a serious health to cigarette smokers. The Secretary has no authority to regulate any hazardous products that may be identified through this collection process. Under the existing law there is insufficient information from the industry to permit analysis of the health effects of exposure (US Office of Smoking and Health). Smokeless product companies must also report the nicotine content of their products to the Secretary (Chitanondh, 2000).

Canada

On 31 July 1998 the Government of British Columbia became the first jurisdiction in the world to require tobacco companies to reveal the additives and ingredients in each brand of cigarettes, and to provide a detailed chemical analysis of the smoke of each brand of cigarettes. The Tobacco Sales Amendments Act requires companies to test their products for the presence of 41 toxic chemical constituents of smoke in addition to nicotine, tar and carbon monoxide (these chemicals include formaldehyde and arsenic). In December 1997 the Liggett & Myers Tobacco Company in the United States became the first company to disclose the ingredients contained in its products (Bates et al., 1999).

Thailand

Thailand passed the Tobacco Product Control Act in March 1992. The law became effective from 5 June 1992.

Section 11 of the Tobacco Product Control Act states that

“ tobacco products to be sold shall have a composition in accordance with the standards prescribed in the Ministerial Rules.

In cases where the composition of any product does not comply with the standards prescribed in paragraph one, the Minister shall have the power to order the prohibition of sale or import of such tobacco product.”

Violation of this section incurs the following penalty:

“ Any manufacturer or importer failing to inform the particulars or informing incomplete particulars or informing false particulars or selling or importing the tobacco products in violation of Section 11 shall be subject to an imprisonment not exceeding six months or a fine not exceeding one hundred thousand baht¹ or both”.

(Section 29)

The implication of the “Ministerial Rules” referred to in Section 11 is that the item must be submitted to the Thai Juridical Council for legal scrutiny and to the cabinet for final approval. In the case of the Tobacco Product Control Act 1992, the Ministerial Rules pursuant to Section 11 were withheld for more than five years due to tobacco industry lobbying. The Rules became effective on 13 February 1998 (Chitanondh, 2000). Now cigarette ingredients submitted in Thailand shall be occasionally inspected, “between sunrise and sunset” (Siem, 2000).

19. Current forms of government action to regulate tobacco products

Voluntary agreements

Voluntary agreements are agreements between the government and the tobacco industry. They establish principles of trust under which the industry agrees to abide by certain restrictions. A number of governments have replaced such agreements with legislation as a more effective method of control. Voluntary agreements are a weak means of controlling the tobacco industry; they are difficult to monitor, and are subject to more differences in interpretation than legislation, as lengthy negotiations are often needed. Voluntary agreements are not considered to be effective (Siem, 2000).

Legislation

Siem (2000) describes five broad categories in which tobacco can be regulated as a product:

Agriculture

In tobacco-producing countries tobacco can be regulated as an agricultural product. It can be included in legislation concerning pesticides, fertilizers, genetic modification, harvesting, drying, storage and blending. Such inclusion would have a limited benefit: of contributing to ensuring knowledge and control of the products that reach the factories.

¹ At the time the law was enacted, Baht 100 000 was equivalent to US\$4000.

Foodstuff and related products

The regulations would typically aim to exclude harmful products, ensure the declaration of additives, assure hygienic handling and set standards to help guide consumers. Regulations might include aspects of production, storage, transportation, import and sales of products. Products can be excluded from the market because they are unfit for consumption for known reasons of toxicity, poor quality or poor hygiene, as well as for suspected or unknown effects, on a precautionary basis. This is the case for certain genetically modified products today. The control of compliance with the regulations is typically decentralized to local authorities, as the food is produced by many providers and sold locally.

Safe food is a high priority. Siem (2000) notes that tobacco regulation fits well into this frame of regulation in some countries, and could do so elsewhere also.

Consumer regulations

Consumer regulations are to protect the consumer in all fields of trade and services and are typically more general than the regulations on foodstuffs. Consumers increasingly demand information about the products they buy. Claims must be true, products must be safe, standards be met, ingredients and methods of production be revealed to the authorities or declared to the buyer. The producer can be asked to produce guarantees of quality and documents of no-known risk, or to evaluate risks which might be associated with the product.

Drugs

Drugs are tightly regulated with regard to the production, composition, import, sales, purpose and advertising of the products (see Section 23 on the regulation of pharmaceuticals). A product with drug-like characteristics can be classified as a drug (pharmaceutical or proprietary medicinal product) based on its content or based on its intended use. If tobacco were to be introduced today, it might well be classified as a drug based on its content of nicotine. It would not, however, fit the requirement of having a desired medical effect.

In 1999, at the Ninth International Conference of Drug Regulatory Authorities, WHO called upon international food and drug regulators to bring cigarettes and other tobacco industry products under the same regulatory framework as other drugs. If this were to happen, it would give the authorities a strong basis for regulating tobacco products.

