

1. Introduction

The WHO Expert Committee on Specifications for Pharmaceutical Preparations met in Geneva from 10 to 14 March 2003. Dr A. Asamoah-Baah, Executive Director, Health Technology and Pharmaceuticals, welcomed the Committee members and other participants on behalf of the Director-General, Dr Gro Harlem Brundtland.

In his opening remarks Dr Asamoah-Baah explained that since the last meeting of the Committee there had been more evidence of the globalization and harmonization of specifications for pharmaceutical preparations in general, and for pharmaceuticals used in the treatment of HIV, tuberculosis and malaria, in particular. He indicated that WHO was committed to helping to ensure the quality of pharmaceuticals and to treating HIV, tuberculosis and malaria. He added that although some patients were fortunate in having easy access to drugs, others were less so. However, there was cause for optimism with the creation of alliances to finance measures to fight HIV, tuberculosis and malaria. Dr Asamoah-Baah also highlighted the problem of counterfeit medicines which appeared to be greater than had originally been feared, and he emphasized the necessity for more heed to be paid to this problem. The issue of quality and safety of pharmaceuticals required appropriate attention.

The Committee was briefed on the WHO strategy for medicines and its focus on increasing access to quality medicines. He mentioned that the 20th century had been a period during which medical advancement had led to improved life expectancy, but that there was a gap between potential and reality due to lack of access to quality medicines. The Committee was also informed of the nomination of Dr J.W. Lee from the Republic of Korea, to replace Dr Brundtland as the Director-General of WHO. Dr Lee had been involved in the vaccine programme and will assume his new position in July 2003. His nomination coincided with the forthcoming period of consolidation which should result in better links between policy decisions and implementation of WHO activities. Medicine was a priority area in terms of support, developing pharmacopoeial standards and programmes focused on AIDS, tuberculosis and malaria. The Committee was assured of the commitment of the Essential Drugs and Medicines Policy Department to assuring quality medicines, from starting materials to the distribution of finished drugs to procurement agencies.

The WHO Strategy for Medicines laid out the basic aims from 2000 to 2003. Currently the strategy was being updated and comments sought on the main objectives, i.e. access and affordability, quality and safety,

rational use and policy development, which will put norms and standards in place to accomplish these objectives.

The Committee was informed about the wide range of activities undertaken by the Quality Assurance and Safety: Medicines (QSM) team. They were told of the need to continue work relating to the quality of medicines at WHO and to run activities in parallel so that there would be more rapid benefits at country level. Positive changes had already been seen but there was still much to be accomplished. Counterfeiting continued to be a major problem. The next International Conference of Drug Regulatory Authorities (ICDRA) scheduled for 2004 in Madrid, Spain would include a pre-conference meeting on counterfeit drugs which would be open to relevant parties. The Committee was informed about the new activities related to the model quality assurance for procurement and to pragmatic approaches in setting priorities. The safety of certain drugs was also a concern and required investigation. There had been increasing collaboration in the area of quality assurance of medicines within the Health Technology and Pharmaceuticals Cluster, with other clusters in WHO and with outside partners.

2. **General Policy**

2.1 **Tenth International Conference of Drug Regulatory Authorities, China, Hong Kong, Special Administrative Region**

Conference reports and recommendations made to the countries and to WHO were made available to the Committee. The Committee was informed that the next ICDRA would be held in Madrid, Spain in 2004, when a special session dedicated to pharmacopoeias had been proposed. In addition a pre-conference meeting on counterfeit drugs was planned.

2.2 **Side meeting to the tenth International Conference of Drug Regulatory Authorities**

The Committee was provided with the meeting report of the ICDRA side meeting entitled “Pharmacopoeial specifications — need for a worldwide approach?” dated 24 June 2002. The following recommendations were made during that meeting:

1. to hold an international meeting for those involved in the development of pharmacopoeial specifications;
2. to include the topic of pharmacopoeias on the agenda of the forthcoming ICDRA;

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3. to encourage international harmonization efforts by WHO to develop common specifications and international reference standards, with special focus on medicines for which no pharmacopoeial monographs currently exist, e.g. new drug entities and combinations or priority disease programmes of major health impact;
 4. to make every effort to help combat counterfeit drugs;
 5. to reinforce the close links between regulatory authorities and pharmacopoeias; and
 6. to discuss the importance of impurity profiles and limits at an international level, especially for internationally traded starting materials.

