

Expert committees and study groups¹

Report by the Secretariat

WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Fifty-sixth report²
Geneva, 24–28 October 2005

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. The use of international reference materials for designating the activity of biological substances used in prophylaxis or therapy, or for ensuring the reliability of quality control or diagnostic procedures, allows comparability of data worldwide. Based on the results of international collaborative laboratory studies, the Expert Committee established 15 new or replacement international reference materials. An up-to-date list of WHO International Standards and Reference Materials is available on the WHO web site.³
3. The Expert Committee recommended adoption of guidelines for DNA vaccines and rotavirus vaccines, and advised that recommendations should be adopted for whole-cell, pertussis vaccine, human plasma for fractionation and rabies vaccine. The Committee also adopted guidelines that provide a risk assessment and define conditions for the safe production of pandemic-strain influenza vaccines.

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, 2007, in press.

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

Significance for public health policies

4. Recommendations published by WHO provide guidance for national regulatory authorities and manufacturers on production, quality control and associated safety and regulatory issues for biological medicines. 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 safe production of pandemic-strain influenza vaccines have implications for countries wishing to start or expand influenza vaccine production. Vaccine manufacturers are responding to the threat of an influenza pandemic by gearing-up production of vaccines against currently circulating highly-pathogenic influenza viruses. This step is an essential part of preparedness planning but carries risks to the public health if, for example, the virus strains were to escape from the production facilities. The new guidelines define conditions to minimize this risk; however, the guidelines will be effective only if they are properly implemented by the countries where the vaccine is produced.

6. The revised recommendations for biosafety in production and quality control areas for rabies vaccines do not cover those produced in mammalian neural tissues. Although such rabies vaccines have been in worldwide use for many years, their use has led to serious adverse reactions following vaccination, such that the safety profile of such vaccines is considered unacceptable. Moreover, there is evidence for a lack of potency of certain vaccines produced in neural tissues, leading to inadequate protection in humans. The revised recommendations, therefore, provide specifications for rabies vaccines produced in cell cultures or purified from embryonated eggs since these vaccines are safe and have dramatically decreased the number of human deaths throughout the world, most notably in countries where canine rabies is endemic. Countries where vaccines produced in neural tissue have not yet been replaced by cell culture and purified embryonated egg derived rabies vaccines will need to consider appropriate strategies for future rabies control.

Implications for the Organization's programmes

7. The Expert Committee on Biological Standardization 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 this area. Its observations, conclusions and recommendations have significant implications for several of WHO's activities. In particular, they 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.

8. Rotavirus vaccines are at an advanced stage of development and there is considerable interest in WHO's facilitation of vaccine-introduction projects and pre-qualification. Until this Expert Committee meeting WHO had made no recommendation on production and quality control in order to provide regulatory guidance; now, these projects can progress.

9. The new recommendations for human plasma for fractionation will guide blood establishments in understanding and facilitating the implementation of appropriate procedures for the production and control of the starting plasma material, and in facilitating the provision of safe fractionated plasma

products at country level. They should also be helpful in instituting supervision by national regulatory authorities of the quality and safety of plasma for fractionation, either prepared locally or imported, thereby contributing to improved quality and safety of human plasma products worldwide. WHO has given priority to strengthening the regulation and regulatory oversight of the quality and safety of blood products, haematological products and in vitro diagnostic devices worldwide but, nevertheless the Committee strongly reiterated its opinion from 2004 that human and financial resources at WHO in this important field of global health remain inadequate and urgently need to be augmented.¹

EVALUATION OF CERTAIN VETERINARY DRUG RESIDUES IN FOOD

Sixty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives Rome, 22–28 February 2006²

Main recommendations

10. The Committee made recommendations on the safety of veterinary drug residues in food. Residues for monitoring purposes were defined, where appropriate, and maximum residue limits were recommended for drugs administered to food-producing animals in accordance with good practice in the use of veterinary drugs. It also made some general comments of relevance to its work and to the Codex Committee on Veterinary Drug Residues in Food, including considerations on compounds for which an acceptable daily intake or maximum residue limit could not be set or recommended, and recommendations on the principles and methods used in deriving those limits, for instance a new procedure for estimating chronic dietary intakes.

11. The Committee established acceptable daily intakes and recommended maximum residue limits for seven veterinary drugs: three antimicrobial agents (colistin, erythromycin and flumequine), two production aids (melengestrol acetate and ractopamine hydrochloride), one insecticide (trichlorfon (metrifonate)), and one anthelmintic (triclabendazole). In addition, the report describes the attempt by the Committee to investigate tylosin toxicologically on the basis of published data as none of the requested data had been provided. WHO will publish toxicological monographs on veterinary drug residues, which summarize the data.³ FAO will publish further information on the residues.⁴

Significance for public health policies

12. The Committee's work identifies and, if possible, quantifies the public health significance of veterinary drug residues in food through a scientific risk assessment. It highlights the complexity of the process, which includes assembling and analysing all relevant data; interpreting studies of, for instance, carcinogenicity, genotoxicity, reproductive toxicity and teratogenicity; extrapolating to human beings the effects observed in experimental animals; evaluating the relevance of available human data; and characterizing hazards to human beings on the basis of available toxicological and epidemiological data.

¹ WHO Technical Report Series, No. 932, 2005.

² WHO Technical Report Series, No. 939, in press.

³ *Safety evaluation of certain food additives*. WHO Food Additives Series, No. 57 (in press).