Environmental pollution

Smoking can be regulated within the framework of labour protection or environmental protection legislation. Siem (2000) comments that these frameworks seem relevant for the regulation of tobacco consumption, but less so in the context of regulating tobacco as a product. The issues of how much smoking and “sidestream” smoke pollute might become issues in the future, if smoke-free and reduced smoke cigarettes are further developed (see section 12 on novel tobacco products).

20. Country-specific regulation

International tobacco product regulation

In most nations, manufacturers are required to disclose the ingredients, including flavourings and other additives, of any product intended for human consumption. Few governments have applied these same rules to tobacco companies. Siem (2000) describes the vast differences between countries in their approach to or implementation of tobacco regulation. A full account of the legislation is given in the International Digest of Health Legislation. Siem (2000) notes that a survey of the current legislation gives an indication of the difficulties that would be presented by the creation of transnational strategies, as called for by the first conclusion of the Helsinki conference on the Regulation of Tobacco Products in 1999.

International regulation of tobacco products requires full disclosure of additives and other product design features, and assessment of product risk. Risk assessment should be based not only on smoking machine tests of tar and nicotine, but also testing of toxic smoke constituents in mainstream and sidestream smoke, human typography and exposure studies, and more complete information about internal industry testing of products.

Additive/ ingredient disclosure

Regulation of additives

In a number of countries, including Germany and the UK, the government publishes lists of ingredients that are permitted or prohibited for use in tobacco. The UK sets a maximum limit for each additive based on percentage added by weight of tobacco. Germany prohibits use of a number of additives. In both cases, disclosure of additives is not required from manufacturers, although the UK House of Commons Health Committee recently required the companies to submit additives by brand to them. These were then published in full, by brand, on the Health Committee's website, although flavourings are not broken down into their constituent parts.

A proposed EU Directive which is going through the legislative process, as currently drafted requires, *inter alia*, a list of all ingredients, and quantities thereof, used in the manufacture of tobacco products sold in the Member States, by brand name and type. This list shall be accompanied by reasons for inclusion of these ingredients, toxicological data in burnt and unburned form, and their effects on health taking including their addictiveness. This information will be disseminated by any appropriate means in order to inform consumers, without prejudice to measures intended to protect the confidentiality of information on manufacturing processes.

Composite lists

In the United States, New Zealand, and Chile, tobacco manufacturers report a composite list of additives which may be present in any tobacco product. New Zealand additionally requires manufacturers to provide the maximum levels of each additive present in various types of tobacco products, including cigarettes.

Australia has been negotiating with Australian cigarette manufacturers for the disclosure of ingredients. Philip Morris and Imperial Tobacco have voluntarily submitted their own composite additive lists.

The Tobacco Manufacturers Association of Denmark disclosed in July 2000 a list of 37 additives used in cigarettes on the Danish market which also included the additives' purpose of use.

Brand-by-brand disclosure

Several governments have taken the lead in requiring tobacco companies to disclose ingredients on a brand-by-brand basis:

Thailand: Thailand passed legislation requiring brand-specific ingredient disclosure in 1992. Tobacco companies did not comply with the law until 1998, after securing agreements from the Thai Government that certain ingredients would remain secret.

British Columbia, Canada: The province of British Columbia passed ingredient disclosure requirements in 1998 that include the power of the Minister of Health to make information public. The collected information has been made available via the Internet.

Massachusetts, United States: The state of Massachusetts passed ingredient disclosure regulations in August 1997 requiring manufacturers to report added constituents, by cigarette brand, in descending order by weight. These regulations are still being challenged in federal court, and no additives information has yet been disclosed. Proposed amendments to these regulations would provide stronger confidentiality protection to any submitted list of added constituents.

Texas, United States: The state of Texas also passed ingredient disclosure regulations in 1998 requiring manufacturers to report added constituents, by cigarette brand, in descending order by weight, and including stronger trade secret protections. Additive information has been submitted by manufacturers but is not publicly available.

Canada passed legislation in 1997 granting authority to require information on tobacco products including ingredient disclosure and prescribing substances that may not be added to tobacco products. Regulations proposed in June 2000 will require reporting of the quantity and cost of each ingredient employed by manufacturers, and the amount of added constituents by brand used separately in the tobacco, filter, and paper. In addition, all product testing and research activity conducted by manufacturers over the past year must be reported on an annual basis, including research on ingredients, product taste and flavour, and product modifications.

Nicotine testing and product characterization

Nicotine yield

The United States has received voluntary data on nicotine yield from manufacturers for more than three decades using a smoking-machine based standard developed by the FTC.

These ratings serve as a relative measure of nicotine yield but do not reliably measure human intake.

Since 1972, in the UK cigarettes have been tested at regular intervals using the FTC test which was adopted by the ISO to determine nicotine (and tar and from 1981 carbon monoxide) yields by the Laboratory of the Government Chemist Ltd (LGC), on behalf of government. The test included establishing average (tar and) nicotine yields and the accuracy of the statement of the yields displayed on all cigarette brands marketed in the UK. Again, these tests do not reliably measure human exposure. The proposed EU Directive (see section 21) requires a machine-tested limit of 1mg nicotine per cigarette by 2003.