2.3 International Conference on Harmonisation

WHO is an observer to the International Conference on Harmonisation (ICH) and liaises with non-ICH countries by distributing information about ICH Guidelines. The Committee was provided with a paper entitled “The impact of implementation of ICH guidelines in non-ICH countries”. This report includes the issues relating to the application of ICH quality documents to generic drugs. The Committee was provided with an update on the new ICH guidelines on impurities and stability testing.

The Committee endorsed the collaboration between WHO and ICH, especially WHO’s participation in the working groups related to quality.

2.4 Pharmacopoeial Discussion Group¹

The Committee was updated on the collaboration between WHO and the Pharmacopoeial Discussion Group (PDG). WHO has participated as an observer at the last three PDG meetings. The next meeting is scheduled to be held in Brussels, Belgium in July 2003.

2.5 Counterfeit drugs

The Committee was informed about the increasing problem of counterfeit drugs. The Committee members stressed the need for a consistent definition of what constitutes a counterfeit drug that would help to assess the real extent of the problem and improve the clarity of case reporting. A working group composed of WHO, pharmaceutical industry associations and Centrale Humanitaire Medico-Pharmaceutique (CHMP), is working to devise solutions to this

¹ The Pharmacopoeial Discussion Group is composed of the United States Pharmacopeia and the European and Japanese Pharmacopoeias, with WHO as an observer.

widespread problem. In addition, a new project in Asian countries is under way to study the situation in the national context. Notwithstanding the difficulties identified, the Committee re-endorsed the recommendation made in its previous report (*I*).

2.6 **Traditional medicine**

The Committee was presented with a progress report on WHO's work related to herbal medicine and which introduced the WHO Traditional Medicines Strategy: 2002–2005 for which the four major objectives are:

- framing policy;
- enhancing safety/efficacy/quality;
- ensuring access; and
- promoting rational use.

Several new technical documents on herbal medicines had been produced and had been circulated for comments before their finalization, while other finalized documents had been translated into various languages.

The Committee noted that in some countries herbal medicinal products were considered as food or as dietary supplements and their regulation might therefore be different from that of normal pharmaceutical products.

Members offered their support for the implementation of the new guidance documents the subjects of which included safety monitoring and quality assurance.

The Committee was informed that resolution EB 111.R12 on traditional medicine had been recommended by the one-hundred and eleventh session of the WHO Executive Board for adoption at the fifty-sixth World Health Assembly in May 2003.

The Committee commended the good work undertaken by WHO in this area and encouraged its continuation.

2.7 **Malaria**

The Committee was updated on the progress of the Roll Back Malaria programme and was informed that the past year had seen a rapid emergence of resistance to antimalarials and suggested that one-drug therapy might no longer be appropriate. It was reported that in 2000–2001 increased resistance to common antimalarials used in monotherapy had been recognized; WHO had therefore recom-

mended the use of combination drugs as more appropriate. However, quality standards for these combinations might not exist in the public domain. It had therefore been recommended by experts on malaria that the development of specifications for quality control should be expedited. The Committee expressed concern that fixed-dose combination drug products were more complicated to manufacture and analyse. In some cases the information available about their safety, efficacy and quality was inadequate. The Committee was also concerned about the results of a study undertaken in the sub-Saharan region that reported on the distribution of substandard quality and counterfeit antimalarial products.

The Committee urged the WHO Secretariat to address these pertinent issues.

2.8 **Biologicals**

The Committee was informed about a current joint effort with QSM in the area of vaccines to assess the capacity of some national regulatory agencies and to identify their needs. One of the major deficiencies identified so far in the assessment had been in the area of postmarket surveillance monitoring. Another example of collaboration with the Expert Committee on Biological Standardization was its technical advice to the International Nonproprietary Names Programme.

