

WHO Library Cataloguing-in-Publication Data

WHO Study Group on Tobacco Product Regulation.

Guiding principles for the development of tobacco product research and testing capacity and proposed protocols for the initiation of tobacco product testing : recommendation 6 / WHO Study Group on Tobacco Product Regulation.

1.Tobacco - chemistry 2.Tobacco industry - legislation 3.Laboratories - standards
4.Research - standards 5.Product packaging - standards 6.Treaties 7.Guidelines I. Title.

ISBN 92 4 159208 7

(LC/NLM classification: HD 9130.6)

© **World Health Organization 2004**

All rights reserved. Publications of the World Health Organization can be obtained from Marketing and Dissemination, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 2476; fax: +41 22 791 4857; email: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to Publications, at the above address (fax: +41 22 791 4806; email: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

Printed by the WHO Document Production Services, Geneva, Switzerland.

Preface

In November 2003, the WHO Director-General formalized the Scientific Advisory Committee on Tobacco Product Regulation (SACTob) by changing its status to that of a study group. Following the status change, the SACTob became the "WHO Study Group on Tobacco Product Regulation" (TobReg). It is composed of national and international scientific experts on product regulation, tobacco dependence treatment, and laboratory analysis of tobacco ingredients and emissions. Its work is based on cutting edge research on tobacco product issues. It conducts research in order to fill regulatory gaps in tobacco control. As a formalized entity of WHO, TobReg reports to the Executive Board through the Director-General in order to draw the Member States' attention to WHO's efforts in tobacco product regulation. This recommendation was approved and adopted by TobReg during its first meeting on 26 to 28 October 2004 in Montebello, Canada.

WHO Study Group on Tobacco Product Regulation

Recommendation 1: Guiding Principles for the Development of Tobacco Product Research and Testing Capacity and Proposed Protocols for the Initiation of Tobacco Product Testing

Background and purpose

This recommendation is the first formulated by the WHO Study Group on Tobacco Product Regulation (TobReg).¹ The purpose of this recommendation is to promulgate the principles that should guide the development of the laboratory capacity required to enable implementation of Articles 9, 10 and 11 of the WHO Framework Convention on Tobacco Control and the initiation of tobacco product testing. Such laboratory capacity provides government regulatory authorities with the means to guide and validate tobacco product testing, including any testing that may be carried out by the tobacco industry itself. The considerations and principles discussed in this recommendation are intended to provide guidance for establishing laboratory capacity that meets the highest standards of excellence, transparency, reliability and credibility.²

The WHO Framework Convention on Tobacco Control includes three articles that lay the groundwork for the regulation of the contents, disclosures, and packaging and labelling of tobacco products (*I*). They are:

- Article 9: Regulation of the contents of tobacco products
- Article 10: Regulation of tobacco product disclosures
- Article 11: Packaging and labelling of tobacco products.

Article 9: Regulation of the contents of tobacco products. The Conference of the Parties, in consultation with competent international bodies, shall propose guidelines for testing and measuring the contents and emissions of tobacco products, and for the regulation of these contents and emissions. Each Party shall, where approved by competent national authorities, adopt and implement effective legislative, executive and administrative or other measures for such testing and measuring, and for such regulation.

¹ For details of the five recommendations formulated by the former WHO Scientific Advisory Committee on Tobacco Product Regulation (SACTob), see references 12–16.

² The various regulatory strategies and considerations discussed in the publications listed in references 2–10 provide useful background information for the present recommendation. The reports and recommendations previously published by WHO and the publications of other institutions that are listed in references 11–20 form the basis of the present recommendation and therefore make essential background reading.

Article 10: Regulation of tobacco product disclosures. Each Party shall, in accordance with its national law, adopt and implement effective legislative, executive, administrative or other measures requiring manufacturers and importers of tobacco products to disclose to governmental authorities information about the contents and emissions of tobacco products. Each Party shall further adopt and implement effective measures for public disclosure of information about the toxic constituents of the tobacco products and the emissions that they may produce.

Article 11: Packaging and labelling of tobacco products

1. Each Party shall, within a period of three years after entry into force of this Convention for that Party, adopt and implement, in accordance with its national law, effective measures to ensure that:
 - (a) tobacco product packaging and labelling do not promote a tobacco product by any means that are false, misleading, deceptive or likely to create an erroneous impression about its characteristics, health effects, hazards or emissions, including any term, descriptor, trademark, figurative or any other sign that directly or indirectly creates the false impression that a particular tobacco product is less harmful than other tobacco products. These may include terms such as “low tar”, “light”, “ultra-light”, or “mild”; and
 - (b) each unit packet and package of tobacco products and any outside packaging and labelling of such products also carry health warnings describing the harmful effects of tobacco use, and may include other appropriate messages. These warnings and messages:
 - (i) shall be approved by the competent national authority,
 - (ii) shall be rotating,
 - (iii) shall be large, clear, visible and legible,
 - (iv) should be 50% or more of the principal display areas but shall be no less than 30% of the principal display areas,
 - (v) may be in the form of or include pictures or pictograms.
2. Each unit packet and package of tobacco products and any outside packaging and labelling of such products shall, in addition to the warnings specified in paragraph 1(b) of this Article, contain information on relevant constituents and emissions of tobacco products as defined by national authorities.
3. Each Party shall require that the warnings and other textual information specified in paragraphs 1(b) and paragraph 2 of this Article will appear on each unit packet and package of tobacco products and any outside packaging and labelling of such products in its principal language or languages.
4. For the purposes of this Article, the term “outside packaging and labelling” in relation to tobacco products applies to any packaging and labelling used in the retail sale of the product.

These three articles are the result of the consensus view that such regulation would serve public health goals by providing a meaningful regulatory oversight of tobacco products and related communications made to consumers. The articles imply the need for an objective, science-based approach to the implementation of the provisions of the Framework Convention.

Unfortunately, as indicated in the recommendations and conclusions contained in the reports of the Scientific Advisory Committee on Tobacco Product Regulation (see references 12–16), the current methods for product testing adopted by the International Organization for Standardization (ISO) and the United States Federal Trade Commission (FTC) are inadequate since they fail to provide the appropriate scientific basis for tobacco product regulation. New laboratory capacity is needed and guidance in initiating the testing of existing and anticipated tobacco products is a critical factor in advancing the regulatory process.

Laboratory capacity: research and testing

Laboratory capacity refers to the physical and human resources needed to conduct research, develop standards for product performance, develop product testing methods, and conduct product testing. A report by the Institute of Medicine on tobacco harm reduction (18) summarizes the science base for testing the physical attributes of tobacco products that contribute to addiction, morbidity, and premature mortality. It is useful to distinguish the two main types of laboratory capacity required to enable implementation of Articles 9 to 11 of the Framework Convention: research and testing.

Research

The main goals of research are to understand better the nature of tobacco products, how they work, their effects, and how they might be modified to alter their effects (e.g., by new ingredients and designs). This research can include molecular, *in vitro*, animal, and human research, addressing topics such as the relationship between tobacco-specific nitrosamines (TSNAs) and lung cancer risk, the relationships between ingredients and addiction risk, and the relationships between particle size and lung retention of cigarette smoke toxicants. Research on human patterns of use and how they interact with product characteristics is also essential.

Testing

The repetitive examination and evaluation of products according to standardized methods to assess product performance is generally referred to as testing. Testing can occur at several stages. To aid the regulatory process, it is useful to test products according to a standardized protocol in order to characterize their delivery of substances such as carbon monoxide, nicotine, and nitrosamines. Annex 1 lists the standardized methods for testing tobacco products.

Laboratory research and testing must be coordinated

Although research, testing and performance standards may be distinguished for conceptual and organizational purposes, they are not mutually exclusive; indeed, they must be interactive. Performance standards require the testing of a broad range of product characteristics, conducting research to determine which toxicity-reducing goals are feasible, and developing standardized testing protocols. This process will continually evolve and rapidly expand to address the challenges posed by existing products. As the number of new tobacco products

increases, it is reasonable to assume that the need to develop new performance standards will similarly increase. Research and testing need to include assays of the physical characteristics, the chemical composition and the performance of products, *in vitro* and *in vivo* toxicology testing, and the assessment of human use patterns to determine the interactions between behaviour and product characteristics as well as actual human exposures.

Tobacco product diversity

Tobacco product diversity increases the range of challenges; thus it is essential to consider both existing products and emerging product alterations in establishing laboratory capacity. The various forms and methods of use of tobacco products include orally or nasally administered products (e.g., snuff), smoked cigarettes, which are designed to maximize exposure, and cigars, in the use of which inhalation of smoke is not generally needed for sufficient nicotine absorption (11, 18, 21, 22). The major categories of products include cigarettes as well as extensively modified cigarettes, cigars, bidis, and smokeless tobacco products, including various forms of snuff, chewing tobacco and Swedish snus (23, 24) (see Annex 2).