British Columbia promulgated regulations in 1998 which require testing and reporting of nicotine yield ratings, smoke pH, and filter efficiency for all brands sold in the province. Testing is performed according to FTC/ISO machine standards and an "intense" machine smoking condition (see section 4). The regulations make this information publicly available, and collected information is currently available via the Internet.

Massachusetts promulgated regulations in August 1997 requiring manufacturers to report information pertaining to cigarette nicotine yield, including total nicotine in the whole tobacco, percent filter ventilation, puff by puff pH and nicotine smoke yield under machine testing in accordance with protocols established to better reflect human smoking behaviour. Approximately 175 brands (about 75% of the US market) are currently tested. Based on these results, a multiplier has been developed using FTC nicotine yield ratings to predict nicotine yield under the Massachusetts test for the remaining brands.

Texas promulgated regulations in 1998 which mirror those from Massachusetts. Regulations proposed by Canada in June 2000 would require testing of nicotine yield according to two smoking machine protocols—both the FTC/ISO standard as well as the British Columbia "intense" condition—as well as pH and puff count, for all brands sold. In addition, all product testing and research activity conducted by manufacturers over the past year must be reported on an annual basis, including research on product modifications and the manner in which products are used by consumers.

Massachusetts has proposed amendments to its nicotine reporting regulations requiring more detailed reporting of cigarette design features that affect nicotine yield. These include such features as moisture content, paper porosity, burn rate, circumference, density and weight of tobacco.

Human typography/nicotine intake

Massachusetts has proposed amendments to its nicotine reporting regulations requiring two additional tests for each of 15 brands selected as a representative sample: human smoking typography (smoking behaviours that may affect nicotine intake) and nicotine intake. This testing would involve having 65 subjects who have smoked a particular brand for at least six months tested on a smoking machine to determine how the brand is smoked in a "real world" setting. Subjects also would submit urine samples over 24 hours that would be tested for metabolites of nicotine.

Smoke constituents and toxicity testing

The United States receives voluntary data on carbon monoxide and "tar" yields from manufacturers using a smoking-machine based standard developed by the FTC. These data serve as a relative measure of nicotine yield but do not reliably measure human intake. No data is collected on individual smoke constituents.

The UK routinely tests cigarettes for tar and carbon monoxide yields as outlined above. The proposed EU Directive as currently drafted, requires a machine-tested limit of 10 mg tar per cigarette and 10m carbon monoxide per cigarette by the end of 2003, although it requests in the first report following implementation of the Directive, *inter alia*, 'Methodologies for more realistically assessing and regulating toxic exposure and harm'. The LGC in the UK has completed several surveys for the government of individual chemicals and entities occurring in tobacco smoke.

The province of British Columbia passed smoke constituent requirements in 1998 with protocols for testing and annual reporting of 44 identified mainstream and sidestream smoke constituents for all brands sold. The testing is based on a smoking machine protocol using both standard FTC/ISO and "intense" conditions. The regulations make this information publicly available, and it is currently available via the Internet.

Regulations proposed by Canada in June 2000 would require testing of the same 44 mainstream and sidestream constituents for all tobacco products. In addition, all product testing and research activity conducted by manufacturers over the past year must be reported on an annual basis, including research on toxicity and health effects.

Massachusetts proposed regulations in August of 1998 requiring manufacturers to test a sample of 75 cigarette brands for 44 known or probable toxins in mainstream and sidestream smoke. In February of 1999, tobacco manufacturers requested a delay in promulgation of the regulations while they conducted an inter-company benchmarking study of 26 brands (about 33% of the US market). Results of the study were submitted to the Department in March of 2000 and are publicly available.

Proposed amendments to Massachusetts' smoke constituent regulations would require manufacturers to test a representative sample of 15 brands for the metabolites of two major carcinogens: NNAL (a metabolite of NNK) as well as metabolites of benzene. Status of these regulations is under discussion with manufacturers.

