The main points addressed in this short summary are the basics of all the World Health Organization (WHO) Expert Committees. Addressed specifically will be the WHO Expert Committee on Specifications for Pharmaceutical Preparations together with the outcome and recommendations of its 44 meetings and their conclusions.

**WHAT IS A WHO EXPERT COMMITTEE?**
An Expert Committee is the highest official advisory body to the Director-General of WHO as well as to all the Organization's Member States. An Expert Committee is established by the WHO World Health Assembly (WHA) by an Executive Board (EB) decision. It is governed through rules and procedures that have to be strictly adhered to. Within the WHO Expert Committee meetings there are different types of participation. There are “members” who are selected from WHO Expert Advisory Panels; there are “temporary advisers” and there are “observers” such as international organizations, nongovernmental organizations and professional associations.

The Expert Committee Rules and Procedures of WHO can be found in the WHO Basic Document series. More importantly they can be found in the WHO Constitution. Reference is made to Expert Committees in Chapter V, Article 18, as well as in Chapter VIII, Articles 38-40. The normative function for pharmaceuticals can be found in Chapter 2, Article 2 (u), which reads that “the function of WHO is to develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products”.

In addition to the Constitution, regulations for Expert Advisory Panels and Committees are also included in a special Annex which is entitled *Rules of Procedure for Expert Committees*, and all these are published, as mentioned before, in the WHO Basic Documents series. There are various types of WHO Expert Committees. For example, there is the Expert Committee on Biological
Standardization which is as old as the Expert Committee on Specifications for Pharmaceutical Preparations. In addition there is the Expert Committee on Drug Dependence, the Expert Committee on the Selection and Use of Essential Medicines and there is a joint WHO/FAO Expert Committee on Food Additives. These Expert Committees are presently the most active in WHO.

When did the work of the Expert Committee on Specifications for Pharmaceutical Preparations start? This goes back far into the 20th century when the so-called Brussels agreement was signed in 1929, which mentioned the “International Pharmacopoeia” for the first time. The work continued under the League of Nations and the first international pharmacopoeia meeting was held in 1937, again under the auspices of the League of Nations, where experts from Belgium, Denmark, France, the Netherlands, Switzerland, the United Kingdom and the United States of America participated. In 1947 the Interim Commission of WHO took up the health-related work of the League of Nations and with that also the work of the international pharmacopoeia. In 1948 during the first World Health Assembly, the Expert Committee on Unification of Pharmacopoeia - which was the title at the time - was established.
The International Pharmacopoeia

In 1951 the World Health Assembly modified the name to the Expert Committee on the International Pharmacopoeia. Again, there was a renaming in 1959 by the World Health Assembly where it was modified to the Expert Committee on Specifications for Pharmaceutical Preparations, a title which remains to this day. Going back to the meetings, the first WHO Expert Committee on Specifications for Pharmaceutical Preparations was actually held prior to the first World Health Assembly from 13 to 17 October 1947. The report of that first meeting was published in English and French in the Official Records of WHO, No. 8, page 54ff, in 1947. The report of the fourth meeting of this Expert Committee was published as the very first WHO Technical Report Series, No. 1 in January 1950. Again, this report was published in English and French.

The International Pharmacopoeia is available for implementation and is ready for use by WHO Member States. Since 1975 the focus of The International Pharmacopoeia has been changed. Prior to that date it encompassed all the medicines that are available and sold globally. The focus is now on the Model List of Essential Medicines and those medicines recommended by WHO specific disease programmes, for instance malaria, tuberculosis, HIV/AIDS and medicines for children.

WHO has been working on the Fourth Edition of The International Pharmacopoeia with its first supplement; the second supplement being in preparation. The International Pharmacopoeia, Fourth Edition, is available in CD-ROM format, online, on the Web and is also in printed form. Together with the pharmacopoeia, there are the International Chemical Reference Substances (ICRS) which are needed in order to validate the procedures. From 1946 until 2009 the WHO Collaborating Centre for Chemical Reference Substances was in Sweden. Since 2010 the European Directorate for the Quality of Medicines and HealthCare (EDQM) located in the Council of Europe, Strasbourg, France, has been taking care of these activities.

NOWADAYS this Expert Committee covers far more than just pharmacopoeial issues. It covers all the quality assurance aspects within the medicines area, as well as recently the development of medicines. For a long time it has covered production, quality control, quality control regulatory guidelines, inspection and distribution. Thus it covers the entire chain from development through to delivery to the patient, meaning that everything is included in the entire supply of medicines.
**MEDICINES QUALITY ASSURANCE**

There are currently 56 official WHO guidance texts and guidelines for medicines quality assurance, and in 2009 seven guidelines were adopted; four were updated and there were three new ones.