2.9 **Risk related to transmissible spongiform encephalopathy**

The Committee was informed of the results of the WHO consultation held in February 2003 on transmissible spongiform encephalopathy (TSE) and indicated that the main concerns with this disease were its transmission from animals to humans and possibly from human to human. There were links between variant Creutzfeldt-Jakob disease (vCJD) and bovine spongiform encephalopathy (BSE). There had been fewer cases of BSE reported in recent years in the United Kingdom as a result of precautionary measures, whereas in the rest of Europe and other parts of the world the trend was increasing, although on a much smaller scale. It is not yet known if the current situation will continue. Products of ruminant origin of interest to the Committee were gelatin, bovine blood derivatives, tallow derivatives, milk and milk derivatives (lactose) and amino acids. In addition to measures already taken, the Committee re-emphasized the need to continue to raise awareness of the possible risk associated with these products through publication of guidelines, inclusion of requirements in pharmacopoeias, and improving the traceability of products. The

possibility of applying WHO's rapid alert system to starting materials had also been discussed.

2.10 **Bioequivalence**

The Committee was presented with the first results on comparative dissolution testing studies, using in vitro testing under conditions that may be used to indicate bioequivalence. The subjects of discussion included bioequivalence studies for fixed-dose combination products; the difficulty in conducting bioequivalence studies in some countries; the need for proper guidance; and the possibility of phasing in bioequivalence requirements for certain drugs or of waiving in vivo bioequivalence requirements for some dosage forms (e.g. liquids) based on existing knowledge.

The Committee acknowledged the good guidance provided by WHO and the need to apply a risk analysis-based approach in the field of bioequivalence. Future work should include the review and update of current guidance, noting that in vitro dissolution testing could be considered as an indicator of possible bioequivalence problems.

Bioequivalence is significant only if compliance with good manufacturing practices and sourcing of active pharmaceutical ingredients (API) are well controlled. The Committee endorsed the need for a review and an update of the existing WHO guidelines on bioequivalence.

3. **Quality control — specifications and tests**

3.1 ***The International Pharmacopoeia***

Volume 5 of the third edition of *The International Pharmacopoeia* is now available. The Committee was informed that revision of some of the general methods of *The International Pharmacopoeia* described in other volumes, as well as the development of new methods, are needed. It is intended that the amendments made to previous volumes will be incorporated in an updated version, to be made available in CD-ROM format.

The Committee endorsed the recommendation and assured WHO of their continued support and willingness to participate in this exercise.

3.2 **Dissolution test requirements**

The work on "In vitro dissolution testing methods for oral immediate-release drug products containing Biopharmaceutical Classification

Scheme (BCS) class I drugs”, was presented to the Committee. The methods include a recommended test procedure for inclusion in *The International Pharmacopoeia*.

The Committee praised this work. It recommended that the document be circulated for comments and for validation of the proposed methods prior to its adoption.

3.3 Specifications for radiopharmaceuticals

The representative of the International Atomic Energy Agency (IAEA) presented an update of the joint effort of WHO and the IAEA in radiopharmaceuticals, as well as a draft report of the consultation on monographs and specifications for radiopharmaceuticals held in Geneva on 16–17 December 2002. It was reported that the expert group had recommended that the general methods as contained in the third edition of Volume 1 of *The International Pharmacopoeia* be replaced with the revised version.

The Committee endorsed the recommendation and also recommended that work commence on the specific monographs.

3.4 Quality specifications for antituberculosis drugs

The Committee was presented with a status report on work undertaken on methods for conducting screening tests and specifications for antituberculosis drugs that were currently being developed and validated entitled “Quality specifications for antituberculosis drugs”.

The Committee recommended that this work should continue.

3.5 Quality specifications for antimalarials

The Committee received a status report on work carried out on screening test methods and specifications for antimalarials that were currently being developed and validated entitled “Quality specifications for antimalarials”. Reference was made to Volume 5 of the third edition of *The International Pharmacopoeia* where it was indicated that International Chemical Reference Substances were required for these tests. These were being developed by the WHO Collaborating Centre for Chemical Reference Substances in Sweden. During the discussion, questions were raised about the issue of different strengths of the same medicine being recommended and leading to irrational drug therapy. This issue will be referred to the Roll Back Malaria programme.