Table 3: Summary of international tobacco product regulation

	Additive/ ingredient disclosure	Nicotine testing/ product characterization	Smoke constituent/ toxicity testing
Australia	Voluntary disclosure Composite	None	None
British Columbia	Regulatory authority Brand specific Publicly available	Regulatory authority Standard/ intense machine test Smoke pH and filter efficiency Publicly available	Regulatory authority Standard/ intense machine test 44 smoke constituents Mainstream/sidestream Publicly available
Canada	Regulatory authority <i>Proposed/ not yet enacted: Brand specific Ban/ limit substances</i>	Regulatory authority <i>Proposed/ not yet enacted: Standard/ intense machine Smoke pH, filter efficiency Internal tests reported Publicly available</i>	Regulatory authority <i>Proposed/ not yet enacted: Standard/ intense machine 44 smoke constituents Mainstream/sidestream Internal tests reported Publicly available</i>
Germany	Ban/limit substances	None	None
Ireland	Regulatory authority Brand specific Publicly available	None	None
Massachusetts	Regulatory authority Blocked in federal court Brand specific Limited public availability	Regulatory authority "Massachusetts" machine test Unburnt nicotine, pH, filter Publicly available <i>Proposed/ not yet enacted: Cigarette design features Human smoker typography Human exposure testing</i>	Voluntary agreement Machine test of sample brands 44 smoke constituents Mainstream/sidestream Publicly available <i>Proposed/ not yet enacted: Human smoker typography Human exposure testing</i>
New Zealand	Voluntary disclosure Composite Maximum levels reported	None	None
Texas	Regulatory authority Brand specific No public availability	Regulatory authority "Massachusetts" machine test Unburnt nicotine, pH, filter Publicly available	None
Thailand	Regulatory authority Brand specific Limited public availability	None	None
United Kingdom	Ban/limit substances	None	None
United States	Voluntary disclosure Composite Limited public availability	Voluntary testing Standard smoking machine Publicly available	Voluntary testing Standard smoking machine Tar and CO Publicly available

21. The European Union directive on tobacco products

Background

The European Commission has announced that it is considering legislation concerning cigarette tar and nicotine yields, additives, and labelling. Its proposal is expected to be based largely on the recommendations of the high-level cancer experts committee of the "Europe Against Cancer" programme of the European Commission made in October 1996. On 16 November 1999, The Commission of the European Communities adopted a Directive for the consolidation, harmonization and approximation of the laws, regulations or administrative provisions of the Member States regarding the manufacture, presentation and sale of tobacco products. The proposal substitutes three existing directives (89/622/EEC; 90/239/EEC and 92/41/EEC) and aims at updating existing provisions in the light of new developments. It still requires the approval of the Member States and the European Parliament.

It is likely that the new Directive (which has to be introduced into national law in all 15 EU Member States by September 2002 with most of it in effect within two years) would contain provisions on: maximum yields; warning labels; warning texts; use of colour photos or graphics; reporting requirements; misleading descriptors; traceability with batch numbers; and monitoring mechanisms.

Adoption of the Directive

Siem (2000) and Piha (2000) describe the implications of the action taken by The Commission of the European Communities.

The proposed EU law would reduce, by 2004, the maximum tar level of cigarettes from 12 to 10 mg per cigarette. The maximum amount of nicotine is 1 mg of nicotine and 10 mg of carbon monoxide per cigarette. It calls for the elimination by EU Member States of the use of terms such as "light" and "mild", which are considered to be misleading descriptions of some tobacco products. Tar, nicotine and monoxide yields are to be measured on the basis of ISO methods, but Member States may also require tobacco manufacturers or importers to carry out any other test as may be laid down by the appropriate national authorities in order to assess the yields and other substances produced by their tobacco products on a brand-for-brand basis. The proposal includes detailed printing requirements for health warnings. In addition, the Commission proposes to increase the size of the warnings and to revise their content. There would be two warnings: a general warning "Smoking kills" and an additional message, occupying at least 25% of the most visible surfaces, if a country has one official language.

The Directive would also force cigarette manufacturers to declare non-tobacco ingredients, including additives, in their products. Article 7 on Further Product Information tackles this issue, stating:

“Not later than 31 December 2003, Member States shall require all manufacturers and importers to submit to them a list of all non-tobacco ingredients and constituents, including additives and quantities thereof, used in the manufacture of their tobacco products by brand. The list shall be accompanied by a statement setting out the reasons for the inclusion of

such ingredients and constituents in their tobacco product. Member States shall also require manufacturers and importers to provide toxicological data on these non-tobacco ingredients and constituents in burnt and unburned form, and to demonstrate that the said ingredients are safe for the health of the consumer when used as intended in their tobacco products....”

Piha (2000), notes that the European Union has opted for a range of measures of which the directives on tobacco products represent simply the legislative aspect. With the caveat that such resolutions and recommendations by Community institutions are expressions of political will with variable impact in practice he also draws attention to the useful enabling role of Community funding in running Union-wide projects. These projects are very important for sharing information and experience as well as for initiating practical action.

The Council of Ministers, in November 1999, urged the development of an overall strategy which included the following elements:

- an effective system to monitor tobacco consumption, tobacco policies and their effects throughout the Community as well as the implementation of Community legislation,
- a coordinated range of Community instruments and activities in all relevant policy areas,
- strengthened cooperation between Member States, and
- international cooperation, in particular with the World Health Organization.

22. The tobacco industry’s resistance

International collaboration

- A global team of experts, facilitated by WHO is needed to help countries deal with industry arguments and development of tobacco product regulations.

(Recommendations from the Oslo conference)

One persistent element common to both Canadian and US attempts to regulate the tobacco industry is that, regardless of the action taken, the industry has challenged the government's action in court, thereby delaying, and sometimes preventing, implementation for many years. Consequently, regulation in both countries has taken significant periods of time to accomplish. As a result, federal regulators in both countries have increasingly premised their regulatory action on extraordinarily complete research and investigations in order to increase their chances of prevailing in court (Wilkenfeld, 2000).