**MANUFACTURE AND PRODUCTION**

Within the area of manufacture and production there are currently 18 (different) guidance documents mainly covering the aspects of good manufacturing practices (GMP), which consist of 12 major guideline texts. Work is ongoing on five texts discussed during the 45th meeting of the Expert Committee held in 2010, four proposals for revision and one new text. The area of production and manufacturing also covers training materials with training slides, a training video and the full GMP text on a CD-ROM and also in printed form.

In this area WHO also published in 2001 a risk analysis document in accordance with the hazard analysis and critical control point (HACCP) principles. Regarding inspection, currently there are six documents and guidelines including a quality system for inspectorates, pre-approval inspection and inspection of manufacturers and distribution channels. Regarding quality control, there are currently 12 guidance documents and guidelines including, most importantly, good laboratory practices and its training materials, guidelines for establishment of chemical reference standards, model certificate of analysis and, of course, *The International Pharmacopoeia*, which is additional to the aforementioned 12 guidance documents, and also to the basic test series.
OTHER REGULATORY GUIDELINES
There are 17 guidance documents and guidelines available as regulatory standards, including stability testing requirements for regulatory purposes, and various guidance texts regarding the interchangeability of generic/multisource products. Fixed-dose combination is also addressed in a separate guidance and several prequalification procedures are also available under this category.

DISTRIBUTION
Under the category of distribution, the Expert Committee has adopted nine current guidance documents and guidelines, including a certification scheme for finished products circulating in international commerce and also a certification scheme for pharmaceutical starting materials. There is also a guidance on the quality system for procurement and good distribution practices for starting materials and finished products; and last but not least good storage practices.

PARTNERS
Partners in the WHO Expert Committee on Specifications for Pharmaceutical Preparations are numerous. Most importantly we work with representatives from national and regional authorities, international organizations such as the Joint United Nations Programme on HIV/AIDS (UNAIDS), United Nations Population Fund (UNFPA), United Nations Children's Fund (UNICEF), the World Bank, World Intellectual Property Organization (WIPO), World Customs Organization (WCO), World Trade Organization (WTO), international professional and other associations, nongovernmental organizations including consumer associations, Médecins sans frontières (MSF), as well as industry associations such as International Federation of Pharmaceutical Manufacturers Associations (IFPMA), International Generic Pharmaceutical Alliance (IGPA) and World Self-Medication Industry (WSMI); and not forgetting the health professionals such as the International Pharmaceutical Federation (FIP) and the World Medical Association (WMA), etc. One of the pillars of the work is, of course, carried out by the members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations. The selection and nomination of this panel is governed by the strict rules and procedures adopted by the WHO World Health Assembly.
WHO EXPERTS

How does one become a World Health Organization expert in the real sense of being able to use the title? There is an official nomination process to a WHO Expert Advisory Panel; a proposal based on the education and background as well as the experience of the person to be nominated in consultation with the Member State of which the expert is a citizen. In addition to clearance through the Member State, the respective WHO regional office is also consulted as well as colleagues in headquarters. The first nomination is for four years and there is the possibility of a renewal for one, two, three or four years.

Most partners in the work of the Expert Committee on Specifications for Pharmaceutical Preparations are specialists from different quality assurance areas. For instance, when there is work on heating and ventilation systems engineers are consulted to ensure that the guidelines reflect the current knowledge in this specific area. We also work closely with WHO collaborating centres which are also nominated through an official process by representatives of WHO Member States. Most of the time in connection with this Expert Committee the WHO collaborating centres are situated within the national authorities and usually constitute national quality control laboratories. WHO also works closely with pharmacopoeia commissions and secretariats, national institutions and institutes that deal with matters concerning quality assurance of medicines. There is also close collaboration with regional and interregional groupings such as the International Conference on Harmonisation (ICH), the Association of South-East Nations (ASEAN), Pan American Network for Drug Regulatory Harmonization (PANDRH), etc.
WHAT IS THE OUTCOME OF A WHO EXPERT COMMITTEE?

The outcome is a printed report and the report is structured as follows: first, there is a summary of the discussions and all the recommendations to WHO and its Member States are listed therein. The most important part of the report comprises the recently adopted guidelines which are attached as an annex to the report. Before the report is made available it is cleared within WHO up to the Director-General’s office and then it is presented to the WHO Governing Bodies for final comments and endorsement, and finally implementation by the Member States. Once the whole process has been completed the report plus the attachments, i.e. the guidelines, constitute WHO technical guidance in a specific area, consisting of the field of medicines quality assurance for the Expert Committee on Specifications for Pharmaceutical Preparations.
As mentioned previously, the Expert Committee on Specifications for Pharmaceutical Preparations meets every year and all the work that is in process is presented. If the members of the Expert Committee consider that a guideline or a specification has passed through enough rounds of consultation and a consensus has been formed for a certain guideline or specification, it will be adopted during that meeting. If it is adopted the guideline will be annexed to the next Expert Committee report and specifications will be made available for publication in *The International Pharmacopoeia*. Should the experts consider that more work needs to be carried out then the guideline or monograph goes back into the consultation process. Once the report is edited and has been cleared through the internal channels, it is presented to the WHO Governing Bodies for recommendation of implementation to WHO Member States and other parties.
NEW GUIDELINES