New tobacco products

In addition to a diverse array of conventional tobacco products, new product types and tobacco product substitutes continue to proliferate rapidly (25). The development and marketing of new tobacco products by the tobacco industry appear to be in response to the health concerns associated with conventional products. Moreover, the range of new products is expected to expand as the pressures for reduced toxicity implicit in the terms of the Framework Convention increase. New products marketed in the last several years include an electronically heated and computer-controlled cigarette substitute, cigarettes containing a carbon heating element, a fibreglass-packed cigarette substitute, cigarettes that are claimed to contain reduced carcinogens and to be nicotine-free, tobacco lozenges, and tobacco patches.

Non-tobacco nicotine products (medicines)

This recommendation does not address non-tobacco nicotine products (e.g., nicotine water and lollipops) or medicines (e.g., smoking cessation medicines) as it is assumed that drug regulatory authorities will continue to regulate such products. The current regulation of medicinal nicotine products is appropriately stringent and consistent with that of other drug products, whereas tobacco products are regulated much less rigorously (3, 26, 27). It is expected that the implementation of the Framework Convention will narrow the regulatory gap between tobacco products and pharmaceutical products by increasing the regulatory oversight of tobacco products. In some countries, the same agency holds regulatory authority for both tobacco and drug products (e.g., Health Canada in Canada and the National Agency for Sanitary Surveillance (ANVISA) in Brazil) in the interest of ensuring regulatory consistency.

Potential providers of laboratory research and testing

There are a variety of potential providers of laboratory research and testing for tobacco product regulation. No one laboratory possesses the requisite expertise and capacity to meet the extensive research and testing needs of an entire region. Indeed, different institutions are needed for research, performance standard development and testing. For example, academic laboratories have a limited interest in developing performance standards for products and establishing repetitive testing operations, since these activities generate little by way of publishable scientific papers and are less likely to provide a fertile ground for the training of students and the production of dissertations. Conversely, companies wishing to set up contract laboratories for repetitive testing are more interested in high-throughput testing and long-term commitments and would find research less appealing from both a commercial and a management perspective.

Funding the development of laboratory research and testing capacity and operation

It is essential that adequate funding is secured in order to establish and maintain laboratories that conduct the independent and credible research and testing for tobacco product regulation called for in this recommendation. There is little question that simply establishing the capacity for developing performance standards and objective tests could cost a few million US dollars each year, in addition to the several million US dollars that would be required to cover start-up costs. But this cost represents an insignificant fraction of the value of the global tobacco market, which is estimated to be in the region of US\$ 300–400 billion. However, in absolute terms, the cost of developing laboratory capacity and operation represents a significant financial commitment which is not likely to be readily undertaken by individual nations. It may therefore become essential that tobacco companies be required to finance laboratory capacity and testing.

There are many challenges to establishing a funding strategy. For example, in developing approaches for obtaining and distributing funds from the tobacco industry, account needs to be taken of the risk that financing laboratories with funds from industry could compromise the transparency, independence and integrity of those laboratories, especially if the expertise developed by the tobacco industry were needed to establish such laboratories. As the provisions of the Framework Convention imply, international collaboration is crucial in controlling transnational tobacco companies (see in this respect the Conclusions of the Conference on the Regulation of Tobacco Products (Helsinki, 1999), mentioned in reference (17). However, the collection and dissemination of funds from sources other than the tobacco industry in order to serve the development and application of laboratory science worldwide in the interests of global public health also constitute a considerable challenge.

In anticipation of the funding challenges posed by the implementation of the provisions contained in the Framework Convention, paragraph 1 of Article 26 of the Convention states that “the Parties recognize the important role that financial resources play in achieving the objective of this Convention”. Moreover, as discussed during the negotiations on the Framework Convention, it is possible that the Conference of the Parties established under the Convention will adopt a protocol to address the area of tobacco product regulation in more

depth. Furthermore, in line with the premise that the Framework Convention provides a global minimum standard for tobacco control, a Party acting as a sovereign entity can develop and implement legislation to ensure funding of its national tobacco control programme. For example, in Brazil, ANVISA is authorized to collect an annual per brand registration fee from tobacco manufacturers, and a part of this fee funds Brazil's tobacco control laboratory.

Protocols for tobacco product testing

The implementation of Articles 9, 10 and 11 requires the empirical testing of tobacco products using standardized methods. As indicated in other publications (18, 28) and in an earlier recommendation by the Scientific Advisory Committee on Tobacco Product Regulation (SACTob) (12), the methods adopted by the International Organization for Standardization (ISO) and the United States Federal Trade Commission for testing cigarettes are severely flawed, both in terms of the measurements used and the parameters selected. For other tobacco products, relatively little effort has been made to standardize testing protocols, although progress has been made with respect to the standardized testing of cigars (29), smokeless tobacco (19), and bidis (24). The Study Group has taken into consideration the information contained in the sources cited in this document in developing recommendations for testing protocols and in selecting parameters to enable countries to begin implementing the Framework Convention as rapidly as possible. In accordance with the principles provided in this document, the recommended testing protocols are intended to be subject to empirical verification, to be supported by complementary existing and emerging research capacity, and to be adaptable to changing findings and consequences.

Issues and limitations in establishing product testing protocols

There is no single product testing model that is perfectly adaptable to tobacco product testing, although experience in testing foods and drugs and knowledge of tobacco product emissions have provided the basis for the observations and protocols contained in this recommendation. For example, foods are generally labelled on the basis of ingredient content, while drugs are labelled on the basis of either content or estimated systemic delivery. In the case of noncombusted tobacco products, content provides an important starting point, but consideration must also be given to the components emitted from the product under the conditions in which it is actually used (e.g., nicotine delivery in the oral cavity from snuff, as described in an earlier recommendation by SACTob (14). In the case of combusted tobacco products, the complexity of assessment is escalated dramatically because the hundreds of constituents in the unburned product can result in more than 4000 products in the emitted smoke, and many of these newly created products are among the most deadly emissions. The generation of these products involves a complex chemical process that is influenced by factors ranging from the product's ingredients and design to the way in which the product is physically smoked (12, 14, 17). In turn, the health effects can be determined as much by how the product is used as by its emissions (e.g., the pattern and intensity of puffing a cigarette influence the nature and amount of emissions, and the number of years of smoking influences disease risk). Finally, the products themselves are rapidly evolving, as indicated above, and this rapid change means that a testing protocol that is well suited to one product may be inadequate for a modified or novel product.

The core principles that follow have been formulated in an attempt to overcome the limitations inherent in any one product testing method. Regulatory authorities that use product testing data to assist in the implementation of Articles 9, 10 and 11 of the Framework Convention will need to take these limitations into account, as will the research and testing laboratories in their ongoing evaluations of the reliability, validity and appropriateness of the testing methods used. For example, machine testing may offer information on cigarette engineering and the differences in the constituents that result from differences in cigarette design; however, no single machine testing protocol can predict human exposures. Furthermore, differences between emission by-products using any single machine testing protocol will mislead consumers if they are used as estimates of the levels to which they are likely to be exposed through the use of different products (12). It is not practically feasible to test for all of the thousands of constituents in cigarette emissions; however, it is plausible that smoking techniques (whether those practised by a human or those simulated by a machine) will affect the levels measured for various toxicants differently (e.g., some levels might be maximal under intensive smoking conditions while others might be lower under less intensive smoking conditions). Machine testing protocols are not likely to provide a valid basis for predicting health effects or for making claims about health effects because such protocols do not predict how the products will be used by individuals or at the population level. These limitations demonstrate the importance of laboratory research to evaluate patterns of human tobacco use, and of surveillance and epidemiological research to assess population trends and health effects, as reflected in the core principles set out below.

Other limitations will surely emerge; however, the Study Group concludes that, if these constraints are recognized and the following principles are adhered to, the product testing protocols described in this recommendation will provide a scientific basis for initiating implementation of Articles 9, 10 and 11 of the Framework Convention.

Core principles applicable to the assessment and development of laboratory capacity

The principles set out below are aimed at ensuring that research and testing laboratories have the scientific and technical capability required to ensure that their output is credible and consistent with the most rigorous of international standards. These principles apply to the development of laboratory capacity intended to serve regulatory authorities. Laboratories maintained by or serving the tobacco industry may or may not adhere to these principles. It is anticipated that the tobacco industry will continue to conduct its own research and that it may be required to provide product information to regulatory agencies; those agencies may then refer such information to the newly developed research and testing facilities for evaluation.

It is recommended that the following principles be considered in establishing laboratory capacity, whether through contracting mechanisms to supplement the capacity of existing laboratories or the development of new laboratories:

1. The primary goal of establishing laboratory research and testing capacity is to provide a science base for improving public health through tobacco product regulation.