Tobacco industry arguments against regulation typically stress their concerns that regulation could interfere with trade secrets and intellectual property rights, and could create discrimination against international manufacturers. For example, they argue that

by imposing restrictions or requiring disclosure of product ingredients it may become possible for rival manufacturers to create identical competing brands using the formula used to manufacture their brands.

Chitanondh (2000) describes how each step of the Thai Tobacco Product Control Act, but especially Section 11 on ingredient disclosure, met resistance from the tobacco industry. The requirement for brand-specific disclosure of ingredients resulted in strenuous lobbying of politicians, regional organizations and governments of the major companies. The seven years it took to pass the Ministerial Rules can be attributed in part to the successful lobbying of politicians by foreign companies in order to hold up the Act's passage. Even after the law was enacted, the tobacco industry tried to persuade the Ministry of Health to allow a collective list of ingredients rather than disclosure individually by brand. At the next stage, when the draft rule was in the Juridical Council, the Prime Minister, the Ministries of Foreign Affairs and Commerce were petitioned. When the final deadline came the industry tried, unsuccessfully, to negotiate with the Prime Minister and his party during an official visit to the United States at the time of Thailand's economic crash.

Thailand's case provides useful lessons to be learned about the difficulties to be faced and overcome in passing such a law, especially in developing countries. However, exceptionally strong advocates supported by international bodies can together stand up to the formidable tobacco industry.

Table 4: General tobacco industry tactics

Tactic	Goal
Intelligence gathering	To monitor opponents and social trends to anticipate future challenges
Public relations	To mould public opinion using the media to promote pro-industry positions
Political funding	To use campaign contributions to win votes and legislative favours from politicians
Lobbying	To make deals and influence the political process
Consultancy programme	To produce "independent" experts critical of tobacco control measures
"Smokers Rights" Groups	To create the impression of spontaneous, grassroots public support
Creating alliances	To mobilize farmers, retailers, advertising agencies to influence legislation
Intimidation	To use legal and economic power to harass and frighten opponents
Philanthropy	To buy friends and social respectability – from arts, sports and cultural groups
Litigation	To challenge law
Bribery	To corrupt the political system, allow the industry to by-pass laws
Smuggling	To undermine tobacco excise tax policies and increase profits
International treaties	To use trade agreements to force entry into closed markets

Source: Saloojee (2000)

Yach (2000) comments on the role of the tobacco industry that it is important to understand the structure, functioning and behaviour of the tobacco industry to be able to develop effective policies and actions. Recent information made public through court action has illustrated the role of the "front group" in the construction of risk in the mind of policy-makers and the public. Such groups support the views that the risks of tobacco use equate with other risks associated with daily living and that moderation is the key to managing all these risks.

ARISE (Associates for Research into the Science of Enjoyment) is an example of an industry group that has played a key role in promoting these ideas. Their meetings have been funded by Philip Morris, Rothmans, BAT, Nestle and the Coffee Science Information Center, among others. According to a Philip Morris document, the concept was to create a vehicle to offset puritanical zealots who diminish the quality of life.

Yach (2000) observes that it is important to be aware of the speed of change in the structure of the tobacco industry, in their development of new products and their desire and search for new respectability. Tobacco product modification is only one part of a comprehensive approach to tobacco control. The issue of product regulation has a considerable direct impact on the tobacco and possibly the pharmaceutical industries. Real progress will require even greater access to both industries' knowledge about nicotine and other constituents of tobacco products, how they are best measured and what the public health consequences of varying the composition of ingredients might have.

During the conference in Oslo, the working groups discussed the several, well-documented, approaches used by the tobacco industry to oppose tobacco control in general. All such approaches involve the tobacco industry spending large amounts of money and exerting its influence through multiple channels. Specific methods used include: lobbying; use of third parties; questioning the science and raising public doubt about health and addiction effects; warning governments about the cost of regulation; use of scientists with unproven ideas; dissemination and repackaging of legislative/regulatory problems from other countries; use of "divide and conquer" tactics across bureaucracies, countries and public health groups; legal and media attacks on regulatory agencies; as well as constitutional challenges.

In developing countries, weaker knowledge about health impacts, weak regulatory and scientific capacity and greater vulnerability of the media and politicians to the power of the industry meant have that industry strategies have often been more intense and successful.

When the tobacco industry cannot prevent new laws and regulations, it finds ways, for example through voluntary agreements with governments and scientists, to ensure that regulations favour their interests.

Inter alia, the working groups at the Oslo Conference proposed proactive global responses for dealing with tobacco industry resistance:

1. A global team of experts is needed to help countries deal with industry arguments.

2. An international alert and response system linking media and experts should rapidly mount public responses to industry claims and critique. More effective use of the media should aim to reframe the debate away from tobacco industry claims.
3. Engagement with the tobacco industry should be discussed with the proposed expert group (see the full recommendations of the meeting, Annex 1) and aim to achieve public health objectives. In the process of engagement the burden of proof for demonstration of less harm should be placed on the industry.

