

Annual Report of Activities of the EDQM – 2008

The activities of the European Directorate for the Quality of Medicines & HealthCare are described in terms of its 5 main areas of responsibility.

- The European Pharmacopoeia, including reference substances and preparations, the biological standardisation programme, publication and communications activities and international relations
- The Procedure for Certification of Suitability
- The European network of Official Medicines Control Laboratories (OMCLs)
- Blood Transfusion and Organ Transplantation
- Pharmaceuticals and Pharmaceutical Care

The year 2008 saw the successful integration of new activities, in the areas of combating counterfeits and of pharmaceutical care, into the portfolio of the EDQM.

1. THE EUROPEAN PHARMACOPOEIA

PARTIES TO THE CONVENTION AND OBSERVERS

The European Pharmacopoeia Convention has been signed by 37 parties including the European Community and the following countries: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "The former Yugoslav Republic of Macedonia", Turkey and the United Kingdom.

This year, Argentina, Armenia and Moldova have obtained observer status to the European Pharmacopoeia Commission so that now in total 23 observers regularly participate in the work of the European Pharmacopoeia Commission, namely: the World Health Organisation (WHO) plus 8 European countries (Albania, Armenia, Belarus, Georgia, Kazakhstan, Moldova, the Russian Federation and Ukraine) and 14 non-European countries (Algeria, Argentina, Australia, Brazil, Canada, China, Israel, Madagascar, Malaysia, Morocco, Senegal, Syria, Tunisia and the United States of America (FDA)).

1.1. EUROPEAN PHARMACOPOEIA

GENERAL ACTIVITIES

The European Pharmacopoeia Commission continued its work on the preparation of supplements to the 6th Edition (6.3 to 6.5), which were published in June 2008, October 2008 and January 2009, respectively. The corresponding implementation dates are 1/1/2009, 1/4/2009 and 1/7/2009.

At its 3 sessions in March, June and November 2008, the European Pharmacopoeia Commission adopted 193 new and revised monographs and general chapters. A revised version of the general monograph 2.2.46.

Chromatographic separation techniques was adopted, which is of major importance for all related substances tests and assays using chromatographic methods. In 21 monographs on active substances, modern HPLC methods either were newly introduced or replaced the existing test for impurities using TLC, in order to align the monographs with modern requirements. 47 new items (monographs and general chapters) were added to the work programme during 2008.

The Commission appointed 5 new working parties: Alkyl mesitates, Pharmaceutical preparations, Process analytical technology, Instrumental determination of colour, and Compounding of radiopharmaceutical preparations. In addition, it was decided to reinstate group 16, which deals with plastic materials. A new pilot group for the elaboration of monographs on biologicals via a P4 procedure was authorised; this will, on one hand, facilitate the collaboration between the EDQM and innovators of biotechnological products and, on the other hand, build a basis for further inclusion of biosimilar products in Ph. Eur. monographs. A policy document on how to deal with potentially genotoxic impurities when elaborating or revising existing monographs was adopted by the Commission. It reflects the approach of the EMEA guideline on this matter.

In reaction to contaminants of heparins, which caused over 100 deaths in the United States and several hundred severe side effects in Europe, the Commission took measures for the rapid revision of the corresponding monographs in order to introduce screening for the presence of the contaminant. These measures have been in force since 1 August 2008. Moreover, Ph. Eur. experts have started to undertake general revisions of the monographs in order for their specifications to reflect the quality of currently marketed products and to bring them up to date with current methodologies

The European Pharmacopoeia Commission pursued its activity with regard to the reduction, replacement and refinement of tests on animals: during its 132nd session, 4 monographs on blood products were revised to allow for the use of an *in vitro* test such as the bacterial endotoxin test as a replacement of the pyrogen test. The test for abnormal toxicity has been removed from the general monograph on allergens; as a result, the test no longer has to be carried out routinely for all allergen products.

The European Pharmacopoeia Secretariat and the Chair of the Inorganic Working Party contributed to a meeting concerning testing methods for heavy metals. The meeting, initiated by the United States Pharmacopoeia, was held by the USA's National Academies of Science in Washington in August 2008. At the November session, the European Pharmacopoeia Commission agreed to review its methods concerning heavy metals, in particular with a view to implementing the new CHMP guideline on the limits for metals used as catalysts and reagents, which came into effect in 2008.