When does the WHO Expert Committee on Specifications for Pharmaceutical Preparations start the development of a guideline or a new guidance. Trigger action is given at the highest level in the World Health Assembly, for instance in a resolution. Taking the example of good manufacturing practices (GMP), they were triggered by WHO World Health Assembly Resolution 20.34. The next level of trigger action can be an Executive Board Resolution, for example EB.37.R9 delegated certain functions of the International Nonproprietary Names (INN) Programme to the Director-General based on advice from experts.

Another body that can trigger action for the work of the Expert Committee is the International Conference of Drug Regulatory Authorities (ICDRA). For example, during the 10th and 11th ICDRAs, the fixed-dose combination guidelines and also the Certification Scheme for pharmaceutical starting materials moving in international commerce were recommended and action was taken thereafter by the Expert Committee and the WHO Secretariat. Further trigger actions can be from other programmes and clusters within WHO, for instance expressing the necessity for quality control specifications for specific medicines of major public health interest. Expert Committee members can also, of course, recommend certain courses of action or certain work to be carried out by the Secretariat.

The advantages of the Expert Committee’s standards which it imposes are numerous and include the following: firstly, all guidelines and specifications are validated internationally through an independent scientific process and adopted by the members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations; secondly, collaboration with standard-setting organizations and parties includes regional and international pharmacopoeias and thus has a vast network of organizations that work in this specific field; thirdly, there is networking and close collaboration with WHO Member States, medicine regulatory authorities, national medicines quality control laboratories and any national or regional authority involved in this type of work; fourth, there are links with other WHO activities; fifth, there is a reality check and input is taken into account from manufacturers, including international associations of research, global generic and self-medication associations; six, there is a consideration of costs which are kept as low as possible in the sense that, for instance, the need for reference standards for monographs is kept to a minimum without compromising the quality so that costs do not increase. This means that there is a minimum requirement for the maximum benefit of the analysis; and seven, the service is free for use by all Member States.
How does the WHO Expert Committee Consultation process work?

The first step is usually either a first draft written by an expert in the area or the development of a first draft in the area bringing together experts in a specific field. Once the draft guidelines are put together and edited and put into the correct format by the Secretariat, they are circulated worldwide for comments. All comments received are assembled and discussed at an informal consultation by experts in the field where the new guideline is to be developed. Once the informal consultation has been deliberated and the draft has been rewritten the draft guideline is again circulated for comments. This process is repeated as often as necessary and every year the drafts that are in the pipeline are presented to the WHO Expert Committee. In order to cover the development of specifications, additional practical steps are included in this process.
SAMPLES
Manufacturers provide samples to WHO, for instance all manufacturers are contacted and asked for samples or specifications regarding a specific product or active ingredient. Laboratory studies or scientific research are then carried out by, for example, a WHO collaborating centre, for the suitability of a specific test specification.

44TH WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS
During the 44th WHO Expert Committee on Specifications for Pharmaceutical Preparations numerous texts were adopted for The International Pharmacopoeia, including medicines for HIV and related conditions, antimalarial medicines, antituberculosis drugs, other medicines and radiopharmaceuticals.

Regarding global quality assurance; seven new guidelines were adopted: good distribution practices for pharmaceutical products; good practices for pharmaceutical quality control laboratories; GMP for active pharmaceutical ingredients; a GMP text for sterile pharmaceutical products; GMP for pharmaceutical products containing hazardous substances; a guideline on the preparation of a contract research organization master file; and requalification of prequalification dossiers.


FUTURE WORK
The list of recommendations for future work includes advice on the work in progress, a work plan for specifications for new monographs to be developed for inclusion in The International Pharmacopoeia, advice for the WHO quality assurance assessment scheme for quality control laboratories, and so forth.
FUNDING

The funding resources of the WHO Expert Committee on Specifications for Pharmaceutical Preparations and its related activities have changed over the past decades. In the past this activity was largely based on WHO’s Regular Budget. During the last two biennia now only around 10% of funding is taken from the Regular Budget, 20% is paid by the European Union and WHO Member States and 70% comes from donors, mainly including the Bill and Melinda Gates Foundation and UNITAID. In addition, the programme can count on at least three times the above budget in the form of additional in-kind contributions and support by Member States, especially through national quality control laboratories and national support to WHO collaborating centres as well as, very importantly, time given by individual experts.

The future for funding is uncertain as it appears this will depend more and more on donors only.