The Committee commended the availability and quality of the monographs on antimalarials published in Volume 5 of *The International Pharmacopoeia* and recommended that the work be continued (see also section 2).

3.6 **Pharmacopoeial monographs on antiretrovirals**

The Committee was provided with a document entitled “Quality specifications for antiretrovirals” which described work being carried out on the development of specifications of certain antiretroviral drugs. This project was developed as a result of a recommendation made by the Expert Committee at its thirty-seventh meeting, and of the tremendous political pressure to make quality antiretroviral agents more readily available to disadvantaged HIV-positive persons. It was indicated that when these monographs become available they should be widely distributed for further consultation and validation.

The Committee expressed its support for the work and asked to be kept informed of its progress and results.

3.7 **Quality control — specifications for excipients**

The Committee was informed of the work in progress by the Pharmacopoeial Discussion Group (PDG) on harmonizing specifications for excipients. The discussion that followed highlighted the fact that some excipients were of a potentially high-risk nature. It was agreed to accept the offer of the PDG to publish monographs on those excipients harmonized to date in the next volume of *The International Pharmacopoeia*. It was further recommended that WHO should indicate differences in tests where they exist, in order to facilitate a better understanding of the harmonized monographs.

4. **Quality control — International Reference Materials**

4.1 **International Chemical Reference Substances**

The reports of the WHO Collaborating Centre for Chemical Reference Substances for 2001 and for 2002 were presented to the Committee.

It was reported that, despite staffing problems, the Centre continued to meet the demand for reference standards. Questions were raised on the absence of expiry dates on the reference substances supplied. During the discussion it was emphasized that reference substances were monitored by the issuing laboratory. The Committee acknowl-

edged the opinion of the EDQM representative who clarified that auditors using ISO 17025 had agreed to consider the practice of not giving expiry dates as acceptable. General guidelines for the establishment, maintenance and distribution of chemical reference substances can be found in the Thirty-fifth report of the Expert Committee on Specifications for Pharmaceutical Preparations (2).

The report for 2001 was accepted and the Committee expressed its appreciation of the support given by Apoteket in providing these reference standards at a minimal cost. Any further comments received on the Centre's report within the deadline will be forwarded to the Centre for appropriate action.

The Centre's report for 2002 was circulated for distribution and further comments. A document was presented to the Committee and a proposal made to disestablish some 13 of these standards as they are no longer required or requested. In addition, it was recommended that where the reference substances had either been disestablished (e.g. biological reference materials), or were subject to international customs controls, that monographs in *The International Pharmacopoeia* be revised.

It was noted that because there would be a delay between the disestablishment of reference standards and publication of the new monographs, the old standards should be temporarily retained. The proposals were accepted.

The Centre for International Chemical Reference Substances can be contacted at the following address:

WHO Collaborating Centre for Chemical Reference Substances
Apoteket AB
Produktion & Laboratorier
Centrallaboratoriet, ACL
Prismavägen 2
SE-141 75 Kungens Kurva, Sweden
Fax: + 46 8 740 60 40 or e-mail: who.apl@apoteket.se

The International Reference Materials available from the Centre, including both International Chemical Reference Substances (ICRS) and International Infrared (IR) Reference Spectra, are listed in Annex 1.

4.2 International Infrared Reference Spectra

To promote a more efficient process for the review and adoption of pending and future IR Spectra, it was proposed to take advantage of

new technology such as e-mail to transmit spectra. Only contentious spectra would be discussed at meetings. The proposal was endorsed and the Committee acknowledged the contribution of the WHO Collaborating Centre for International Infrared Reference Spectra, Zurich, Switzerland. Members expressed their appreciation to the Swiss Federal Institute of Technology for providing the resources necessary for the activities of the Centre.

5. Quality control — national laboratories

5.1 Equipment for model quality control laboratories

The Committee was informed that the document providing information on the cost of equipment for model quality control laboratories entitled “Cost estimate of equipment for model quality control laboratories” was being revised to include the technical specifications for each item of equipment as requested by the Expert Committee at its thirty-seventh meeting.