2. Both the research and testing capacities of laboratories must be supported, developed, maintained and adapted as conditions dictate. Research and testing operations have overlapping but distinct missions that must be recognized.
 - a. *Research laboratories*: A major characteristic of research endeavours is the presence of considerable flexibility to pursue the process of scientific discovery and analysis.
 - b. *Testing laboratories*: A major characteristic of testing operations is the capability of adhering to reliable, standardized, high-throughput protocols.
3. At least two distinct sets of issues require expert consideration when addressing the task of coordinating and facilitating the emerging laboratory capacity internationally in order to implement certain provisions of the Framework Convention:
 - a. *Administrative issues*, such as how to develop, fund and contract for laboratory capacity, should be addressed. Mechanisms for funding may need to vary to meet differing needs on a country-specific or region-specific basis.
 - b. *Scientific issues*, such as the prioritization and sequencing of the potential targets of tobacco product testing, both in terms of a product's design and its ingredients, must be addressed and a mechanism for the international sharing of knowledge and coordination of action should be implemented.
4. In view of the vast number of potential targets for study and testing, as well as the need for funding and developing standardized protocols, the priorities for tobacco product testing and a timetable for their implementation, in light of the provisions of the Framework Convention, must be developed in order to guide the sequencing. The setting of such priorities must be driven to the greatest extent possible by the existing science base and public health needs, following their review by appropriate scientific advisory groups in order to provide oversight and guidance. WHO and its advisory committees shall identify the means whereby such priorities are established. In this regard, certain provisions of the Framework Convention call on the Parties to cooperate in the scientific, technical, and legal fields and to provide the related expertise.
5. The vital importance to public health of product regulation necessitates the development of laboratory capacity as quickly as possible. However, the Study Group recognizes the clear need for laboratory research and testing capacity to develop gradually as funding is obtained, as expertise is developed, and as laboratory facilities are established. The pace of development needs to reflect the critical importance of ensuring that the high standards of integrity and quality of the science are preserved.
6. Research and testing laboratories must develop mechanisms to share information, both nationally and internationally, and to collaborate as necessary to ensure that the emerging science base guides the activities of all such laboratories. Mechanisms for sharing methods and results to ensure standardization of testing protocols are vital.

7. Transparency in laboratory operations is necessary in order to inspire confidence among regulatory authorities and the public in the integrity of laboratory operations and findings.
8. The risk to humans, as documented in human studies and studies involving animal models, must largely dictate the overall requirements of laboratory testing; therefore, laboratory capacity must encompass physical, chemical, and biological testing, and must also enable testing procedures to be modified and corrected following the findings of assessments of actual human use.
9. Surveillance of health effects and changes in the patterns of tobacco use in individuals and populations, for example, as a consequence of changes in marketing messages, is essential in order to guide the process and to provide an objective basis for changing and improving the priorities for research and protocols for testing.
10. The laboratories must provide mechanisms for training new scientists and for building the greatly expanded base of physical and human resources and expertise that will be needed in the future in order to fully implement the provisions of the Framework Convention.
11. Funding must be predictable, sustained, and long term, with gradual growth potential provided as needed to enable laboratories to keep pace with emerging product issues and the emergence of broader technical expertise that will enable laboratory expansion. Examples of such funding approaches include the levying of a surcharge on tobacco products, as has been done in other areas of product regulation.
12. Regardless of the funding mechanism adopted, it should ensure that the independence and integrity of research and testing operations are not compromised or inappropriately influenced.
13. These principles do not address the establishment of laboratory capacity for the regulation of non-tobacco nicotine products (smoking cessation medicines). However, it is urged that the regulation of tobacco products and medicines be mutually informed so that there are not inappropriate inconsistencies in regulation.
14. Existing independent laboratories serving the tobacco industry have the potential to provide laboratory capacity, but if they are to be used to serve public health regulation, mechanisms must be put into place to ensure the independence of their operations and the credibility of their findings. Appropriate “firewalls” must be developed in the drawing up of contracts for such laboratories.
15. It is vital that regulatory testing procedures are readily adaptable to meet the testing requirements of altered or new tobacco products, particularly since modified cigarettes and smokeless tobacco products have already led to the problem of the inadequacy of the protocol adopted by the International Organization for Standardization and the Federal Trade Commission (ISO/FTC protocol). Recent years have witnessed even more radical changes in cigarette design and the introduction of novel cigarettes and smokeless products, and further changes need to be anticipated. It is therefore essential that regulatory research and testing laboratories anticipate the rapid evolution of products and are able to adjust their procedures accordingly.

16. For countries with little or no existing laboratory capacity and insufficient resources for establishing laboratories, which is the case of many developing countries, it is vital that networks are established to enable resources to be shared and collaborative efforts to be undertaken in order to achieve the recommended laboratory capacity.
17. It is urged that all new tobacco products and modified existing products be subject to pre-market review by regulatory authorities. Rigorous pre-market review is especially important when claims such as “harm reduction” are made or anticipated.
18. Pre-market review and product evaluation, which the effective implementation of the provisions contained in certain articles of the Framework Convention would require, are neither intended to ensure nor would be capable of ensuring the safety of the products.

Tobacco product testing

As indicated earlier, the implementation of Articles 9, 10 and 11 of the Framework Convention requires the empirical testing of tobacco products. This section provides the rationale and recommended protocols for the implementation of such testing. It is recognized that there may be a variety of options that may be considered in selecting specific parameters. However, the Study Group recommends that these options be based on the current state of the science and that due consideration be paid to the limitations of product testing methods already discussed in this recommendation as well as to the foregoing principles. It is recognized that the machine testing of products does not provide information that is directly applicable to the way in which people consume tobacco products. As further research becomes available, the protocols that are recommended here should be altered to better reflect the state of ongoing science. It is important to consider the principles for research and testing set out above as product testing protocols are designed and implemented.

Outlined below are various regulatory and scientific considerations in the protocol development process that may serve as an information base as well as recommended guidelines for tobacco product testing protocols.

Regulatory considerations for product testing protocol development

This Study Group recommendation has been developed primarily to support implementation of Articles 9, 10 and 11 of the Framework Convention. However, testing protocols are specifically covered by the provisions of Article 9, which states that “the Conference of Parties, in consultation with competent international bodies, shall propose guidelines for testing and measuring the contents and emissions of tobacco products, and for the regulation of these contents and emissions”.

The provisions of the Framework Convention reflect the efforts undertaken by various countries and states within those countries to bring tobacco products into a regulatory framework. The following specific examples of regulatory action by national, federal and state governments provide precedents, and such regulatory action may also be served by this Study Group recommendation.

Canada, British Columbia. The Tobacco Testing and Disclosure Regulation of the Tobacco Sales Act requires cigarette manufacturers to submit quarterly reports that identify and list, by brand, all ingredients and additives in every brand of cigarette offered for sale in British Columbia during the previous quarter, including the quantity of the ingredient or additive as a proportion of the total weight of the cigarette or cigarette equivalent. The Act also requires cigarette manufacturers to submit annual reports that list the yield ratings from all smoke constituents, the pH of whole tobacco smoke, and the efficiency of the cigarette filters. Finally, the Act requires reporting of an extensive list of smoke constituents by cigarette manufacturers. These smoke constituents include levels in mainstream and sidestream smoke under non-ISO smoking conditions (55 ml puff volume, 30-second puff interval, 2-second puff duration, and 100% of ventilation holes blocked) (see Table 1). The constituents to be reported in mainstream and sidestream smoke are ammonia, aromatic amines, benzo[a]pyrene, selected volatile carbonyls, hydrogen cyanide, mercury, toxic trace metals, nitric oxide, TSNAs (tobacco-specific nitrosamines), selected basic semi-volatiles, phenolic compounds, tar, nicotine, carbon monoxide, and selected volatiles. (http://www.qp.gov.bc.ca/statreg/reg/T/TobaccoSales/282_98.htm, 12/18/2003)

Brazil. In 1999, the National Agency of Sanitary Surveillance (ANVISA) was created as the responsible agency for regulating the control and surveillance of cigarettes and other tobacco products. Each tobacco company must register its brand with ANVISA and pay annual taxes. As a regulatory agency, ANVISA has the authority to issue binding rules under existing laws. In addition, ANVISA has been given the mandate and obligation to establish and maintain a tobacco testing laboratory in Brazil. Also, ANVISA Resolution No.46 (21 March 2001) establishes maximum tar, nicotine, and carbon monoxide yields for cigarettes and prohibits the use of any labelling or advertising of tobacco products as “mild”, “light”, “ultra-light”, or “low tar”. Finally, the tobacco industry is required to submit annual reports that identify and list by brand all ingredients and additives in every tobacco product produced in Brazil.

European Union. In 2001, the European Parliament issued a directive for Member States concerning the manufacture, presentation, and sale of tobacco products (<http://www.who.dk/document/e74524.pdf>, 12/18/2003). The provisions limited the maximum yield of tar, nicotine, and carbon monoxide in cigarettes. The directive also included the requirement that the tobacco industry submit to Member States a list of ingredients used in tobacco product manufacture.