In 2008, the European Pharmacopoeia Department (Scientific Secretariat) organised 78 meetings of groups of experts and working parties, 3 sessions of the Commission, 6 meetings of the Presidium and the annual meeting of National Pharmacopoeia Authorities, which was hosted by the Irish Medicines Board. EDQM staff regularly attended as observers and actively participated in meetings of EMEA committees and working parties: the Committee on Herbal Medicinal Products, the Biologicals Working Party, the Immunologicals Working party, the Quality Working Party, the GMDP Inspectors Working Group, and the PAT team. At the beginning of 2008, the annual EDQM-EMEA joint forum was held in London with representatives of the Secretariat and the Presidium of the European Pharmacopoeia, the EMEA and the chairs of the latter's working parties to discuss items of common interest and compare work programmes.

Members of the Secretariat continued to participate in training courses on the use of monographs. These well-attended courses not only provide information to participants but also give interesting feedback to the Secretariat on the concerns of users.

INTERNATIONAL HARMONISATION WITH THE PHARMACOPOEIAS OF JAPAN AND THE USA

The Pharmacopoeial Discussion Group (PDG) met on 1-5 June 2008 in Portland, USA and on 9-14 November 2008 in Brussels. Newly harmonised monographs for carmellose, magnesium stearate, polysorbate 80 and stearic acid were signed off together with a general chapter for laser diffraction analysis of particle size.

In response to evaluations carried out by the ICH Q4B Expert Working Group, an important number of revisions have been accepted. Concerning the evaluation of pharmacopoeial texts for regulatory interchangeability, the interactions between the PDG and the ICH Q4B Expert Working Group continued to evolve in a positive manner. Meanwhile, the first topic-specific annex reached ICH step 5 (residue on ignition). 3 annexes have reached step 4 (extractable volume, particulate matter, microbial contamination), whereas 4 annexes could be signed-off at step 2 (disintegration, uniformity of dosage units, dissolution, sterility) by the Q4B Expert Working Group.

Following a discussion between the PDG and Q4B to widen the scope of Q4B activities, the ICH Steering Committee approved the addition of 5 general chapters to the Q4B work program, namely tablet friability, analytical sieving, bulk and tapped density, capillary electrophoresis, and polyacrylamide gel electrophoresis. The PDG agreed to submit the respective packages for evaluation during the year 2009.

Meetings were held in Portland and Brussels with Tri-PEC (IPEC Europe, IPEC Americas and the Japanese Pharmaceutical Excipients Council), who are important stakeholders in the work on harmonisation of excipient monographs. The active involvement of these stakeholders in the PDG process is encouraged, particularly for inter-regional collaborative testing to strengthen further the harmonisation process.

During its 132nd session, the European Pharmacopoeia Commission decided to include information on the harmonisation status of 10 general methods in Ph.

Eur. chapter 5.8. *Pharmacopoeial harmonisation*. The chapter will refer to equivalent texts published in the JP and the USP and provide assistance to users willing to employ the methods in the 3 regions. The exercise will be continued in 2009, in particular for harmonised excipient monographs.

STANDARD TERMS

Since 2006, national authorities have been responsible for entering the translations of standard terms into the specialised database via the EDQM website. Standard terms are now available in 31 languages, including Chinese. Russian translations are currently being developed.

TRANSLATIONS AND PUBLICATIONS

The European Pharmacopoeia is published in both official languages of the Council of Europe, namely English and French. A Spanish version is also available, but for now only online (up to Supplement 5.5). The 6th Edition is currently being translated into Spanish and the texts will be made available within the online subscription as they become available. In 2008, 281 texts were translated from English to French (equivalent to 1476 pages with 300 words per page) and 337 from French to English (equivalent to 748 pages with 300 words per page).

In the area of publications, the 2008 issues of *Pharmeuropa* comprised a total of 788 pages in French and 750 in English, *Pharmeuropa Bio* (issued in English only) comprised 39 pages, and *Pharmeuropa Scientific Notes* (issues in English only) comprised 40 pages. The 3 Supplements published in 2008 for the 6th Edition comprised 1188 pages in French and 1132 in English.

The 6th Edition (including Supplement 6.5) consists of 2090 monographs, 324 general texts and 2440 descriptions of reagents, and is published in both electronic and book form.