5.2 External quality assurance assessment scheme

Two documents and the summary report from the European Directorate for the Quality of Medicines were presented to the Committee. It was noted that 36 laboratories, i.e. six in each WHO Region, randomly numbered in each report, had participated in this second phase of the external quality assessment scheme.

The Committee noted that this was a valuable exercise providing insight into the realities of the proficiency of drug quality control laboratories. It was also seen as a tool to help laboratories to improve their performance by serving as a benchmarking exercise.

The Committee expressed its appreciation of the work done and recommended continuation of these efforts. It was further recommended that the names of participating laboratories be included in the list of acknowledgements of the Expert Committee report.

6. Quality assurance — good manufacturing practices

6.1 Excipients

The Committee was informed of the efforts made by various parties in the area of good manufacturing practices (GMP) for excipients.

However, the Committee saw no need to revise the current version of the WHO supplementary GMP for excipients as it was found to be satisfactory in its present form (3).

6.2 **Heating, ventilation and air conditioning**

The Committee was provided with the first draft of the supplementary guidelines on GMP for heating, ventilation and air conditioning (HVAC) systems. The document will enter the consultation process and be included in the agenda of the next meeting of the Expert Committee.

The Committee commended WHO for its work on this subject.

6.3 **Herbal medicinal products**

The Committee was informed that a process for the revision of the WHO supplementary guidelines for the manufacture of herbal medicinal products had been initiated (4). A modified version of the guidelines would be submitted to the Expert Committee at its next meeting. Although some concerns about validation requirements were expressed, the Committee recommended the retention of the validation requirements as an important part of quality assurance of drugs. It also stressed the importance of proper packaging and labelling for these products.

6.4 **Validation**

The Committee was informed that a new WHO text for a supplementary GMP guideline on validation had been prepared and circulated for comments. A modified version would be submitted to the Expert Committee at its next meeting.

6.5 **Water for pharmaceutical use**

The Committee was informed that the supplementary GMP text on water for pharmaceutical use was being distributed for comments. The document had been written in a format different to that of the usual GMP texts. The Committee recommended that the document be separated into two parts: a general section and a section on GMP.

7. **Quality assurance — inspection**

7.1 **Strengthening of Pharmaceutical Manufacturing Inspection project and development of training modules for inspectors**

A presentation on the Strengthening of Pharmaceutical Manufacturing Inspection (SPMI) project and on the new training modules recently developed for inspectors was made to the Committee.

The aim of the SPMI project was to consolidate and extend upon the achievements of the first project entitled: “Promoting of the Implementation of GMP” (1998–2000) and to focus on strengthening the pharmaceutical manufacturing inspectorates by developing networks and using the CD-ROM of WHO basic training modules on GMP. A total of 240 participants from 47 countries had undergone the training and about 5800 copies of the CD-ROM had been distributed. The materials had been translated into Spanish by the WHO Regional Office for the Americas/Pan American Health Organization (PAHO) and into Chinese by the State Drug Administration (SDA), China. The Spanish version had been utilized by PAHO in the Region of the Americas, where 571 individuals had received training. The SDA had run five training courses during 2002.

Supplementary training modules on the subject of “Validation”, “Water for pharmaceutical use” and “Air handling systems” had also been developed and were almost ready for distribution.

The efforts undertaken with the SPMI project may assist in providing a consistent application of the requirements in the inspection process. The Committee acknowledged that the project would assist in strengthening and improving the inspection process. Members commended the WHO project staff for their initiative and their success in raising the awareness of GMP around the world.

8. **Quality assurance — distribution and trade-related**

8.1 **Good trade and distribution practices for pharmaceutical starting materials**

The Committee was informed that a number of incidents involving diethylene glycol had resulted in a World Health Assembly resolution (WHA52.19) which had triggered the preparation of the GTDP and of the recommendations on good trade and distribution practices for pharmaceutical starting materials. The Committee was informed that the new guidelines, which focused on GMP and good storage

practices (GSP) related to activities, such as repackaging and relabelling, involved in the distribution of starting materials, had been widely circulated and the resulting comments incorporated. It was recognized that the implementation of this guidance could also assist in reducing the occurrence of counterfeit drugs. After discussion the Committee recommended the adoption of this guidance (Annex 2) with some minor additions reflecting the outcome of the discussions.