United States. The Comprehensive Smoking Education Act of 1984 (15 U.S.C. 1331 et seq., Pub. L. 98-474) requires that each person who manufactures, packages, or imports cigarettes provide the Secretary of Health and Human Services annually with a list of ingredients added to tobacco in the manufacture of cigarettes. The Comprehensive Smokeless Tobacco Health Education Act of 1986 (15 U.S.C. 4401 et seq., Pub. L. 99-252) requires that each person who manufactures, packages, or imports smokeless tobacco provide the Secretary of Health and Human Services annually with a list of ingredients added to tobacco in the manufacture of smokeless tobacco products. Section 4403(a) of the Comprehensive Smokeless Tobacco Health Education Act of 1986 (15 U.S.C. 4401 et seq., Pub. L. No. 99-252) requires that each person who manufactures, packages, or imports smokeless tobacco is required to submit annually to the Department of Health and Human Services a specification of the quantity of nicotine contained in each smokeless tobacco product. The Office on Smoking and Health of the Centers for Disease Control and Prevention has been delegated the responsibility of

implementing these provisions. Individual states (i.e., Massachusetts, Minnesota, and Texas) have also developed regulations based on product testing, and the process of development has provided additional basis for developing this present Study Group recommendation.

Massachusetts. According to the Tobacco Disclosure Act (General Laws of Massachusetts, Chapter 94, Section 307B Manufacture of tobacco products: annual reports, including added constituents and nicotine yield ratings; disclosure; exclusions), 1997, manufacturers of cigarettes, snuff, or chewing tobacco sold in the commonwealth are required to report added constituents other than tobacco, water, or reconstituted sheet and nicotine yield ratings that accurately predict nicotine intake for the average consumer.

Minnesota. In 1997, the State of Minnesota legislature passed the Minnesota Tobacco Substance Reporting Law. Under the provisions of this Law, manufacturers of tobacco products must provide the Commissioner of Health with information about detectable levels of ammonia or any compound of ammonia, arsenic, cadmium, formaldehyde, and lead in their products.

Texas. According to Subchapter P, Disclosure of Ingredients in Cigarettes and Tobacco Products, of Chapter 161 of the Public Health Provisions of the State of Texas, manufacturers of cigarettes or tobacco products must file an annual report identifying the ingredients in the product other than tobacco, water, and reconstituted sheet. They must also state the product's nicotine yield rating.

Scientific considerations for product testing protocol development

It cannot be overemphasized that, as indicated in the principles set out above, the following testing protocols are intended to provide a starting point to aid implementation of Articles 9, 10 and 11 of the Framework Convention. It will be essential to combine such tobacco product testing with laboratory research on actual human smoking patterns and exposure, including studies involving biomarkers to assess human exposure, and epidemiological studies to assess actual human use patterns and health effects, which have been described in other publications (11, 18). The recommended testing protocols should therefore be considered as initial proposals that should be updated from time to time as additional research is completed and as changes in tobacco products occur.

There is a need to identify, use and validate standardized methods, to assess existing capacity (gaps, opportunities, barriers) and to develop a strategic plan for strengthening laboratories at the global, regional and national levels. Furthermore, Member States will need guidance in setting levels for the contents and emissions of tobacco products both consumed by users and emitted into the environment. This guidance still has to be developed.

Surrogate measures

Although the focus of the present recommendation is on product testing protocols, it is important briefly to address surrogate measures which have also been discussed as a means of characterizing the biological effects of tobacco products. In 1999, the American tobacco companies carried out a study for the Massachusetts Department of Public Health (30). This study was intended to investigate whether surrogate measures of emissions such as tar,

nicotine, and carbon monoxide could be used to predict levels of other emission products of concern, such as polyaromatic hydrocarbons (PAHs) and TSNAs. The samples examined in this study were 26 United States-brand cigarettes containing tobacco commercially blended in the United States. The companies stated that the test cigarettes emphasized differences (i.e., design features) in products in the United States cigarette market. However, this sample of United States-brand cigarettes does not reflect many of the possible differences that can result from changes in blending, additives, and tobacco processing around the world. In evaluating the data from the benchmark study, Harris (31) concludes that the Federal Trade Commission's ratings for tar, nicotine, and carbon monoxide are not adequate to compare the yields of toxic substances. Thus, it may be concluded that benchmarking is not an appropriate way to determine levels of toxins in tobacco products.

Additional considerations for product testing protocol development

The proprietary blending and processing of tobacco can have a significant effect on levels of toxic chemicals in tobacco. In a recent study (32), researchers identified a wide range of TSNA levels in tobacco in cigarettes purchased in the 14 countries surveyed.

Mainstream smoke levels can also be altered significantly by changes in product characteristics (33). The types of materials used in filters and filter design can alter the chemical composition of the smoke that is inhaled, including the levels of carbon monoxide, nitrogen oxides, hydrogen cyanide, acrolein, and benzene. The amount of expanded tobacco or reconstituted tobacco in the products can alter the level of toxic chemicals in the smoke. The level of reconstituted tobacco can change the smoke yields of tar, nicotine, phenols, PAHs, and TSNAs. The use of expanded tobacco can have a significant effect on the amount of tobacco required to fill a cigarette rod and thus, the contents of the smoke. Cigarette length, circumference and packing density can also alter the chemical composition of the smoke.

It is important to measure sidestream smoke in addition to mainstream smoke. One study (34) found that the distribution of constituents in sidestream smoke between the particulate phase and the gas phase components of smoke varied according to certain product characteristics. In another report (35), scientists reported that the addition of filters to cigarettes significantly reduced the mainstream smoke levels of specific toxic agents without having a significant impact on sidestream smoke levels. Thus, cigarette design changes intended to reduce the levels of mainstream smoke may have a different impact on sidestream smoke.

It is therefore important to take into account the many manufacturing practices and product characteristics in evaluating a tobacco product's potential toxic delivery.

Although the existing machine-smoking methods employed/adopted by ISO and the Federal Trade Commission do not accurately reflect human smoking behaviour, and consequently do not accurately reflect the delivered dosages of toxic and carcinogenic constituents of smoke (12, 14, 15, 18, 28), it is recommended that such testing be continued to the extent that it provides a basis for a comparison of the results with new testing protocols until protocols that reflect variations in human smoking behaviour according to different cigarette designs are developed. In those settings where sufficient resources are available, a second set of puffing parameters is recommended to test cigarettes under more intense smoking conditions. It is possible that differences between the results derived from the use of these new parameters and

those yielded by using the ISO/FTC protocol would be useful in product evaluation. For example, if the ISO/FTC protocol yielded higher levels of important toxicants, then it is possible that data from that test would be considered in estimating the potential maximal exposure of that toxicant. Furthermore, because the ISO/FTC methods are based on smoking regimens that draw smaller, fewer, and more widely spaced puffs than does the average smoker, these methods might provide a model for estimating emissions from non-intensive smoking. A further complication is that the degree of underestimation of human smoking intensity is not constant across all existing cigarette designs but is exaggerated in low-yield cigarettes because smokers tend to compensate by increasing both puff frequency and the volume of smoke inhaled. In addition, the ISO/FTC protocol does not take into account the important aspect of the compensatory smoking behaviour of blocking the ventilation holes of ventilated or low-yield cigarettes. Finally, the ISO/FTC test method has not been validated for new cigarette designs (e.g., Eclipse® or Accord®) and may not be valid for subsequent new tobacco product designs.

Recommended tobacco product testing protocols and guidance

Outlined below are recommendations for tobacco product testing protocols and guidelines for tobacco product manufacturers and regulators. Also presented is a set of recommended guidelines for testing tobacco products (smoked and smokeless) and a proposed framework for laboratory requirements for research and testing.

Reporting by manufacturers

Manufacturers should report, at least annually, the product characteristics given below and the contents and emissions of tobacco products according to the protocols described below in the section on guidelines for testing. Manufacturers should also report to regulators the contaminants and product characteristics of all tobacco products offered for commercial sale. These reports should include data on both the contents (e.g., raw materials, pesticide residues, contaminants, flavourings, and processing aids) and the emissions (e.g., materials formed in the process of product use, such as carbon monoxide) of tobacco products.

The product characteristics to be reported by manufacturers should include:

- aerosol particle size (mean and 95% confidence intervals)
- filter ventilation
- filter length
- filter fibre residues
- filter charcoal content
- cigarette circumference
- paper porosity
- percentage of reconstituted tobacco
- percentage of expanded tobacco
- moisture content
- product firmness.

Additional considerations for reporting product characteristics

If the design of the product or the steps involved in processing the tobacco or manufacturing the product are changed, the manufacturers should report all changes to the regulating authority, as well as the reasons for the change and the impact of the change on product characteristics, contents, and emissions.

The frequency of sampling and the number of measurements required for determining the chemical characteristics should be based on production volume. The higher the production volume for the product, the more often the sampling of the product for those characteristics should be undertaken.

The same standards should be applied to all existing products available in the marketplace.

In addition to the information on existing products that manufacturers are required to submit to the regulators, information on new products, including modified products, should be required to be submitted. Such information should include the design of the product and its intended method of use by the consumer and the results of any toxicity studies performed on the product.