A hologram for EDQM publications has been developed to protect against unauthorised copying and is now used for all EDQM publications. It contains a number of security features (see <http://www.edqm.eu/site/Hologram-699.html>). In addition, each publication has a unique 'EDQM Publication ID' (EPID), which serves for registration of the electronic versions and allows users to verify their genuine EDQM publication using an online registration. For *Pharmeuropa*, access to additional online services is granted after registration.

The cumulative electronic edition of the European Pharmacopoeia is available in 2 different formats: a CD-ROM version, intended mostly for individual use, and an online version. Both electronic editions are based on browser technology and contain powerful search engines. Hyperlinks between monographs, general methods, reagents, printable PDF files of the texts, which are identical to those of the paper version, and links to the online database for reference substances and the Knowledge database are established. For the online version of the 6th Edition a new publication platform has been implemented, in order to cope better with the increased number of customers using this version. More advanced searches and export functions have been implemented in this new online version. The licensing system is now based on the registration of computers. Additional administration and reporting

functions, basically intended for large accounts, and user interfaces in English, French and Spanish have been added in 2008. Subscribers to the online version of the European Pharmacopoeia will soon have access to an archive version of all previous editions of the European Pharmacopoeia.

Pharmeuropa (including Pharmeuropa Bio and Pharmeuropa Scientific Notes) is available online. All issues dating back to Volume 0 (1987) have been indexed and are available as searchable PDF files. The online access is included for subscribers to the current paper version of Pharmeuropa. The necessary access code can be generated using the information from the label on the back cover of the first issue of the volume.

Standard Terms is now only available as an online version, and access can be acquired by using the EPID number obtained from the EDQM sales department.

1.2. PROVISION OF REFERENCE SUBSTANCES AND PREPARATIONS

127 new (chemical) reference substances (or spectra) and biological reference preparations (including 10 for plants) were adopted in 2008, bringing the number of substances available to users of the European Pharmacopoeia to 2143. Extensive collaborative studies were required for 36 of these substances (including 3 for plants) to determine the content of the substances used in the assays. In addition, 139 reference substances were replaced and the EDQM laboratory regularly monitored 435 substances and carried out quality control tests during the production of 395 batches. The number of chemical reference substances and biological reference preparations distributed to users continued to climb: 225 194 vials in 2008 compared to 203 967 in 2007, and the number of orders increased from 26 075 to 28 462. Taking bulk substances selected by the European Pharmacopoeia Commission for use as reference substances, the Production Unit of the EDQM prepared 512 batches (filling 475 098 vials).

1.3. PREPARATION AND DISTRIBUTION OF SAMPLES

3260 new samples were received by the EDQM in 2008 compared to 2826 in 2007. The total number of samples in stock was almost 22 000. 403 studies were carried out by the EDQM laboratory to compare or check the analytical methods proposed for new monographs or for revisions of monographs at the request of the groups of experts of the Commission. The Production Unit had to prepare 4819 samples for these laboratory studies to check the quality of the substances available on the market (multisource substances) or to check the robustness of draft European Pharmacopoeia monographs. In addition, 21 944 samples were prepared for distribution to the various experts of the EDQM (for the elaboration of monographs and the organisation of collaborative studies, market surveillance studies and biological standardisation projects).

1.4. BIOLOGICAL STANDARDISATION PROGRAMME

The Biological Standardisation Programme (BSP) continued to pursue the following goals in the area of standardisation of biologicals:

- the establishment of Ph. Eur. (working) standards;

- the development and validation of new analytical methods;
- the validation of alternative methods in the framework of the 3R concept (i.e. the Refinement, Reduction and Replacement of animal experiments).

To this end, collaborative studies are performed involving all interested partners (e.g. OMCLs and manufacturers). Participation in a collaborative study is not restricted to members or observers of the Ph. Eur. The results of the collaborative studies are published in Pharmeuropa Bio, which, since 2001, is referenced in MEDLINE and Index Medicus of the National Library of Medicine (USA).

Since the programme's start in 1992, 106 BSP projects have been initiated and 96 BRPs (new or replacement batches) have been established.

In 2008, the following projects were pursued.