⁴ *Compendium of food additive specifications*. FAO Food and Nutrition Paper, in preparation.

13. Although all Member States face the problem of assessing potential risks of veterinary drug residues in food, only a few scientific institutions can assess the relevant toxicological and related data on a national or regional basis. Therefore it is important to provide Member States with valid information on both the general aspects of risk assessment and the specific evaluations on veterinary drug residues covered in this report. The Committee's complex work in reaching an international consensus in the evaluation of these compounds means that no other organization has a comparable importance and impact on public health decisions related to food safety.

14. The Committee's recommendations are used by the Codex Alimentarius Commission for setting international food safety standards. Such standards are established only for substances that have been evaluated by the Committee and have been allocated an acceptable daily intake or other relevant safety statement, so ensuring that food commodities in international trade meet strict safety standards.

15. The scientific advice from the Committee also directly serves Member States in setting up their national food safety programmes.

Implications for the Organization's programmes

16. The evaluation of chemicals in food by the Committee is an ongoing activity.

17. WHO is a partner in the Joint FAO/WHO Food Standards Programme, which administers the Codex Alimentarius Commission. The Committee's work is very important for the Commission.

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

EVALUATION OF THE ABUSE LIABILITY OF CERTAIN SUBSTANCES AND OTHER RELATED MATTERS CONCERNING CONTROLLED SUBSTANCES

Thirty-fourth report of the WHO Expert Committee on Drug Dependence¹ Geneva, 28–31 March 2006

Main recommendations

19. The Committee recommended that dronabinol and its stereoisomers should be rescheduled from Schedule II to Schedule III of the United Nations Convention on Psychotropic Substance, 1971. Also, the Committee recommended that oripavine be scheduled in Schedule I of the United Nations Single Convention on Narcotic Drugs, 1961, as amended by the 1972 Protocol. The Committee evaluated some other substances for their dependence-producing liability and decided not to recommend their scheduling in the drug-control conventions. However, for khat (*Catha edulis*) it recommended that national educational campaigns should be adopted in order to discourage use that may lead to adverse consequences.

20. The Committee recommended the pre-review or critical review of a number of substances during its next meeting.

¹ WHO Technical Report Series, 2007, in press.

21. The Committee decided to advise the Secretariat to draw the attention of countries to the fact that both the conventions include procedures for informing the United Nations: where a Party has information, which, in its opinion, might require an amendment to any of the Schedules, it should notify the Secretary-General and furnish him or her with the information in support of the notification, after which the Secretary-General will transmit such notification to WHO and other bodies.

22. The Committee also advised the Secretariat to urge countries once more to respond to questionnaires sent out by WHO in the preparation process for the evaluation of substances.

Significance for public health policies

23. The Committee discussed the scheduling of buprenorphine. This substance, used in the treatment of patients with opioid dependence, is included on the 14th edition of the WHO Model List of Essential Medicines. At present it is scheduled in Schedule III of the Convention on Psychotropic Substances, but its transfer to the Single Convention on Narcotic Drugs was proposed to the Committee's thirty-third meeting. No decision was taken then.

24. Buprenorphine is recognized as an efficacious and cost-effective treatment for opioid dependence (as are other medicines used in substitution therapy, such as methadone). Buprenorphine maintenance treatment programmes provide opportunities for prevention of HIV infection among opioid-dependent injecting drug users and support the implementation of directly observed antiretroviral therapy for people with opioid dependence who are infected with HIV. Such programmes can also act as a platform for promoting adherence to medical treatment of opportunistic infections.

25. A concern was expressed that transfer from one convention to the other could result in rescheduling at the national level, which would have the unintended effect of restricting access to buprenorphine for use in opioid substitution therapy. The Committee, having considered the unique pharmacological actions of buprenorphine and its expanded role in the treatment of opioid dependence, did not recommend any change in the present scheduling of the substance.

26. The Committee agreed that the Secretariat would organize a discussion on how to make best use of pharmacovigilance data for the evaluation of dependence and abuse potential.

27. The Committee noted that more than 80% of the world's population has no proper access to opioid analgesics, if required, and stressed that the appropriate national authorities should be encouraged to cooperate with WHO in consultation with the International Narcotics Control Board in order to assist in improving access to these medications. The Committee asked the Secretariat to suggest inclusion in the proposed agenda of the Committee's next meeting of an item on the impact of scheduling on the balance between medical availability of controlled substances and the prevention of their abuse.

Implications for the Organization's programmes

28. The evaluation of psychoactive substances for their dependence-producing liability is a continuing activity. If the budget will allow to do so, a next meeting will be organized in 2008.

29. The Committee agreed that its collaboration with the WHO Programme for International Drug Monitoring would be intensified.

30. The Committee noted, as it had already concluded on other occasions, that access to controlled medicines is insufficient in many cases, and it was therefore regarded as appropriate to establish an assistance mechanism for improving access to, and rational use of, such medicines. Therefore, the Committee agreed that it could contribute to promoting education and information about the appropriate use of controlled medicines.

31. The Secretariat is working on a plan to improve access to, and rational use of, controlled medicines, pursuant to resolutions of the Health Assembly and the United Nations Economic and Social Council requested the International Narcotics Control Board and WHO to examine jointly the feasibility of a possible assistance mechanism that would facilitate the adequate treatment of pain using opioid analgesics¹. The Committee recommended that a formal, regularly accessible forum would enhance the consultation of experts in this field and indicated its willingness to act as such.

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¹ Respectively resolutions WHA58.22 and 2005/25.