23. The regulation of pharmaceuticals

Regulatory approaches applied to pharmaceutical products to treat tobacco dependence are so far out of balance with tobacco product regulation that innovative treatment development tends to be impeded and not fostered (Page, 1998; Slade and Henningfield, 1998; Henningfield and Slade, 1998; Warner et al., 1998). For example, Bates et al. (1999) describe the difficulties faced by pharmaceutical companies wishing to add flavourings to nicotine gum. In such an instance the manufacturer has to conduct studies that may take several years and millions of dollars to satisfy the pharmaceutical regulator that the additive does not:

- interfere with the efficacy or safety of the product;
- increase the abuse potential of the product;
- encourage a different pattern of use (indication) for the product;
- alter the drug delivery characteristics of the product.

Such demands are considered reasonable from the perspective of drug development in general but stand in striking contrast to the relatively unencumbered ability of tobacco companies to alter the flavour and dosing characteristics of existing products without being held accountable for whether the changes alter toxicity or addictiveness. It is not suggested that standards for medicines be reduced, but that consideration be given to raising the standards for the development and manufacture of tobacco products (Warner et al., 1998; Bates et al., 1999).

The tobacco industry itself has made this link (in the *Research planning memorandum on the nature of the tobacco business and the crucial role of nicotine therein*, quoted by Professor Channing Robertson in his expert court report to the State of Minnesota).

" In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry. Tobacco products, uniquely, contain and deliver nicotine, a potent drug with a variety of physiological effects."

"Our Industry, is then based upon design, manufacture and sale of attractive dosage forms of nicotine, and our Company's position in our Industry is determined by our ability to produce dosage forms of nicotine which have more overall value, tangible or intangible, to the consumer than those of our competitors."

Annex 1

Recommendations of the International Conference: Advancing knowledge on regulating tobacco products 9-11 February 2000, Oslo, Norway.

These recommendations were developed by representatives from 20 countries from all WHO regions. While some recommendations suggest the need for additional research, countries are urged to act rapidly on the basis of a large body of existing knowledge. Exposure reduction policies must aim to achieve meaningful reductions in harm while avoiding decreased quitting or increased initiation.

1. All countries need to introduce comprehensive tobacco control policies and strategies along the lines recommended by the World Health Organization.

These should be adequately financed and managed by institutions with a clear mandate for tobacco control. The emphases of policies should be to prevent initiation, increase the quit rate, and eliminate exposure to passive smoking. Within the context of a comprehensive policy, product regulation should be given explicit and urgent attention in order to reduce the health impact of tobacco use among smokers. Product regulation needs to apply to all forms of tobacco and nicotine products.

2. Governments are urged, individually or at a regional level, to take the following actions:

- Evaluate and implement the most effective ways to achieve a unified regulatory framework for nicotine delivery products, including tobacco products, products for treating tobacco dependence, and novel nicotine delivery devices, whether or not these are based on tobacco products. Key terms of reference are to
 - Maintain a primary focus on harm reduction
 - Develop better measurement of the constituents and impact of tobacco products with the aim of substantially reducing their toxicity
 - Promote international comparability
 - Implement a pre-market approval and post marketing surveillance system.
- Ban the use of misleading terms such as “light”, “mild”, and other words or imagery (including certain brand names) which have the aim or effect of implying a reduced health risk attributable to low tar or nicotine measurements on tobacco products and in advertising/promotional material.
- Remove tar and nicotine measures derived from ISO/FTC methods from packages. Warning labels should emphasize the addictiveness of tobacco products.
- Require tobacco manufacturers to disclose the contents, purpose and effects of constituents in all their products at regular intervals.

- Discontinue harm reduction strategies based on naïve interpretation of tar and nicotine yield measurements. This means abandoning the strategy of seeking lower nominal tar yields and instead, finding approaches that genuinely reduce harm to nicotine users.
- Give urgent priority to studying the implications for harm reduction of reducing levels of nicotine and other possible addictive constituents in tobacco products over time.
- Give greater attention to increasing public access to the range of effective methods of treating tobacco dependence, including nicotine replacement therapies (NRTs), and to encourage development and marketing of additional effective products.
- Develop and implement a comprehensive long-term communication program to accompany all the above actions that stresses that there is no safe cigarette and that nicotine addiction is a major public health concern.

3. Research is needed to advance further progress.

- Global tobacco control research needs to be better supported. Within such a plan, emphasis should be given to research to support product regulation within developing countries. Existing research institutions should work together to implement such an approach.
- In order to reduce the addictiveness of tobacco products, research is urgently needed to evaluate the benefits and/or hazards of reducing nicotine and other possible addictive constituents in tobacco products over time. Particular attention should be given in research to determining whether a threshold exists for addictiveness.
- Develop better measures, including biomarkers, to assess the health impact of the use of “less harmful” tobacco products in order to drive future regulatory actions. For exposure, a composite measure of toxicity is needed. In addition the unintended consequences of such products should be investigated.
- Expand behavioural research on how “cigarettes affect smokers” and how the population (of smokers and nonsmokers) responds to claims about new products and to new packaging rules.
- Determine whether regulators should encourage the development of substantially less harmful nicotine delivery devices.
- Determine whether countries should forbid addition of all new additives and explicitly address the possibility of reducing the use of additives that make tobacco products more attractive and/or taste better.
- Evaluate how regulatory approaches developed for cigarettes could be adapted to cover all forms of tobacco use.