In the field of vaccines for human use:

- validation of serological method for potency assay of acellular pertussis vaccine;
- standardisation of test for residual pertussis toxin in acellular pertussis vaccine;
- validation of alternative method for potency assay of whole cell pertussis vaccine (Kendrick test);
- standardisation of human influenza vaccine serology;
- validation of NMR methods for quality control of polysaccharide vaccines;
- establishment of (non-adsorbed) hepatitis A vaccine BRP;
- establishment of varicella vaccine BRP;
- establishment of diphtheria vaccine BRP; replacement batch;
- establishment of tetanus vaccine BRP replacement batch.

In the field of vaccines for veterinary use:

- validation of alternative method for potency assay of rabies vaccine.

In the field of plasma-derived products:

- establishment of BRP for assay of SD-plasma and fibrin sealant kits;
- validation of *in vitro* assay method for tetanus immunoglobulin;
- establishment of von Willebrand factor BRP for ristocetin cofactor assay;
- establishment of BRPs for determination of anti-A, anti-B haemagglutinin titres in human normal immunoglobulin for intravenous administration;
- establishment of human coagulation factor VII BRP replacement batch;
- establishment of human coagulation factor VIII BRP replacement batch;
- establishment of human coagulation factor IX BRP replacement batch;

- establishment of BRP replacement batches for determination of prekallikrein titres in human albumin;
- establishment of human immunoglobulin BRP replacement batch.

In the field of biotechnology products

- establishment of an HPLC assay for alfa-2 interferon;
- establishment of BRPs and ELISA assays for 2 major recombinant allergens (Bet v 1, Phl p 5a);
- establishment of low-molecular-mass heparin for assay BRP replacement batch.

The studies led to the adoption of the following reference preparations by the Commission in 2008:

- prekallikrein activator (PKA) in albumin BRP, batches 2 & 3;
- human coagulation factor IX BRP, batch 2;
- immunoglobulin (positive control for anti-A, anti-B antibodies test) BRP, batch 1;
- immunoglobulin (negative control for anti-A, anti-B antibodies test) BRP, batch 1;
- immunoglobulin for anti-A, anti-B antibodies limit test BRP, batch 1.

The full reports on the concluded collaborative studies are published in *Pharmeuropa Bio 2008-1*.

In the field of vaccines for human use, a collaborative study was started for the second phase of a project that aims at a better standardisation of the serological methods used for clinical evaluation of influenza vaccines during the annual licensing procedure according to the EMEA Committee for Medicinal Products for Human Use (CHMP) guidelines; this had been requested by the CHMP Biologics Working Party (BWP) of the EMEA. In the first part of the project, which was completed in 2006, the influence of test variability on compliance with the CHMP guidelines for inter-pandemic influenza vaccines was investigated. Sera from elderly patients were tested using the haemagglutination inhibition (HI) test. The study showed that reproducibility of the HI test is not satisfactory for this purpose and that standardisation of the serological methods is urgently needed. The second part of the project examines the influence of the use of a sheep serum standard on the variability of the HI and single radial haemolysis (SRH) test and how this affects compliance with the CHMP criteria. The complex collaborative study started in mid-2008; the report is expected for spring 2009.

The strong efforts to apply the 3R concept to the field of quality control of biologicals were continued in 2008. Two 3R projects were advanced and are now close to conclusion. One project aims at the replacement of the *in vivo* challenge assay for tetanus immunoglobulin by an *in vitro* assay. Following the evaluation of the results from the collaborative study, additional experiments were found to be necessary. The project will be concluded in early 2009. A second project extends previous projects on the development of serological assays to replace the *in vivo* challenge as the batch potency test for vaccines containing diphtheria and tetanus components to acellular pertussis vaccine. The goal is to enable

the performance of the potency assay for vaccines containing all these components using serum from the same animals. This will reduce enormously the number of animals needed for these assays. The collaborative study was started and concluded in 2008, the report is in preparation. For both projects, first results were presented at the EDQM symposium 'Alternatives to animal testing: new approaches in the development and control of biologicals', which was held in Dubrovnik, Croatia, on 23-24 April 2008.

2 new projects in the area of alternatives to animal experiments were started in 2008. Both projects aim to validate methods for the potency assay of vaccines in fields where alternatives have long been sought. In both cases, it is intended to replace the currently used challenge tests by serological assays. One project targets the Kendrick test, the potency assay for whole cell pertussis vaccines, the other project targets the NIH test, the potency assay for rabies vaccines for veterinary use. For both new projects preparatory work started in late 2008.