8.2 **WHO Pharmaceutical Starting Materials Certification Scheme for use in international commerce**

The Committee considered the new WHO Pharmaceutical Starting Materials Certification Scheme (SMACS) for which two model certificates were proposed: one for issue by national authorities and the other for completion by manufacturers of starting materials. The concept of this scheme was presented and discussed during the tenth ICDRA as suggested by the Expert Committee at its thirty-sixth meeting.

After a discussion about the implementation of the minimum requirements by the relevant authorities, it was suggested that the scheme should be reviewed after a pilot phase. Additionally, QSM should develop training materials on this subject. The Committee members supported the proposal and adopted the document for submission to the World Health Assembly (Annex 3).

8.3 **WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce**

The Committee was briefed on the implementation of the scheme in which about 140 members were participating. The Committee was also briefed on the recommendations made at the ICDRA in 1999 on the issue of certificates.

The Committee was informed of some cases where WHO-type certificates were issued:

- by authorities that did not meet the conditions specified in the WHO guidelines for the implementation of the scheme;
- for manufacturers not meeting WHO GMP standards; or
- by authorities that were not party to the scheme.

The issue of differences in the implementation of GMP requirements was also raised. The Committee suggested that every effort should be made to ensure the credibility of the certification scheme which was based on self-assessment by the participating country.

The Committee agreed that a small working group be formed to discuss the current status of the certification scheme, and recommended further measures to improve its effectiveness for presentation to the next Expert Committee meeting.

9. **Quality assurance — risk analysis**

9.1 **New approach to inspections and manufacture**

Documents related to the use of parametric release and a risk analysis approach for the inspection process were provided for the Committee's information and discussion. It was noted that the principle of risk analysis was being used in a variety of settings and could possibly be used by drug regulatory authorities, especially those with limited resources.

The Committee considered the approach to have value and recommended that the issue be reconsidered in the future.

10. **Quality assurance — drug supply**

10.1 **Pre-qualification of manufacturers for the procurement and sourcing of pharmaceutical products**

The Committee was informed of the background and progress of the WHO procedure for the pre-qualification of suppliers and pharmaceutical products (5).

The purpose of this procedure was to verify that pharmaceutical products and manufacturers met the specifications and standards set by WHO. As an additional benefit, those manufacturers that adopt this programme would serve as an example to others because the manufacturers that did adopt it would receive international recognition. The Committee emphasized the need for preserving the confidentiality of information and for selecting competent inspectors and evaluators.

The Committee discussed issues related to the inspection of sites per product rather than a global GMP inspection, to donations of drugs that might not be subject to inspection, and to confidentiality. The Committee noted that pre-qualification for vaccines was handled by another department in WHO and the focus of the project discussed here was on medicines used in treating HIV/AIDS, tuberculosis and malaria.

The Committee noted that drug regulatory authorities would also benefit as inspections were carried out by teams of inspectors, including those from the Pharmaceutical Inspection Co-operation Scheme (PIC/S), signatories, WHO staff and local representatives from the drug regulatory authority inspectorates of the countries involved.

The Committee commended the good work in developing the documents discussed below and acknowledged the need for a pre-qualification programme.

10.2 **Pre-qualification of quality control laboratories**

A draft procedure for assessing the acceptability, in principle, of quality control laboratories for use by United Nations Agencies was presented to the Committee. Suggestions for additions to the document were made (e.g. a standard operation procedure document describing the infrastructure of the laboratories, etc.). The Expert Committee suggested that laboratories that were accepted following this suggested procedure could also be used by other countries for the same activities. It was recommended that certification under ISO 17025 should be taken into consideration when laboratories were assessed by WHO.

The Committee accepted, in principle, the text as a working document. Suggestions made would be taken into consideration by the Secretariat and a revised version would be distributed by e-mail for approval (the final document will be published as an annex) (Annex 4).