4. International collaboration

- Establish under WHO authority, an international expert group on tobacco and nicotine delivery devices. It needs to be well-financed and have access to the best technical expertise available. It would guide international policy development

with respect to product regulation and could facilitate access to scientific information needed for tobacco regulation. Its first task would be to study the recommendations of the Oslo meeting and recent scientific reports on the topic and make recommendations for action to WHO.

- A global team of experts, facilitated by WHO is needed to help countries deal with industry arguments and development of tobacco product regulations.
- Ensure that issues related to product regulation are incorporated into the Framework Convention for Tobacco Control and related protocols.
- Communicate the outcome of this meeting to all appropriate national, regional and international agencies in an attempt to foster uniform approaches.

Annex 2

Conference on the Regulation of Tobacco Products

Conclusions

18 October 1999, Helsinki

Conclusions. The Helsinki meeting addressed both tobacco product regulation (18, October) and treatment regulation (19, October). The present summary provides some of the main conclusions of the exceedingly rich and thoughtful discussion of issues provided by the presenters and other participants on the topic of tobacco product regulation. Following the first conclusion, which appeared absolutely fundamental to the participants, the order of the remaining conclusions does not necessarily reflect their priority.

- (1) Tobacco control requires transnational strategies.** There was overwhelming consensus that tobacco control efforts must be transnational. It was observed that virtually every level of the regulatory process, as well as ultimate regulations require such an approach. This includes the need to share data from research and analysis of tobacco industry documents to the need to regulate the toxin delivery limits for cigarettes. This conclusion was also supported by the facts that the tobacco industry itself is a consummate transnational industry in which a small number of companies dominate much of the global tobacco market and account for many of the innovative approaches to spread the tobacco epidemic across borders. Several examples were discussed in which tobacco control strategies adopted in one country were undermined by inconsistencies in a neighboring country.
- (2) Cigarettes are highly addictive and toxic nicotine delivery devices and they warrant regulation of physical characteristics and marketing that is more consistent with their health effects.** Cigarettes are highly engineered nicotine delivery devices in which the expressed intent of the manufacturers (in their previously secret documents) is to provide sufficient doses of nicotine to consumers to derive pharmacological effects including mood enhancement, body weight, and dependence. However, they are presently exempted from the regulatory controls, including stronger warning labels that could enable consumers to make informed choices. It was recognized that the addictive effects of tobacco delivered nicotine might serve as part of the basis for exerting regulatory authority. Therefore, appropriate control of nicotine in tobacco products is warranted, however, this does not necessarily imply the elimination of nicotine from tobacco products.
- (3) The harms caused by cigarettes go well beyond the adverse effects upon their users, and should be subject to consumer protection laws and regulations that is more consistent with the dangers they pose.** Cigarettes are consumer products whose physical nature results in their producing a broad range of undesirable effects pertaining to health, safety (e.g., they are the most common cause of household fires in many countries), and pollution of the air, water, and land (via discarded cigarette butts and matches). However, they are presently excluded from many basic consumer

product protection laws which might be utilized to reduce risks such as their ability to cause fires.

- (4) Consumers should be provided information regarding the dosages of tar, nicotine, carbon monoxide, and other substances to which they are actually exposed by smoking cigarettes.** The levels of tar, nicotine, and other substances that consumers can obtain by smoking cigarettes bear little relation to the levels that are labelled and/or advertised by their marketers. Yet these substances can have strong toxic and addictive effects. This implies correcting the deficiencies in the current ISO/FTC methods of cigarette testing, and then adequately communicating dosage information to consumers. It was observed that this conclusion is generally consistent with the proposed European Commission draft directive to set limits on tar and nicotine levels because such a directive implies the ability to accurately measure and communicate such information.
- (5) The use and effects of additives in cigarettes needs to be assessed with consideration given to banning the use of additives not deemed warranted by health authorities.** Scientific data from non tobacco industry researchers, as well as insights from tobacco industry documents made it clear that there is little evidence for safety of cigarette additives when they are burned and that some additives may actually increase the toxic and addictive effects of cigarettes beyond that of tobacco cigarettes without additives. One of the more insidious means by which additives can adversely affect public health that was of concern was the reference to additives in tobacco industry documents as a means to decrease the throat irritation and displeasing odors and thereby enable increased exposure. An additional problem is that it is the tobacco companies themselves which presently determine whether various substances used in the manufacture of cigarettes are considered “additives”, “flavorings”, or “extracts”.
- (6) Cigarettes advertised as “light” or “low tar and nicotine” have not been shown to provide health benefits implied by the claims and therefore such claims are unacceptable.** Available data indicates that cigarettes labelled, advertised, or branded, with descriptors implying reduced tar and nicotine (e.g., “light”, “low”, “reduced”) have not been demonstrated to be of health benefit relative to the so-called “full-flavor” cigarettes on the present market. Despite the conclusion that the risk of many smoking associated diseases is related to the amount of tobacco toxin exposure, there is now sufficient evidence to conclude that the tobacco industry has designed its cigarettes to yield lower levels according to the ISO and FTC smoking machine tests while ensuring that even “light” cigarettes can readily provide dosages of tar and nicotine comparable to those provided by “full-flavor” cigarettes. Furthermore, tobacco industry documents confirm that an intent of this strategy was to undermine cessation activity. Therefore tobacco companies should not be permitted to make any such claims that imply health benefits. Related to this conclusion was the expression of concern that if such claims were ever to be sufficiently supported by data to warrant consideration, great care would need to be given before approving such claims to minimize the risk that such a claim would have the unintended consequence of undermining prevention and cessation efforts.