The efforts of the EDQM and the Biological Standardisation Programme in the 3R field are united with those of the EPAA (European Partnership for Alternative Approaches to Animal Testing), a high-level joint initiative of the European Commission and industry.

In 2008 the BSP started to look into possibilities to replace the current Ph. Eur. tests for extraneous agents by PCR methods. The current tests have the disadvantage of being very time-consuming. In addition, in the case of avian vaccines, a high number of animals are used for this test. PCR methods could be a promising alternative to the current methods. In October 2008, a meeting was organised at the EDQM in Strasbourg with all interested parties (manufacturers of veterinary and human vaccines, licensing authorities, OMCLs) to evaluate the potential of the PCR methods. It was decided to elaborate a position paper addressed to all interested parties and to set up a working group with representatives mainly from OMCLs and industry in order to elaborate further and validate methods, reagents and standards for PCR in this field.

As in previous years, co-operation with international partners continued; projects to establish common standards were set up, whenever possible, with the WHO Expert Committee on Biological Standardisation (ECBS). Examples include the establishment of standards for determination of anti-A and anti-B antibody titres in immunoglobulins and for replacement of the current standards of human coagulation factor IX. Both projects were run as tri-partite projects with the WHO and FDA/CBER. Standards emerging from these projects were adopted as International Standards at the ECBS meeting in October 2008. Other examples of collaboration between the EDQM and the WHO include the establishment of replacement batches for the current standards of diphtheria vaccine, tetanus vaccine and human coagulation factor VIII.

1.5. EDQM ACTIVITIES AS WHO CUSTODIAN LABORATORY FOR ANTIBIOTICS

Since May 2006, the EDQM has been the custodian laboratory for the WHO International Standards for Antibiotics (ISA). At the same time, the EDQM took over the responsibility for the establishment, storage

and distribution of ISA from the National Institute for Biological Standards and Control (NIBSC). Batches that were held and distributed by the NIBSC are now being distributed by the EDQM.

The ISA are essential for the standardisation and quality control of antibiotic drug substances and pharmaceutical drug products. They are supplied for use in the microbiological assays performed for quality control.

In 2008, the collaborative study aimed at the establishment of a replacement batch for the current International Standard for gramicidin, the stocks of which will soon be exhausted, was completed. The establishment report was adopted by the WHO Expert Committee for Biological Standardisation (ECBS) at its session in October 2008. At the same meeting, the ECBS approved proposals for replacement of the current batches of the International Standards for bleomycin complex A2/B2, neomycin B and streptomycin, the stocks of which will soon be depleted. The respective collaborative studies will be initiated in 2009. Information on the availability and ordering of ISA is available on the EDQM website (<http://www.edqm.eu/site/WHO-International-Standards-for-Antibiotics-ISA-665.html>).

1.6. COMMUNICATIONS AND PUBLIC RELATIONS

The EDQM continued its comprehensive communication policy with its partners, giving priority in 2008 to developing its website and organising and participating in many conferences, training sessions and visits.

Events for the general public were organised to convey the importance of the activities of the EDQM and the European Pharmacopoeia in ensuring the quality of all medicines and in the fight against counterfeit medicines.

In its international relations, the EDQM strived to consult all its partners by meeting with them or participating in major specialised exhibitions.

Website

The EDQM is working actively to improve and expand its online services not only in scientific and technical areas, but also in the areas of training and informing its users about EDQM products and services.

The number of visitors and visits to the EDQM website continued to increase in 2008, reaching a monthly average of 20 000 visitors and 62 000 visits (data from the statistics tool AWSTATS).

As part of its commitment to service the needs of its users and clients, the EDQM launched the French-language version of its website in February 2008 and the Chinese-language version in March 2008, bringing to 3 the number of languages now offered.

The EDQM recognised the need for a website designed for Chinese-speaking users to be able to inform more effectively potential customers and partners in China about EDQM activities and its different products and services.

The user-friendly website provides detailed information regarding EDQM products, services, activities and news. It also provides opportunities for website visitors,

customers and partners to contact the EDQM through the website using the HelpDesk.