Guidelines for drafting a laboratory information file were presented to the Committee. The Committee accepted, in principle, the document as a working document. Suggestions made would be taken into consideration by the Secretariat and a revised version would be distributed by e-mail for approval (the final document will be published as an annex) (Annex 5).

10.3 **Pre-qualification of procurement agencies**

The draft procedure for assessing the acceptability, in principle, of procurement agencies for use by United Nations Agencies was presented to the Committee and discussed.

Comments were made on the content of the next version of the document, i.e. to include the definition of the term procurement agency, and address the issues of complaint handling, recalls and traceability of the product after distribution, to protect against diversion.

The Committee accepted, in principle, the document as a working document. Suggestions made would be taken into consideration by the Secretariat and a revised version would be distributed by e-mail for approval (the final document will be published as an annex) (Annex 6).

Guidelines for drafting a procurement agency information file were presented to the Committee and discussed. Suggestions were made for the inclusion of additional information to be submitted on requirements regarding personnel and storage requirements.

The Committee accepted, in principle, the document as a working document. Suggestions made would be taken into consideration by the Secretariat and a revised version would be distributed by e-mail for approval (the final document will be published as an annex) (Annex 7).

Draft interim guidelines for the assessment of a procurement agency were presented to the Committee and discussed. These interim guidelines would be used during the transition period until the final document (model quality assurance system) becomes available.

The Committee suggested that the checklist should be considered as basic, some of the criteria be considered as essential, and others should be classed as desirable or expected. The outcome should be monitored to assess its impact on the delivery of quality drugs.

The Committee accepted the document, in principle, as a working document. Suggestions made would be taken into consideration by the Secretariat and a revised version would be distributed by e-mail for approval (the final document will be published as an annex) (Annex 8).

The second draft of a model quality assurance system for pre-qualification, procurement, storage and distribution of pharmaceutical products was considered by the Committee. The Committee was informed about the background that led to the development of this document and received an explanation of the urgent need for this document to be finalized. The Committee was also informed that many comments on the document had already been received and that these were being processed by the Secretariat.

When reviewing the document, the Committee stressed the need to involve the drug regulatory authorities in the approval process and recommended that the role of the regulatory authority be clearly defined in the text. As guidelines related to quality assurance are not always respected, the Committee recommended that the document

should urge countries to ensure that all pertinent activities be performed in accordance with the relevant guidelines. The issues of bioequivalence, storage conditions and delivery were also raised in the discussion, reflecting their importance for the assurance of drug quality.

The Committee accepted the document, in principle, as a model that could be assessed and modified as necessary. It was further agreed that the Secretariat should produce a revised version, taking into consideration the comments made during the discussion. The Committee agreed, on the basis of urgency, to make the revised text available for use as an interim text. As it was anticipated that the document would be finalized before the end of 2003, it was further agreed that it would subsequently be presented for inclusion in the report of the next meeting of the Expert Committee.

10.4 **Pre-qualification procedure for procurement of HIV/AIDS drugs**

The Committee was informed of WHO's pilot project, being conducted in conjunction with the United Nations Children's Fund (UNICEF), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the United Nations Population Fund (UNFPA) and with the support of the World Bank, to test the system for the pre-qualification of suppliers of HIV/AIDS drugs. This included:

- dossier evaluation;
- samples for analysis; and
- manufacturing site inspection.

Only manufacturers of dosage forms were subject to inspection under this programme (the manufacturers of active pharmaceutical ingredients were not to be inspected at this time, but the possibility of such inspections being required in the future was not to be excluded). The Committee was briefed on the number of quality defects found in the course of this project and recommended that all possible efforts should be made to ensure budgetary support for its continuation.

11. **International Nonproprietary Names programme**

The Committee was presented with a progress report of the work carried out since the previous meeting of the Expert Committee. The International Nonproprietary Names (INN) cumulative list was now available on CD-ROM and on a database that would facilitate searches. It was also planned to have applications submitted over the

Internet as well as further computerized processes to facilitate publication preparation. The link with the updated pharmacopoeial database, which is a compilation of monographs available in major pharmacopoeias, was also mentioned.