Manufacturers should disclose the identities of toxic compounds found in tobacco and emissions on the packaging and product labels. No quantitative levels should be displayed on the packs.

Information about product use and exposure should be displayed prominently on the packaging (e.g., "Smoking causes exposure to hydrogen cyanide"). Examples of these kinds of packages can be found on the following web sites: <http://www.hc-sc.gc.ca/hecs-secs/tobacco/legislation/warnings/warnings.html> (accessed 16 February 2004) and <http://www.health.gov.au/mediarel/yr2004/tw/picsindex.htm> (accessed 16 February 2004).

In addition, information regarding product use and exposure can be added as inserts inside the packaging itself, as is the practice in Canada.

Quantitative levels of chemical constituents in tobacco and emissions should be made available to interested researchers or to other public health officials through electronic means (i.e., Internet web sites, etc).

Action by regulators

The regulator must ensure that the proper procedures are followed in identifying laboratories to be engaged in the testing of tobacco products, in verifying the protocols used, examining the reported data, and in taking any corrective action. Set out below is a list of actions that regulators should be required to undertake.

Laboratory identification

The regulator should identify laboratories that are capable of carrying out sampling and/or analysis to the required standard. The laboratory chosen should (a) be independent of the tobacco industry; (b) have a working quality-control system; and (c) be able to provide evidence of internal and external checks demonstrating competency in the required analysis.

Specific criteria for the identification of laboratories to be engaged in the testing of tobacco products are given in the section entitled “Guidelines for testing”.

Sampling

The regulator should ensure that the sampling is appropriate not only for existing products, but also for new products.

Example 1: An oral tobacco product that is claimed to be nicotine-free is about to be introduced onto the market. The regulator wishes to check this declaration before allowing the product onto the market. In this case, a spot check would be appropriate and only a few samples of the product would need to be tested to verify the authenticity of the claim.

Example 2: The regulator wishes to verify that the tar, nicotine and carbon monoxide yields of a top-selling brand of cigarettes in Europe are consistent with the yields declared by the brand’s manufacturer. In this case, a sampling protocol such as that described in ISO 8243 needs to be used to ensure that several samples of the brand (representative of production output from different factories) over a prescribed period of time are obtained for analysis.

Examining reported data and disseminating information

The regulator should have a system in place to ensure that information is properly evaluated and disseminated in a clear and unambiguous style.

Regulators have an obligation, once they have received information, to act upon the findings. Thus, it is essential that regulators require that the information provided by the manufacturers and independent laboratories is compiled and summarized in such a way that conclusions can be drawn from it and those conclusions disseminated. Only if regulators have enough staff in place to examine and disseminate the information will the process of product testing be useful in furthering public health. A possible way of accomplishing this aim is by requiring reporting entities to:

- measure baseline results and report statistically significant deviations from the baseline;
- report relative differences between specific products produced by the same manufacturer;
- provide summary statistics for all products for commercial sale;
- report brands above 75%, 90%, or 95% confidence intervals for all products for commercial sale.

Packaging labels should not carry statements such as, “These cigarettes contain reduced levels of nitrosamines” or “These cigarettes contain half the level of carbon monoxide compared to our regular brand”. These are quantitative statements that imply that one brand is safer than another. The Study Group is very concerned that cigarette testing will be used by the tobacco industry to make claims that imply health benefits in order to market its products. Instead, health information should be disseminated by the display of qualitative facts on the packages, such as “These cigarettes contain nitrosamines that have been shown to cause cancer in laboratory animals” or “Smoke from these cigarettes contains benzene, a known carcinogen”. It is important to publish qualitative information *only*, based on appropriate research that indicates the presence of toxic components in smoke.

Reporting

Complete details of any analysis should be published in a report that can be accessed by public health officials and researchers. The report should include background information on why the analysis was performed, the analytical method used, evidence of method validation, the analytical results, and information on measurement uncertainties. Any opinions and interpretations given in the report, for example, recommendations on the usefulness of the results, should be clearly stated and the basis on which the opinion and interpretations are given should be documented.

Corrective action

The national authorities, in giving authority to the regulators to undertake any disciplinary action (e.g., financial penalty or criminal liability) against any tobacco manufacturer/importer who knowingly makes a false declaration about their product, must specify the administrative or legal measures that should be taken. In addition, the regulator should have the administrative and/or legal powers to request that the product be withdrawn from the marketplace, that packets be relabelled, or that an inspection be carried out of the manufacturer's premises to check that systems are in place to minimize production errors.

Guidelines for testing

Laboratories

Verification of constituents in tobacco products and tobacco smoke should be performed by laboratories that are independent of tobacco industry influence and that are appointed by the national governments. Laboratories that are selected to analyse tobacco products or tobacco smoke must have an accreditation according to the ISO 17025 and the selected analytical methods used must be evaluated on a regular basis for proficiency testing according to ILAC-G13. Finally, the laboratories should follow a stringent quality control regime (e.g., each set of smoking runs or analyses made should contain at least one quality control monitor product).

Smoking regime

The smoking regime used in most countries is the one defined by ISO/FTC and should be supplemented by the more intensive smoking protocol used in some other countries. The more intensive protocol should approximate the maximum exposure level to which an ordinary smoker could reasonably be expected to be subject when smoking the specific product. Research has indicated that there is a need for larger and more frequent puffs than have been used in the ISO/FTC protocol to estimate the emissions produced when smokers use cigarettes with highly ventilated filters. It is understood that non-cigarette products are likely to require different smoking regimes than those used for cigarettes. For cigarettes, it is recommended that the machine-smoking regimes shown in the following table be utilized. National authorities may wish to prescribe one or both of these regimes for analysing emission constituents or types of cigarettes.

Table 1. **Recommended machine-smoking regimes for cigarette testing**

Parameter	ISO/FTC protocol	More intense protocol
puff volume	35 ml	55 ml
puff duration	2 seconds	2 seconds
puff interval	60 seconds	30 seconds
ventilation holes	unblocked	blocked: all (to avoid smoking compensation)
butt length	filter overwrap plus 3 mm	filter plus 3 mm

Note: It is recognized that the more intense protocol will require modification to meet existing mandated standards. If individual smoking patterns change or if new products prevent the intense regime from approximating maximum exposure levels, the more intense protocol will need to be adjusted.

Analytes for regulatory testing purposes

The following lists specify the initial minimum number of substances for which tests should be carried out in analysing the contents and emissions of tobacco products. These lists are not exhaustive and will require regular updating. The test results should be reported per cigarette.

Product content

- Nicotine/free nicotine (smokeless products)
- Ammonia/ammonium ion
- Metals (arsenic, cadmium, chromium, lead, mercury, nickel, selenium)
- Nitrosamines [N-nitrosornicotine (NNN), 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK), N-nitrosoanatabine (NAT), and N-nitrosoanabasine (NAB)]
- Menthol

Product emissions (mainstream and sidestream)

The results of measurements of the yields of the toxic constituents listed below should be reported per milligram of tar.

- Nicotine/free nicotine
- Tar
- Carbon monoxide
- Ratio of nicotine-free dry particulate matter to nicotine yield
- Polynuclear aromatic hydrocarbons: benzo[a]pyrene
- Volatiles: benzene, 1,3-butadiene, formaldehyde, acetaldehyde
- Nitrosamines: NNN, NNK, NAT, NAB
- Metals: arsenic, cadmium, chromium, lead, mercury, nickel, selenium
- Gas-phase compounds: nitrogen oxide, hydrogen cyanide

This list should be supplemented according to testing requirements and revised according to changing product circumstances. It should ideally be extended to include other toxins in the emission profile. Additional volatile and semi-volatile compounds, polynuclear aromatic carbons, nitrosamines, among other toxins, have been included in a list commonly referred to as “the Canadian list”. Recent Canadian tobacco regulations require that manufacturers list six toxic constituents and their emissions on exterior packaging of tobacco products and that an

expanded list of toxic chemicals found in tobacco smoke be reported to the Canadian Government.

Methods

New analytes should be measured using up-to-date, validated and sensitive methods capable of measuring the components at the required levels. These methods include protocols adopted by the United Kingdom authorities (i.e. Laboratory of the Government Chemist), Health Canada, and by the Centers for Disease Control and Prevention, and the Health Department of the State of Massachusetts in the United States. The statistical measures reported should include the mean, the standard deviation, and the coefficient of variation.

Use of the data

The purpose of these measurements is to enable regulators to set upper limits for the nominated priority compounds on a per milligram of tar or a per milligram of nicotine basis. The upper limits could be based on the values measured for the lowest quintile of brands among a commissioned sample of existing international brands. A limit based on the levels achieved by the lowest 20% of the brands in the market is a suggested starting point. National regulators should determine the optimal time frame in which this first step should be achieved.

Additional country-specific list

It is recognized that the use of certain tobacco products is specific to certain countries and that the list of compounds required to be tested will therefore vary from country to country. Analytes and methodologies may therefore need to be altered to meet the analytical requirements of these special products.

