



WORLD HEALTH ORGANIZATION

EXECUTIVE BOARD
104th Session
Provisional agenda item 8

EB104/11
3 May 1999

Matters for information

Report on meetings of expert committees and study groups¹

Report by the Secretariat

SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Thirty-fifth report
Geneva, 21-25 April 1997²

Main recommendations

1. The report covers the extension and revision of *The international pharmacopoeia*, and the adoption of specifications on drug substances and drug products together with new International Chemical Reference Substances (now totalling 203) and International Infrared Reference Spectra (now totalling 69). The Committee also adopted revised General guidelines for the establishment, maintenance and distribution of chemical reference substances.
2. In relation to *The international pharmacopoeia*, the Committee recommended the use of basic tests for quick screening of drugs, for example at ports of entry. It endorsed the concept of using simple test methods to detect counterfeit pharmaceutical products.
3. The Committee recommended the revision of the guidelines on good laboratory practices for government laboratories carrying out drug quality control, as well as the external quality assessment of analytical results by a limited number of national and regional laboratories.
4. Two supplements to the main guidelines on good manufacturing practices for pharmaceutical products (GMP) were adopted, dealing respectively with the role, functions and training of “authorized persons” and with the manufacture of pharmaceutical excipients.

¹ The Regulations for Expert Advisory Panels and Committees provide that the Director-General shall submit to the Executive Board a report on meetings 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. 885, 1999.

5. The Committee recommended the preparation of draft guidelines on quality systems for GMP inspectorates and further review of the draft on pre-approval inspection. It adopted guidelines for the inspection of drug distribution channels, to monitor quality from the point of manufacture of medicines to their delivery.

6. The Committee encouraged the development of a system for the selection of comparator products to facilitate the establishment of interchangeability of multisource (generic) pharmaceutical products.

7. The Committee expressed strong support for the revised text of the guidelines on good pharmacy practice in community and hospital pharmacy settings originally developed by the International Pharmaceutical Federation, which it decided to reproduce in its report.

8. The Committee reviewed progress made on drug terminology, in particular within the International Nonproprietary Names programme, and endorsed the text entitled “National drug regulatory legislation: guiding principles for small drug regulatory authorities”.

Significance for public health policies

9. Ensuring the quality and safety of medicinal products is essential to protect the health of the end-users. This has been underlined by the repeated occurrence in various countries of cases of poisoning with diethylene glycol. Vigorous implementation of GMP in the local production of pharmaceuticals is the first prerequisite for prevention. However, as proposed by the Committee, international agreements should also be considered to strengthen preventive measures.

10. Special efforts have been undertaken to raise awareness of the need for regulatory measures covering the safety of and trade in starting materials - including active pharmaceutical ingredients and excipients - and GMP implementation. The participation and support of policy-makers and the entire public health community are required, involving both the public and private sectors.

11. Evidence shows that problems regarding the quality assurance of pharmaceuticals persist. This applies especially to the growing incidence of production, distribution and sale of counterfeit, spurious and substandard pharmaceutical products in both developing and industrialized countries. The statutory instruments, advice and recommendations provided in the Committee’s report can help national authorities - in particular drug regulatory authorities - to deal effectively with the prevention, detection and control of these problems.

Implications for the Organization’s programmes

12. The Organization must continue to promote a comprehensive approach to quality assurance of pharmaceutical products. It must also lead and coordinate the definition and harmonization of clear and practical standards and guidelines for pharmaceuticals at the international level, in particular to respond to the increased globalization of trade.

13. While the Organization seeks to enhance the rational use of scarce resources and consumers’ confidence in health care, its priority objective must be to ensure the safety, efficacy and quality of medicinal products for improved public health.

EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS

Joint FAO/WHO Expert Committee on Food Additives Forty-ninth report Rome, 17-26 June 1997¹

Main recommendations

14. The Committee evaluated the following food additives using normal toxicological procedures: one antioxidant (*tert*-butylhydroquinone (TBHQ)), three emulsifiers (microcrystalline cellulose and sucrose esters of fatty acids and sucroglycerides), two enzyme preparations ("acetolactate decarboxylase and maltogenic amylase), one flavouring agent (*trans*-anethole), one glazing agent (hydrogenated poly-1-decene), one sweetening agent (maltitol syrup), and salatrim (short- and long-chain acyltriglycerides). Acceptable Daily Intakes (ADIs) or temporary ADIs were allocated to all of these substances except for hydrogenated poly-1-decene and salatrim. The Committee prepared new or revised specifications for the identity and purity of the food additives that were evaluated toxicologically and considered specifications for 33 other food additives.

15. The Committee evaluated 223 flavouring agents belonging to six chemical groups and the flavouring agent allyl-2-furoate using the Procedure for the Safety Evaluation of Flavouring Agents. On the basis of toxicological, metabolic and intake data on these flavouring agents and their structural characteristics, the Committee concluded that all but five were of no safety concern. The evaluation of these five flavouring agents was postponed, pending consideration of other closely related substances.