The HelpDesk service, which has been in operation since April 2006, has received 24 000 questions so far. The topics and frequently asked questions (FAQs) are available in English and French, the official languages of the Council of Europe, thus enabling an even wider audience to communicate with the EDQM. The FAQs are also regularly updated and new ones added so that they reflect all the activities and respond to changing user needs.

Specific customer and contact information are available as well as free publications and brochures. The site also allows easy access to the EDQM online bookshop, EDQM Store, making ordering and paying for products and services even easier.

Organisation of symposia on current issues

International Symposium on 'Alternatives to Animal Testing - New Approaches in the Development and Control of Biologicals', 23-24 April 2008, Dubrovnik, Croatia

This international symposium was essentially aimed at the application of the 3Rs (Reduction, Refinement and Replacement of animal use) in routine quality control of therapeutic biologicals. It was recognised that for the development and characterisation of these products, different approaches and priorities may be necessary.

While considerable progress has been made in setting requirements, especially in Europe, implementation and regulatory acceptance are still key elements that needed further work, in particular for routine application in the control of biologicals. Better transparency and dissemination of existing and future scientific work and achievements are necessary, as well as improved co-operation in method elaboration.

During the symposium, the need for international harmonisation was strongly expressed and supported. Representatives from all the European and international institutions present indicated their willingness to investigate means to improve the situation and to refer the ideas expressed during the symposium to their decision-making bodies and groups of experts so as to facilitate their incorporation into appropriate work programmes.

The symposium was attended by almost 150 participants from 26 different countries, including representatives from industry and key regulatory stakeholders.

Workshop on the Characterisation of Heparin Products, 19-20 June 2008, Strasbourg, France

This workshop was jointly organised by the EDQM, the National Institute for Biological Standards & Control (NIBSC) and the United States Pharmacopoeia (USP) in a series of workshops on heparins to be continued in 2009 to discuss the characterisation and quality control of heparins. The main focus was on unfractionated heparin and the control of impurities, in the light of the contamination of heparins detected worldwide early in 2008.

The different speakers presented their viewpoints and approaches based upon their experience and analyses of samples drawn from their respective markets. The

need for setting a common standard and developing a harmonised approach to define a potency assay based on a common international unitage (IU) was identified.

One of the main outcomes of the workshop was the approach agreed upon by the 3 pharmacopoeias. A 2-step approach was developed to revise their respective heparin monographs. The goal was, in the immediate term, to revise their monographs to include adequate quality control of the observed contaminants, and in the mid-term, to try to establish harmonised monographs for both heparin and low-molecular-mass (LMM) heparins. The workshop attracted 147 experts from 25 countries.

EDQM Symposium: Pharmaceutical Reference Standards

This international symposium, held in October 2008, was dedicated to discussing current topics and future approaches related to pharmaceutical reference standards. Pharmaceutical reference standards are essential for the quality control of medicines.

The symposium, which attracted more than 170 participants from 31 countries, brought together stakeholders involved in the production, characterisation and use of reference standards to exchange their views and opinions on the different issues related to the subject.

The scientific programme included presentations on the Japanese Pharmacopoeia's, United States Pharmacopoeia's and European Pharmacopoeia's reference standards programmes, as well as the World Health Organisation's biologicals programme, viewpoints from the regulators (EU, USA and Russian Federation), audits and inspections, characterisation of primary reference standards, and the establishment and use of secondary standards. Issues related to the development of chemical, herbal and biological reference standards and their role in the quality of medicines were addressed in 2 separate workshops. The programme also included a poster session and a roundtable discussion.

The EDQM and European Pharmacopoeia Commission will take into account the outcome of the symposium discussions when making future policy and work programme decisions.

10th European Day for Organ Donation and Transplantation, 18 October 2008, Ljubljana, Slovenia

The 10th European Day for Organ Donation and Transplantation was organised in collaboration with the Institute for Transplantation of Organs and Tissues of the Republic of Slovenia (*Slovenija-Transplant*), *Slovensko društvo Transplant* and *Združenje društev dializnih in ledvičnih bolnikov Slovenije*, and in the presence of the President of the Republic of Slovenia, Mr Danilo Türk.

The event was an opportunity to strengthen European collaboration, increase the levels of awareness on the different issues, facilitate the exchange of information and, above all, celebrate and express thanks to the professionals, voluntary organisations, organ donors and their families, and to patients for their dedication, generosity and courage. The work of the EDQM in organ transplantation was presented by Dr Per Pfeffer, the Vice-chair of the Steering Committee on Organisational Aspects of Cooperation in Organ Transplantation (CD-P-TO). One of the highlights of the day was a sporting event 'Run for Life and Joy' organised for the general public.