Other smoking and smokeless tobacco products

The wide range of smoking and smokeless tobacco products poses a challenge for standard testing. Annex 2 lists other products available in the market that will require special testing regimes. For non-smoked products, the levels of chemical components in the tobacco filler are the critical determinants.

Reporting format for laboratory results

Reports of laboratory results must contain all the information that is required to evaluate the scientific validity of the data and to link these reports directly to the actual materials tested. All data reported should contain the following information:

- product
- testing conditions
- methods used
- limitations
- results
- quality control
- evaluation
- a declaration on conflict of interest.

Framework for the requirements of research and testing laboratories

Anybody setting out to establish and operate a tobacco product testing laboratory must be able to demonstrate its competence by conforming to ISO/IEC 17025.

Criteria for laboratory operations

It is essential that laboratories are able to make accurate and reproducible measurements of the contents and emissions of tobacco products. To achieve this, laboratories must (a) have trained, competent staff; (b) have equipment capable of making the necessary measurements; (c) follow procedures that are sensitive, selective, accurate, and reproducible; and (d) have a mechanism for cooperating and sharing information with international bodies dedicated to laboratory accreditation. All laboratories must be able to demonstrate that they

- use a valid method of measurement
- use trained and competent staff
- establish traceability through use of calibration standards
- evaluate measurement uncertainty
- evaluate quality assurance
- carry out quality control
- compare results with those obtained by other laboratories (proficiency testing)
- establish and maintain a quality system, supported by third party audit (accreditation).

Resources for the laboratory setting

In order to carry out analyses of tobacco products, laboratories will require an investment in the resources necessary to accomplish the task. The resources required to operate a laboratory are summarized under the following headings:

- infrastructure
- human resources
- specialized equipment/instrumentation.

Infrastructure

Table 2 shows the approximate requirements in terms of surface area and environmental control of a testing/research laboratory.

Table 2. Requirements of a testing/research laboratory

Type of area/ accommodation	Minimum surface area	Expanded laboratory surface area ^a	Research laboratory facilities surface area ^b	
	(m ²)	(m ²)	(m ²)	
Preparation laboratory	20	60	80	Air-conditioned; to house fume hoods/cupboards. Water and drainage required. Metal analysis will require separate 'clean room'.
Smoking laboratory	20	60	60	Contains smoking machine(s). Air- conditioned and humidity- controlled (22 ± 2 °C and 60 ± 5%).
Instrument room	30	80	100	Air-conditioned; specialist instruments will require additional ventilation and other specific conditioning.
Offices	20	40	80	
Stores	15	25	40	
Common areas	15	25	30	
Utility room	15	40	40	
Total	135	330	430	

^a An expanded laboratory would include the necessary equipment for performing all recommended analyses of chemical constituents.

^b The research laboratory facilities could include a small in-vitro or biomarker facility.

Human resources

For many aspects of the laboratory's operations, staff need to be trained and experienced in particular analytical fields and to be confident in the area of data handling, in the production of reports and, above all, in the use of statistics. The number of staff required to operate the testing laboratory will depend on a combination of factors, for example, the frequency of sampling, the total number of tests per brand, the number of brands, the frequency of tests, the complexity of the analyses and the nature of the reporting. A typical laboratory performing tests on approximately 150 brands annually should consist of the following personnel:

- 1 smoke laboratory manager;
- 2 to 3 smoke technicians, who should be familiar with the operation/maintenance of the smoking machine(s);
- 2 to 3 analytical chemists, who should have extensive knowledge of instrumentation; and,
- 1 quality control manager to supervise and control data and methods, and who should be well versed in statistics and data reporting.

Specialized equipment/instrumentation

A testing laboratory should be provided with the following equipment:

- 1 linear smoking machine or rotary smoking machine
- 1 dual-column gas chromatograph with thermal ionization detector and flame ionization detector
- 1 gas chromatograph with thermal energy analyser
- 1 gas chromatography mass spectrometer
- 1 high-performance liquid chromatograph
- 1 environmentally controlled chamber
- 1 continuous flow analyser (2-channel or 4-channel)
- 1 carbon monoxide analyser (non-dispersive infrared spectrometer)
- 1 nitrogen oxide analyser (nitrogen oxide chemiluminescence detector).

For groups of research and testing laboratories

It is recognized that the necessary expertise required for the testing of all the tobacco products of any one country will require input from several laboratories, possibly from national and/or regional reference laboratories. Effective communication and networking between the various laboratories will enable the development of databases, which can be shared and monitored by a coordinating centre. Such a coordinating centre could also offer a range of other benefits, such as:

- providing information on the availability of new/standardized methods;
- improving and increasing awareness of measurement problems;
- informing regulators of science-based developments;
- managing a web site;
- publicity;
- managing collaborative studies between laboratories; and,
- standardizing reporting formats (templates should be agreed upon) in order to facilitate the reading of the reported data for the end-users, the regulator and scientists (36, 37).

Interaction between testing and research laboratories and health research groups

The testing laboratories, which are used principally for regulatory purposes, should network closely with research laboratories that are located in academic institutions and are independent of the tobacco industry's ownership or influence. This interaction will enable the regulatory testing laboratories to keep abreast of product modifications being carried out by tobacco product manufacturers and will also provide them with the latest information on new analytical techniques, which make measurements more accurate. At the same time, the research laboratories will be constantly aware of the need to steer their research efforts towards strengthening regulatory action, especially with respect to new or modified tobacco products.

Testing laboratories should also establish and maintain close links with health research groups involved in epidemiological and behavioural research into the effects of tobacco products and their claims on health, beliefs, behaviours and outcomes. Since the purpose of tobacco product regulation is progressively to reduce the harm arising from tobacco products, it is essential that the regulatory agencies and testing laboratories are kept well informed of the effects of regulatory measures at the population level. This is especially important when information based on regulatory testing is released to consumers by the agencies concerned or is used by the tobacco industry to make product-related health claims.

Special considerations for developing countries

Developing countries are experiencing rising levels of tobacco consumption, and WHO predicts that they will contribute 7 million of the 10 million tobacco-related deaths projected for 2020. Several of these countries are not only tobacco producers, but are also exporters of raw tobacco, tobacco products or both. The existing laboratory capacity for testing tobacco products is very limited. The diversity of tobacco products marketed and consumed in many developing countries makes the need for tobacco product regulation more urgent because of insufficient information about the contents and/or emissions of several tobacco products, and the regulatory process more demanding in terms of the testing methods required to cover different categories of products.

In many developing countries, for example, in Brazil, India, South Africa and Thailand, enacted or intended national legislation is evidence of an increasing interest in tobacco product regulation and related testing. At the Fifty-sixth World Health Assembly, held in May 2003, most of the developing countries made a commitment to sign and ratify the Framework Convention. However, many developing countries can only meet the requirements of Articles 9, 10 and 11 of the Convention for the testing and regulation of and the disclosure to governmental authorities of information about the contents and emissions of tobacco products either by relying on the tobacco industry's own resources for testing and information disclosure or by employing independent testing laboratories located in other countries. The Framework Convention does not require the existence of independent laboratories within the countries for the carrying out of tobacco product testing. However, there is a clear need for independent laboratories that are not owned or influenced by the tobacco industry and that can evaluate accurately and objectively the product claims advanced by the tobacco product manufacturers. Such laboratories would, moreover, need to be established at the regional and

national levels in developing countries, since the capacity currently available in developed countries could not meet the testing needs of developing countries, either in terms of volume or of product diversity.

Strategic plan for capacity building

Capacity building should be undertaken in two phases. In **Phase I**, regional testing laboratories would be established in each of the WHO regions. This would be accomplished either by establishing new laboratories or by scaling up existing laboratories that are currently performing some of the functions required of a testing laboratory. These laboratories could be government-managed laboratories or government-accredited independent laboratories established in academic institutions or by the private sector. The criterion of independence from the tobacco industry must be fulfilled.

Since laboratory capacity is very limited in the developing countries, these testing laboratories may also need to fulfil the functions of a research laboratory. The feasibility of equipping these laboratories for this twin role needs to be examined when selecting or setting up laboratories in the developing countries.

In Phase I, one or two regional laboratories could be established in each of the WHO regions. Initially, a situational analysis would need to be performed in each WHO region to assess current national capacity for laboratory testing, the plans and potential for the future enhancement of laboratory capacity, and the regulatory environment that exists or that is likely to evolve. The technical and financial requirements of countries would need to be mapped, the potential partners for the provision of technical assistance would need to be identified and the capacity for mobilizing financial resources must be assessed. On the basis of this situational analysis, WHO could select one or two countries within each of its regions. Plans for capacity development must then be developed, in close consultation with the national regulatory authorities of those countries. Training programmes must be established and technology transfer must be facilitated through collaboration with suitable international partners. The laboratories must be accredited and subsequently linked to the national regulatory authorities of all the countries that they are expected to serve.

