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Expert committees and study groups¹

Report by the Secretariat

WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Fifty-fifth report²
Geneva, 15-18 November 2004

Main recommendations

1. The Expert Committee on Biological Standardization reviews developments in the field of biological substances used in human medicine, which include vaccines, biological therapeutics, blood products and related in vitro diagnostic devices. It coordinates activities leading to the adoption of recommendations for assuring their quality, safety and efficacy and to the establishment of international reference materials.
2. Comparability of data worldwide is assured by the use of international reference materials in designating the activity of prophylactic or therapeutic biological substances or in ensuring the reliability of quality control or diagnostic procedures. Based on the results of international collaborative laboratory studies, the Expert Committee established eight new or replacement international reference materials and disestablished one preparation. An up-to-date list of International Reference Preparations is available on the WHO web site.³
3. The Expert Committee also adopted new guidelines for the production and quality control of candidate live attenuated tetravalent dengue vaccines, and revised recommendations for the preparation, characterization and establishment of international and other biological reference standards.

¹ The Regulations for Expert Advisory Panels and Committees provide that the Director-General shall submit to the Executive Board a report of expert committees containing observations on the implications of the expert committee reports and recommendations on the follow-up action to be taken.

² WHO Technical Report Series, No. 932, in press.

³ <http://www.who.int/bloodproducts/catalogue>.

Significance for public health policies

4. Recommendations published by WHO provide guidance to national regulatory authorities and manufacturers on production, quality control and associated safety and regulatory issues. These serve as the basis for national regulations. WHO's international standards are used to calibrate regional, national or manufacturers' standards and often form the basis for licensing, routine lot release and clinical dosing worldwide.

5. The guidelines on dengue vaccines were developed in response to interest from many countries in the development of candidate live attenuated tetravalent dengue vaccines. Their scope crosses the broad spectrum of candidate vaccines, from those prepared by the classical method of virus attenuation by application of biological selection pressures to those based on the latest molecular biological approaches to the design of novel virus constructs. The document defines international norms and standards to assure the quality, safety and efficacy of each of these approaches, so as to facilitate national authorities' decision-making on the suitability of candidate dengue vaccines for testing in their own populations.

6. The revised recommendations for the preparation, characterization and establishment of international and other biological reference standards set out the process whereby such reference preparations are established and the technical specifications to which they must comply. The scientific basis for characterization of biological reference materials was reviewed in a series of consultations with the scientific community, national regulatory authorities, international standards setting bodies and users. As a result, the concepts used by WHO for biological standardization were both reaffirmed as appropriate and clarified, thereby ensuring the continued usefulness of this class of reference materials.

Implications for the Organization's programmes

7. The Expert Committee provides up-to-date recommendations on the quality, safety and potency of biological substances used in human medicine and ensures the availability of necessary international reference materials. Its work enables WHO to fulfil its constitutional responsibilities. In particular, its observations, conclusions and recommendations provide timely recommendations and reference preparations for assuring the quality, safety and efficacy of vaccines, and the provision of reference materials for standardizing essential diagnostic assays for the detection of virological contaminants in blood products. The global norms and standards defined by the Committee provide the basis for assessing the acceptability of vaccines for purchase by international agencies, such as UNICEF and WHO.

8. The consultative process for the revision of the recommendations on preparation of biological reference substances (see paragraph 6 above) revealed a need for continued scientific and capacity building in the area of biological standards. The Committee recommended that WHO should consider starting or, as appropriate, continuing work on: (a) predicting and monitoring the stability of biologicals; (b) development of specific training modules for biological standardization through the Global Training Network; and (c) preparing a detailed manual on calibration procedures for secondary (regional or national) standards.

9. In approving the first-ever international standard for a human genetic test for factor V Leiden (a genetic mutation that is a risk factor for thrombosis), the Committee set a milestone in the field of genetic testing procedures. The test provides information on susceptibility to venous thrombosis, and ultimately will benefit people at increased risk of this potentially life-threatening condition. The new

standard will help ensure that this commonly performed test provides accurate results. Cross-Organizational activities are in hand to ensure the proper implementation and use of the standard.

10. The quality of blood grouping reagents is important for safe blood transfusion, yet there is currently no appropriate international standardization of anti-D blood-grouping reagents. Suitable international reference reagents are needed to ensure minimum standards of potency of such reagents. Accordingly, the preparation and characterization of a monoclonal antibody blood-grouping reagent have been initiated and, after critical review of data from an international collaborative study, the Committee established the candidate preparation as a new international standard. Additional work is now required to establish appropriate WHO standards for anti-A and anti-B blood-grouping reagents.