The Committee was informed of the workplan, progress and future challenges of this programme. The Committee was also informed that priority continued to be given to upgrading the database architecture and functionality.

The Committee noted that a small panel of experts had been formed to advise on issues relating to compounds in the area of biologicals in close collaboration with the Expert Committee on Biological Standardization.

The Committee was also informed of the plans for naming excipients. The Committee endorsed this plan because the consistent naming of excipients would be useful for the GTDP effort.

The Committee was informed about a proposed revision of “The procedure for the selection of recommended INNs for pharmaceutical substances” which was under discussion by the Executive Board.

The Committee commended the close collaboration with the WHO Expert Committee on Biological Standardization as well as the success of the INN programme, and encouraged their continued effort.

12. **Miscellaneous**

12.1 **Launch of *The International Pharmacopoeia*, Volume 5**

The new volume of *The International Pharmacopoeia* was presented to the Committee. This document includes 72 new monographs, 15 of which are for antimalarials, and contains monographs for artemisinin derivatives and their dosage forms for finished products. It was noted that no other pharmacopoeia had such complete monographs for this type of drug. In addition, a number of new test methods and general requirements were included in this volume. The Committee highly commended the good work that had resulted in the new volume.

12.2 **Global Alliance for Quality of Pharmaceuticals**

The Committee was provided with an update of the plans to launch a Global Alliance for Quality of Pharmaceuticals. There was evidence to show that problems related to the quality assurance of pharmaceuticals persisted. This applied especially to the growing problem world-

wide of the production, distribution and sale of counterfeit, spurious and substandard pharmaceutical products. In addition to being a waste of money for the people who buy them, counterfeit and substandard drugs prolonged treatment periods, exacerbated the conditions being treated, led to increased drug resistance and could even cause death.

A recommendation was made at the last ICDRA that WHO should work with other partners to address these problems jointly. Partnership was initially envisaged with PIC/S, the International Pharmaceutical Federation (FIP) and national pharmacopoeias. The objectives of the Alliance would be to:

- increase awareness of the importance of the quality, safety and efficacy of medicines through advocacy and promotion;
- promote assistance to countries to improve their access to good quality medicines;
- promote measures to eliminate the manufacture, distribution and sale of poor quality medicines with special focus on those used in the treatment of life-threatening conditions; and
- promote cooperation between international and national organizations to improve the quality of medicines.

There were presently a number of participants, but there is a possibility of others joining in the future.

The Committee was in favour of WHO's efforts to establish a Global Alliance for the Quality of Pharmaceuticals in response to challenges relating to the quality of medicines.

12.3 WHO Medicines Strategy 2004–2007

The Committee was presented with the new proposed framework for the WHO Medicines Strategy 2004–2007 on which comments were being sought by 15 May 2003. The document outlined the policy aspects, the challenges envisaged, measures to meet these challenges and benchmarks for the assessment of achievement. It was emphasized that although there had been some broad consultations with various stakeholders in drafting the document, it was still in its initial consultation phase, and could benefit from input by Committee members.

In discussing the documents, the Committee felt that it would have been easier and more beneficial to compare the objectives and expected outcomes of the 2004–2007 plan with those from 2000–2003. This would have enabled its members to assess to what extent the

objectives of the old plan had been met; this knowledge could then have been used as a measure for the potential success of the new plan. It was also felt that although provision for training was made in the document, greater emphasis on the development of human resources would be desirable, particularly for personnel in community pharmacies in rural areas, such as chemical vendors, and for personnel involved in GMP and GTDP. Members felt that although patent protection could be an incentive to research and development of new drugs for target diseases, its considerable cost could also be a stumbling block to making drugs available more cheaply to vulnerable groups, and to future research on treatments for HIV/AIDS, tuberculosis and malaria in developing countries.

Notwithstanding the questions raised, the members were unanimous in accepting the document as a good working draft. The Committee recommended that the WHO Secretariat should take the suggestions into consideration and re-circulate the revised document for further study.

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