Once the regional testing laboratories are well established, they would serve as resources for developing national capacity in other countries of that region. In **Phase II**, further expansion of capacity would occur through such a process and many more countries would become capable of establishing, running and using tobacco product testing laboratories, which would enable them to perform the desired regulatory functions.

Annex 1. Standardized methods for testing tobacco products

- **Machine-smoking parameters:** Routine analytical cigarette-smoking machine – Definitions and standard conditions - ISO 3308:2000. Special revisions have to be made to cover the new smoking regime specified.
- **Tobacco and tobacco products:** Atmosphere for conditioning and testing - ISO 3402:1999.
- **Protocols for testing contents of smokeless tobacco:** Free nicotine method - US Federal Register 64 FR 14086: Notice regarding requirement for annual submission of the quantity of nicotine contained in smokeless tobacco products manufactured, imported, or packaged in the United States.
- **Tar yield (mg per cigarette):** Cigarettes - Determination of total and nicotine-free dry particulate matter using a routine analytical smoking machine - ISO 4387:2000.
- **Nicotine yield (mg per cigarette):** Cigarettes - Determination of nicotine in smoke condensates – Gas– chromatographic method - ISO 10315:2000.
- **Water yield (mg per cigarette):** Cigarettes - Determination of water in smoke condensates – Part 1: Gas–chromatographic method - ISO 10362-1:1999.
- **Carbon monoxide yield (vapour phase) (mg per cigarette):** Cigarettes - Determination of carbon monoxide in the vapour phase of cigarette smoke - NDIR (Non-Dispersive Infrared) method - ISO 8454:1995.
- **General requirements for the competency of testing and calibration laboratories:** ISO/IEC 17025:1999. Accreditation to ISO/IEC 17025 requires that the laboratory has a quality system meeting the requirements of ISO 9000. Therefore, ISO/IEC 17025 accreditation is a recognition of laboratory competence, while ISO 9000 accreditation alone is simply a recognition of conformance to a quality system.
- **ILAC Guidelines for the Requirements for the Competence of Providers of Proficiency Testing Schemes:** ILAC-G13:2000.
- **International standard on cigarettes sampling:** Cigarettes – Sampling - ISO 8243:2003.
- **Fine-cut tobacco and smoking articles made from it:** Methods of sampling, conditioning and analysis - Part 1: Sampling - ISO 15592-1:2001; Part 2: Atmosphere for conditioning and testing – ISO 15592-2:2001; Part 3: Determination of total particulate matter of smoking cigarettes using a routine analytical smoking machine, preparation for the determination of water and nicotine, and calculation of nicotine-free dry particulate matter – ISO 15592-3:2003.

Annex 2. Tobacco products that will require special testing regimes.

Smoking tobacco products besides cigarettes

Bidis. Bidis (or Beedies) are hand-rolled cigarettes consisting of sun-dried tobacco flakes wrapped in a tendu leaf and secured with a thread at one end. Bidis are made in India and are available in the United States. They are available in a variety of flavours such as vanilla, chocolate, cherry and strawberry. Despite their small size, their tar and carbon monoxide deliveries tend to be higher than machine-made cigarettes because of the need to inhale harder to ensure that the bidi stays alight while being smoked. This is also the case for cigars, where the puffing volume often exceeds 55–70 ml, depending on the length or diameter of the cigar. Bidis form a significant proportion of the South-East Asian market and are now becoming increasingly prevalent in other parts of the world.

Cigars. Any roll of tobacco wrapped in leaf tobacco or in any substance containing tobacco. Small cigars weigh not more than three pounds per thousand (<1.36 g/cigar); large cigars weigh more than three pounds per thousand.

Fine-cut smoking articles (roll-your-own). In the case of **fine-cut smoking articles** (FCSAs), the ISO method 15592 with all four matrices should be adopted for tar, nicotine and carbon monoxide.

Kreteks. Kreteks, also known as clove cigarettes, are commonly used in Indonesia and are a blend of tobacco and cloves, as well as other exotic flavourings and eugenol. Kreteks can be hand-rolled in a corn husk or paper or machine-made with or without filters.

Tobacco used in water pipes (sheesha/narghile/arghile/hookah/hubble-bubble, goza). The term for the water pipe varies according to the region and country in which it is used: it is thus variously referred to as the hookah, hubble-bubble, narghile, arghile, goza, and sheesha. A “water pipe” refers to the method of smoking tobacco in which smoke passes through water (and therefore gets filtered by it) before inhalation. Water pipes come in a great variety of sizes, shapes and ornamentation of the equipment. Generally, the pipe is composed of a tall glass chamber filled part-way with water, a mechanism for heating the flavoured tobacco (usually using charcoal), and one or more hoses from which people smoke the tobacco once it is heated and filtered through the water in the glass chamber.

Smokeless tobacco products

Chew, loose-leaf. Loose-leaf chew is made of leaf tobacco, sweetener, and/or licorice. Examples of brand names are Red Man, Beech-Nut Wintergreen, and Taylors Pride.

Chew, twist or roll. Dark, air-cured leaf tobacco is treated with a tar-like tobacco leaf extract and twisted into rope-like strands that are dried. Typically, no flavouring or sweetener is added. The final product is a pliable, but dry, rope. Some brand names are Conwood (Conwood product), R.C. Owen (R.C. Owen product) and R.J. Reynolds (R.J. Reynolds product).

Chimo. Chimo is a tobacco paste which is packaged in small tins or candy-like wrapped cylinders and is available in Venezuela. Chimo is made of tobacco leaves, sodium bicarbonate, brown sugar, ashes from the Mamón tree (*Melicocca bijuga*), and vanilla and anisette flavouring. The ingredients vary according to the region of Venezuela in which chimo is manufactured. Some brand names are El Sabroso, El Gran Búfalo, El Dragón and El Morichal.

Gul. Gul contains tobacco powder, molasses, and other flavouring ingredients. Gul is machine-produced and sold in toothpaste-like tubes.

Gutkha. Tobacco, betel nut and catechu are mixed together with several other ingredients, flavoured and sweetened. The product is sold in small brightly coloured packets, which appeal to children. Some brand names are Manikchand, Moolchand, Tulsi, Shimla, Sikandar and Pan Parag.

Iq'Mik. Fire-cured tobacco leaves are mixed with punk ash (ash generated by burning a woody fungus that grows on the bark of birch trees). The ingredients are available at grocery stores and retail outlets, but are generally combined by the user before use. It is believed that the punk ash in the mixture raises the pH level in the mouth, increasing the dose and enhancing the delivery of nicotine to the brain.

Khaini. Powdered tobacco and slaked lime paste are combined by the user in his/her palm and formed into a ball. Areca nut is sometimes added. The product is held in the mouth, in a similar manner to moist snuff. Some brand names are Raja and Kuber.

Kimam, see Qiwam

Mawa. Small pieces of sun-cured areca nut are mixed with tobacco flakes and slaked lime (liquid calcium hydroxide). The mixture is rubbed together, placed in the mouth and chewed.

Mishri (Masheri, Misheri). Tobacco is baked on a hot metal plate until toasted or partially burnt, then powdered. Users apply it to the teeth and gums, often for the purpose of cleaning the teeth. Users then tend to hold it in their mouths (because of nicotine addiction).

Nass (Naswar, Niswar). Sun- and heat-dried tobacco leaves, slaked lime, ash from tree bark, and flavouring and colouring agents are mixed together. Water is added and the mixture is rolled into balls. The constituents of Nass are tobacco, ash, cotton or sesame oil, water, and sometimes gum. *Naswar*, or *niswar*, contains tobacco, slaked lime, indigo, cardamom, oil, menthol, water.

Pan masala (betel quid). Pan masala is commercially prepared, vendor-prepared or assembled at home. Areca nut is boiled, roasted or sun-dried. The tobacco may be used raw, sun-dried, and roasted, then finely chopped, powdered and scented. Alternatively, the tobacco may be boiled, made into a paste and scented with rose water or perfume. To assemble, slaked lime and catechu are smeared on a betel leaf. The betel leaf is folded into a funnel shape and tobacco, areca nut and any other ingredients are added. The top of the funnel is folded over, resulting in a *quid*, which is placed in the mouth for use.

Plug or chew tobacco. Enriched tobacco leaves (burley and bright tobacco or cigar tobacco) or fragments are charged into a mould and pressed to acquire a flat bar shape. Most plug tobacco is flavoured and sweetened with licorice. Plug tobacco exists in two forms, dry and moist. Some examples of brand names of moist plug tobacco are Red Man Moist Plug, Totems, RJ Gold (Swedish Match product), Levi Garrett Plus and Taylors Pride (Conwood product). Some brand names of dry plug tobacco are Days Work (Swedish Match product), Conwood (Conwood product) and Brown & Williamson (Brown & Williamson product).

Qiwam. Tobacco leaves processed by removing their stalks and stems, then boiled and soaked in water flavoured with spices (e.g., cardamom, saffron and/or aniseed) and additives (e.g., musk). The resulting pulp is mashed, strained and dried into a paste. It is placed in the mouth and chewed.