- (7) Tobacco industry documents need to be systematically reviewed with findings shared transnationally.** It was quite evident that the previously secret tobacco industry documents contain a wealth of information relevant to product design, intent, and constituents, as well as insights into marketing approaches to various target populations within and across countries, (e.g., women and adolescents, populations in developing countries). It was further concluded that such information would be invaluable in expediting efforts to reverse trends in tobacco-caused disease through prevention, treatment and product regulation.
- (8) Tobacco product regulation must occur in the broader tobacco control context such as being considered in the WHO Framework Convention process.** It was recognized that controlling tobacco caused disease requires a broad range of efforts including economic disincentives toward smoking as concluded by the World Bank in 1999, treatment access provisions as discussed in the Conference on the Regulation of Tobacco Dependence Treatment Products (19, October 1999), transnational control of trade and mitigation of smuggling, and accelerated efforts to prevent youth from taking up smoking. The process of tobacco product regulation must move forward with consideration given to these and other issues to be considered in the WHO Framework Convention proposals so that these various aspects of tobacco control are harmonized so as to not undermine one another.
- (9) It was concluded that the proposed European Commission Directive to restrict tar and nicotine levels and to prohibit “light” cigarette types of claims is consistent with the conclusions of this conference.** Ongoing efforts to develop a European Commission Directive to regulate tar and nicotine delivery of cigarettes was viewed as a positive first step and one that is consistent with the goals and approaches endorsed in the present conference. Subsequent actions of the European Commission would be expected to similarly address deficiencies in the system for testing and communicating levels of tar and nicotine and other constituents, as was concluded to be important in this conference. The European Commission should be encouraged to include a regular review process as discussed in conclusion 12 to ensure that modifications are made as scientific progress and understandings evolve.
- (10) Various national and regional tobacco control approaches were viewed as positive developments but the need to make efforts to ensure better transnational communication and coordination was recognized.** The fact that a variety of national and regional efforts to regulate tobacco products (i.e., the approach of the U.S. Food and Drug Administration, Health Canada, and the European Union) were viewed as constructive and necessary as each is adopting approaches that appear best suited to the particular nation or region, and as there is no certainty as to which of the various approaches will actually be most effective in the reduction of tobacco-associated disease. Nonetheless, the need for continued transnational sharing of communications among regions as was occurring at this conference was concluded to be vital to the global effort to reduce tobacco caused death and disease.

- (11) The regulatory process must nurture a larger base of experts to be able to cope with emerging issues.** It was recognized that a severe limitation of the potential of the WHO to regulate tobacco is the ready availability of expert assistance. Although, as demonstrated by this conference, expertise is sufficient to launch and provide guidance to a systematic regulatory process, many issues are present (e.g., developing more accurate measures of cigarette tar and nicotine deliveries) and more issues emerging (e.g., unraveling the effects of additives and determining appropriate restrictions) that will require a broader base of experts to carry the process of regulation into the future. As expertise is cultivated, it is apparent that to the greatest extent possible, efforts must be made to accelerate the development expertise among the diverse populations which have been targeted by the tobacco industry and in whom tobacco use is prevalent (e.g., women and the diverse ethnic and racial populations of the European Region).
- (12) The regulatory process must be guided by the best available science and the effects tracked so as to maximize health benefits, minimize unintended consequences, and to thereby foster self-correction.** It was recognized that there are limitations to the scientific base for guidance in many key areas (the function and health effects of various additives, and the dimensions along which to measure cigarette dosing characteristics). Similarly, it was recognized that there are differences of opinion as to specific aspects of potential cigarette regulation (e.g., whether nicotine levels of cigarettes should be maintained, increased, or eliminated over time). Nonetheless, there was concurrence that if regulatory strategies were developed on the basis of the best available science, and were continuously monitored and guided by emerging science, overall progress should be ensured towards reduction of tobacco-associated diseases.

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