EVALUATION OF CERTAIN FOOD CONTAMINANTS

Sixty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives Rome, 8-17 February 2005¹

Main recommendations

11. The Committee evaluated the potential health risk of four individual food contaminants and two groups of compounds. Intakes of all these contaminants were assessed in order to identify main source foods and commodities at an international level. The report also contains several general recommendations, for example on the formulation of advice on contaminants that are both genotoxic and carcinogenic, and considerations on the establishment of acute reference doses for contaminants that could present an acute toxicological risk through short-term, high levels of intake.

12. In particular the Committee developed a new approach on how to give more useful advice to risk managers about contaminants that have genotoxic and carcinogenic properties, in light of often incomplete data, a limitation which precludes a quantitative risk assessment. For acrylamide, ethyl carbamate, polybrominated diphenyl ethers and polycyclic aromatic hydrocarbons, the Committee expressed the outcome of this new approach to risk assessment in the form of the margin of exposure, which indicates the difference between the concentration at which, in experimental systems, adverse health effects have been observed and the estimated current human intake. The lower this margin, the higher the level of concern.

13. In addition the Committee assessed the impact on the overall intake of cadmium of different proposed regulatory limits in a variety of commodities. A similar, but less complex, assessment was performed for the intake of inorganic tin from canned foods.

Significance for public health policies

14. The Committee's work identifies and, if possible, quantifies the public health significance of unavoidable contaminants in food through a scientific risk assessment. The new approach enables the Committee to give risk managers more useful advice on certain contaminants, thereby facilitating priority-setting relative to other contaminants and targeted interventions to reduce human exposure.

¹ WHO Technical Report Series, No. 930, in press.

15. Although all Member States face the problem of assessing potential risks of contaminants in food, only a few national or regional scientific institutions can assess the relevant toxicological and related data. Member States therefore need to be provided with valid information on both the general aspects of risk assessment and specific evaluations on the contaminants covered in this report. The Committee's complex work in reaching consensus among independent international experts on the evaluation of these contaminants means that no other body has a comparable influence on public health decisions related to food safety.

16. The Committee's work also contributes to international harmonization in risk assessment of contaminants, which is an important prerequisite for a more coherent set of public health policies on food contaminants.

17. The Committee's recommendations are used by the Codex Alimentarius Commission for setting international food standards. Such values are established only for substances that have been evaluated by the Committee, thereby ensuring that food commodities in international trade meet strict safety standards.

Implications for the Organization's programmes

18. The evaluation of chemicals in food by the Committee is a continuing activity. Four meetings of the Joint FAO/WHO Expert Committee on Food Additives (three on food additives and contaminants, and one on residues of veterinary drugs in food) are scheduled for 2006-2007.

19. WHO is a partner in the Joint FAO/WHO Food Standards Programme, which administers the Codex Alimentarius Commission. The Committee's work is crucial to that of the Commission.

20. Regional offices and WHO Representatives also make use of the Committee's evaluations when advising Member States on food safety regulatory programmes.

THE SELECTION AND USE OF ESSENTIAL MEDICINES

Report of the WHO Expert Committee, 2005 (including the 14th WHO Model List of Essential Medicines) Geneva, 7-11 March 2005¹

21. The Expert Committee, meeting for the third time under new procedures adopted in 2002, noted that the full effect of those procedures was now apparent in the careful and timely presentation of evidence-based applications for addition, deletion or changes to the WHO Model List of Essential Medicines. Early posting of most documents on the WHO web site together with the rounds of review and comments before the meeting ensured the transparency of the process. The Secretariat requested and received agreement from the Committee to hold an open session, the purpose of which was to allow all stakeholders to comment on issues relating to the Model List.

¹ WHO Technical Report Series, No. 933, in press.

Main recommendations

22. The Committee recommended that 18 medicines should be deleted from the Model List and that seven should be added.
23. With regard to methodological issues, the Committee recommended that any reviews of sections of the Model List should be done in the first year after a Committee meeting, so that full applications for new additions, if suggested by the review, can also be submitted at the next Committee meeting.

Significance for public health policies

24. The continuing review of the core and complementary lists, the use of the square box symbol and planned reviews of specific sections continue to make the Model List more consistent in its advice. The deletion of many obsolete items and the addition of more relevant ones have increased the practical value of the Model List as a public health tool.
25. Medicines with similar clinical performance within a pharmacological class are identified and listed in the web-based WHO Essential Medicines Library, which now incorporates the Model List, the WHO Model Formulary and references to most of WHO's clinical guidelines, with links to price information, nomenclature and information on quality and standards.

Implications for the Organization's programmes

26. The drive for consistency between the Model List and WHO's clinical guidelines helps to ensure coordination within WHO, and promotes a systematic evidence-based approach to developing and updating WHO's clinical guidelines

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