Red tooth powder. Tobacco powder most commonly used to clean teeth. One brand name is Dabur.

Snuff, creamy. Tobacco toothpaste made of tobacco, clove oil, glycerin, spearmint, menthol, and camphor.

Snuff, dry. Tobacco is fire-cured, then fermented and processed into a dry, powdered form. It is packaged and sold in small metal or glass containers. Some brand names are Al Capone Powder, Conwood (Conwood product) and Swisher (Swisher product).

Snuff, moist. The tobacco is either air- or fire-cured, then processed into fine particles (“fine cut”) or strips (“long cut”). Some brand names are Copenhagen, Skoal, Skoal Bandits, and Happy Days.

Snus (snuff). Finely ground dry tobacco is mixed with aromatic substances, salts, water, and humidifying agents. The product is kept cold to avoid fermentation. Some brand names are Catch, General, and Timber Wolf.

Toombak. Tobacco and sodium bicarbonate are rolled into a ball called *saffa* and placed in the mouth and sucked slowly for 10 to 15 minutes.

Zarda. Tobacco leaves are broken up and boiled with lime and spices. The mixture is dried and coloured with vegetable dyes, then mixed with finely chopped areca nuts. The mixture is often used as an ingredient in betel quid and is chewed.

References

1. WHO Framework Convention on Tobacco Control. Geneva, World Health Organization, 2003 (http://www.who.int/tobacco/fctc/text/en/fctc_en.pdf, accessed 10 June 2004).
2. Rabin RL, Sugarman SD, eds. Regulating tobacco. Oxford, Oxford University Press, 2001.
3. Bates C et al. The future of tobacco product regulation and labelling in Europe: implications for the forthcoming European Union Directive. *Tobacco Control*, 1999, 8:225–235.
4. Henningfield JE, Moolchan ET, Zeller M. Regulatory strategies to reduce tobacco addiction in youth. *Tobacco Control*, 2003, 12 (Suppl. 1):114–124.
5. Henningfield JE, Slade J. Tobacco dependence medications: public health and regulatory issues. *Food and Drug Law Journal*, 1998, 53:75–114.
6. Henningfield JE, Zeller M. Could science-based regulation make tobacco products less addictive? *Yale Journal of Health Policy, Law and Ethics*, 2002, III:127–138.
7. Kennedy EM. The need for FDA regulation of tobacco products. *Yale Journal of Health Policy, Law and Ethics*, 2002, III:101–108.
8. Myers ML. Could product regulation result in less hazardous tobacco products? *Yale Journal of Health Policy, Law and Ethics*, 2002, III:39–47.
9. Parrish SC. Bridging the divide: a shared interest in a coherent national tobacco policy. *Yale Journal of Health Policy, Law and Ethics*, 2002, III:109–118.
10. Slade J, Henningfield JE. Tobacco product regulation: context and issues. *Food and Drug Law Journal*, 1998, 53:43–74.
11. Advancing knowledge on regulating tobacco products: monograph. Geneva, World Health Organization, 2001 (WHO/NMH/TFI/01.2; http://whqlibdoc.who.int/hq/2001/WHO_NMH_TFI_01.2.pdf, accessed 11 June 2004).
12. WHO Scientific Advisory Committee on Tobacco Product Regulation . Conclusions and recommendations on health claims derived from ISO/FTC method to measure cigarette yield. Geneva, World Health Organization, 2002 (http://www.who.int/tobacco/sactob/recommendations/en/iso_ftc_en.pdf).
13. WHO Scientific Advisory Committee on Tobacco Product Regulation . Recommendation on nicotine and its regulation in tobacco and non-tobacco products. Geneva, World Health Organization, 2002 (http://www.who.int/tobacco/sactob/recommendations/en/nicotine_en.pdf).
14. WHO Scientific Advisory Committee on Tobacco Product Regulation . Recommendation on tobacco product ingredients and emissions. Geneva, World Health Organization, 2003 (http://www.who.int/tobacco/sactob/recommendations/en/ingredients_en.pdf).
15. WHO Scientific Advisory Committee on Tobacco Product Regulation . Statement of principles guiding the evaluation of new or modified tobacco products. Geneva, World Health Organization, 2003 (http://www.who.int/tobacco/sactob/recommendations/en/modified_en.pdf).
16. WHO Scientific Advisory Committee on Tobacco Product Regulation . Recommendation on smokeless tobacco products. Geneva, World Health Organization, 2003 (http://www.who.int/tobacco/sactob/recommendations/en/smokeless_en.pdf).
17. Conclusions of the Conference on the Regulation of Tobacco Products, Helsinki, 19 October 1999. Copenhagen, WHO Regional Office for Europe, 1999.

18. Stratton K, Shetty P, Wallace R, Bondurant S, eds. Clearing the smoke: assessing the science base for tobacco harm reduction. Institute of Medicine. Washington, DC, The National Academies Press, 2001.
19. Food and Drug Administration. Regulations restricting the sale and distribution of cigarettes and smokeless tobacco products to protect children and adolescents; proposed rule analysis regarding FDA's jurisdiction over nicotine-containing cigarettes and smokeless tobacco products; notice. *Federal Register*, 1995, 60:41314–41792.
20. Food and Drug Administration. Regulations restricting the sale and distribution of cigarettes and smokeless tobacco to protect children and adolescents; final rule. *Federal Register*, 1996, 61:44396–45318.
21. Warner KE et al., eds. Reducing the health consequences of smoking: 25 years of progress: A report of the Surgeon General: 1989 executive summary. Rockville, MD, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1989 (DHHS Publication No. (CDC) 89-8411; <http://profiles.nlm.nih.gov/NN/B/B/X/s>, accessed 9 June 2004).
22. Royal College of Physicians. Nicotine addiction in Britain: a report of the Tobacco Advisory Group of the Royal College of Physicians. London, Royal College of Physicians of London, 2000.
23. Shafey O, Dolwick S, Guindon GE. Tobacco country profiles. American Cancer Society and World Health Organization, 2003.
24. Malson JL et al. Nicotine delivery from smoking bidis and an additive-free cigarette. *Nicotine and Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco*, 2002, 4:485-90.
25. Hatsukami DK et al. Biomarkers of tobacco exposure or harm: application to clinical and epidemiological studies. Paper presented at the Conference on Biomarkers for Tobacco Toxin Exposure, 25-26 October 2001, Minneapolis, Minnesota. *Nicotine and Tobacco Research*, 2003, 5:387-396.
26. Warner KE et al. Treatment of tobacco dependence: innovative regulatory approaches to reduce death and disease: preface. *Food and Drug Law Journal*, 1998, 53(Suppl.):1–8.
27. Gray N, Boyle P. The future of the nicotine-addiction market. *Lancet*, 2003, 362:845–846.
28. Risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine. (Smoking and Tobacco Control Monograph No. 13; <http://news.findlaw.com/hdocs/docs/tobacco/nihnci112701cigstgy.pdf>, accessed 9 June 2004). Bethesda, MD, United States Department of Health and Human Services, National Institutes of Health, National Cancer Institute, 2001.
29. Burns D, Cummings KM, Hoffman D, eds. Cigars: health effects and trends. Smoking and Tobacco Control Monograph No. 9. Bethesda, MD, United States Department of Health and Human Services, National Institutes of Health, National Cancer Institute, 1998 ((NIH Publication No. 98-4302).
30. Borgerding MF, Bodnar JA, Wingate DE. The 1999 Massachusetts benchmark study: final report, July 24 2000. Louisville, KY, Brown and Williamson Tobacco, 2000 (<http://www.bw.com/home/html>, accessed 9 June 2004).
31. Harris JE. Smoke yields of tobacco-specific nitrosamines in relation to FTC tar level and cigarette manufacturer: analysis of the Massachusetts Benchmark Study. *Public Health Reports*, 2001, 116:336–343.
32. Ashley DL et al. Tobacco-specific nitrosamines in tobacco from U.S. brand and non-U.S. brand cigarettes. *Nicotine and Tobacco Research*, 2003, 5:323–331.

33. Hoffmann D, Hoffmann I. The changing cigarette, 1950-1995. *Journal of Toxicology and Environmental Health*, 1997, 50:307–364.
34. Guerin MR. Formation and physicochemical nature of sidestream smoke. In: O'Neil IK, Brunneemann KD, Dodet B, Hoffmann D, eds. *Environmental carcinogens. Methods of analysis and exposure measurement*, pp. 11–23. Lyon, International Agency for Research on Cancer, 1987 (IARC Publication No. 81).
35. Adams JD, O'Mara-Adams KJ, Hoffmann D. Toxic and carcinogenic agents in undiluted mainstream smoke and sidestream smoke of different types of cigarettes. *Carcinogenesis*, 1987, 8:729–731.
36. King B. *In-house method validation: a guide for chemical laboratories*. Teddington, LGC, 2003.
37. Lawn RE, Thompson M, Walker R. *Proficiency testing in analytical chemistry*. Cambridge, Royal Society of Chemistry, 1997.