16. Toxicological, epidemiological, and intake data on aflatoxins B, G, and M were evaluated, including qualitative and quantitative information on their hepatocarcinogenicity derived from a wide range of studies in both animals and humans. The Committee evaluated the potency of these contaminants, linked their potencies to intake estimates, and discussed the impact on sample populations and their overall risks of applying hypothetical standards for aflatoxin contamination in food. Using these potency estimates and intake data available at country level, governments can estimate the risks of liver cancer in the population.

17. Summaries of the toxicological and related information which served as the basis for the Committee's evaluation of the safety of these food additives and contaminants have been published separately by WHO.² Specifications have been published by FAO.³

Significance for public health policies

18. The Committee's work emphasizes the public health significance of the risk assessment of chemicals used in food. It highlights the complexity of the process, which includes assembling and analysing all relevant data; interpreting studies of carcinogenicity, genotoxicity, reproductive toxicity, teratogenicity, etc.; extrapolating to humans the effects observed in experimental animals; and assessing risks to humans based on available toxicological and epidemiological data.

¹ WHO Technical Report Series, No. 884, 1999.

² *Safety evaluation of certain food additives and contaminants*. WHO Food Additives Series, No. 40, 1998.

³ *Compendium of food additive specifications, Addendum 5*. FAO Food and Nutrition Paper, No. 52, Add. 5, 1997.

19. Although all Member States face the problem of assessing these risks, only a few scientific institutions can undertake such assessments at this stage; hence the importance of providing all Member States with valid information both on the general aspects of risk assessment and on specific food additives and contaminants.

20. The Committee's recommendations are used by the Codex Alimentarius Commission for setting international food standards. Such standards are established only for substances that have been evaluated by the Committee and have been allocated an ADI (food additives), or for which a tolerable intake level has been established or potencies have been estimated (contaminants). This ensures that food commodities in international trade meet strict safety standards.

Implications for the Organization's programmes

21. The evaluation of chemicals in food by the Committee is an ongoing activity. Provision is made in WHO's programme budget for 1998-1999 for convening four meetings of the Joint FAO/WHO Expert Committee on Food Additives, two on food additives and contaminants and two on residues of veterinary drugs in food.

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

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

THE USE OF ESSENTIAL DRUGS

Eighth report of the WHO Expert Committee Geneva, 1-5 December 1997¹

Main recommendations

24. The Committee reviewed previous work and updated the WHO Model List of Essential Drugs. It reaffirmed the relevance of the concept of essential drugs for national drug policies and outlined the criteria for the selection of listed substances and their pharmaceutical dosage forms.

25. The Committee emphasized the need for rigorous quality assurance and the importance of WHO's Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, particularly in countries with inadequate laboratory facilities for drug analysis and quality control. It stressed the importance of detecting adverse drug reactions and encouraged reporting and coordination in this regard with the WHO Collaborating Centre on International Drug Monitoring, Uppsala, Sweden. It highlighted the need for independent and up-to-date information on all essential drugs, and recommended further development of the WHO Model Formulary.

26. The Model List of Essential Drugs was revised in the light of therapeutic advances and such priority issues as antibiotic resistance and the treatment of asthma and diabetes. Important additions to the Model List include a new drug, triclabendazole, for the treatment of liver and lung flukes. Zidovudine (AZT) was also

¹ WHO Technical Report Series, No. 882, 1998.

introduced, for the specific treatment of HIV-infected pregnant women to reduce mother-to-child transmission and protect the newborn. A note on triple therapy for HIV/AIDS was included, to the effect that this new therapy exceeds the budgets of most national drug programmes and therefore AIDS treatment policies must be decided at country or institutional level. Several drugs were added to the Model List for the treatment of opportunistic infections in HIV/AIDS.

Significance for public health policies

27. More than 120 countries have developed their own essential drugs lists. These lists are used *inter alia* for the development of standard treatment guidelines, procurement and supply of drugs, training of health workers, promotion of local production of drugs of adequate quality, and reimbursement of costs in health insurance schemes. On the basis of the Model List, Member States select the essential drugs that best meet their own health needs and services. Lists of essential drugs should be drawn up locally and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management.

28. The biennial updating of the Expert Committee's report and the provision of complementary WHO model prescribing information must be seen in this context. They serve as an important focus for technical collaboration between industrialized and developing countries, and encourage academia and the pharmaceutical industry to tackle global health problems through continuous reappraisal of therapeutic practice and innovative research.

Implications for the Organization's programmes

29. The concept of essential drugs has been disseminated and promoted extensively at country level by WHO's Action Programme on Essential Drugs and all technical programmes involved in disease control and prevention. The Model List provides the Organization with a useful tool to promote the most cost-effective treatments and help countries to implement national drug policies. This is of particular importance for the cluster on Communicable diseases. The Model List has also been adopted by many international and bilateral agencies which now include drug supply and the rationalization of drug use in their health care programmes. This emphasizes the Organization's pivotal responsibility in coordinating work in this regard.

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