Training sessions / presentation of the missions of the EDQM

The EDQM organised 5 training sessions in 2008, in Shanghai, China (March 2008), in New Jersey, USA (May 2008), in Montreal, Canada (May 2008), in Strasbourg, France (July 2008), and in London, UK (December 2008). The session in the United States was organised at the request and with the support of the New Jersey Pharmaceutical Quality Control Association (NJPQCA).

These training sessions are very much appreciated by users of the European Pharmacopoeia and each attracted the participation of 70 to 80 people from more than 17 countries. At each session, individual consultations with EDQM staff members were offered to participants allowing more meaningful interactions.

Other visits presenting the missions of the EDQM were also organised in response to invitations from national authorities and professional associations of the pharmaceutical industry, for example to countries that are major producers of pharmaceutical raw materials, as with Prescription Pharma Support in Hyderabad, India (80 participants, November 2008).

A training session on CombiStats was held in Strasbourg (November 2008) for members of the European Network of Official Medicines Control Laboratories (OMCLs). 13 participants from 8 countries attended this very specific session.

2 training sessions (in Strasbourg, France, June 2008 and in Larnaca, Cyprus, November 2008) were organised for the different players and partners concerned by the counterfeiting of medicines (such as the police, custom authorities, inspectors, etc.). The sessions focused on methods to gain awareness of the responsibilities, existing control systems, and practical investigation procedures and the standard procedures to apply, as well as the interaction between the different sectors and disciplines concerned. The workshops attracted 30 participants from 20 different countries.

Group visits

In keeping with its policy of openness and transparency, the EDQM welcomed various groups of visitors to its premises.

- Union of Associations of Voluntary Blood Donors of *La Poste* and *France Telecom* (May 2008)
- Permanent representatives at the Council of Europe (September 2008)
- A delegation from Chile representing the Chilean Pharmacopoeia Project (October 2008)
- 20 visiting groups representing both the target groups of the EDQM and a wider audience, totalling 400 people

Open day at the Council of Europe on European Heritage Day, 21 September 2008

This year, the Council of Europe's Agora building, inaugurated in April 2008 by Bernard Kouchner, French Minister for Foreign and European Affairs, was opened to the public. This building houses 3 Directorates General of the Council of Europe: the Directorates General of Human Rights and Legal Affairs, of Social Cohesion, and

of Education, Culture, and Heritage, Youth and Sport. The EDQM had a stand with informational leaflets and brochures available for the 5300 visitors that came. During the day, an institutional film explaining the work of the EDQM was offered to the public.

Exhibition on the European Pharmacopoeia for the general public

Upon request, since 2004, the EDQM has provided exhibition panels such as 'Find out about Pharmacopoeias and Medicine' that can be used as educational tools or for a particular event. Other panels explaining what a pharmacopoeia is and how it guarantees the quality of medicines and describing all the activities of the EDQM in its European and global environment are also available.

This year the exhibition was on display in the National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands, on 19-21 March 2008, and in Jaarbeurs Utrecht, Utrecht, the Netherlands, on 1 April 2008.

The exhibition is on display at all times and accessible to all visitors in the main hall of the EDQM building.

International relations

Relations with the European Medicines Agency (EMA)

In addition to the yearly consultation meeting between the 2 institutions, co-ordination and co-operation activities with the agency continued throughout the year. EDQM representatives participated as observers in all the working parties relevant to the EDQM, notably the Biologicals, Inspection and Immunological and Quality working parties, the PAT team, and the Committee for Herbal Medicinal Products. Representatives of the Agency were also invited to participate in symposia organised by the EDQM in areas of common interest to both institutions and to take part in relevant expert groups of the European Pharmacopoeia as well as the Commission as observers.

The EDQM also gives all of the EMA and its experts free access to the electronic versions of its publications on the Agency's premises to facilitate the work of its European partners.

Relations with the World Health Organisation (WHO)

EDQM representatives participated in the expert groups on setting specifications and the Expert Committee on Biological Standardisation (ECBS) as observers. Several studies were carried out in close collaboration with the WHO and FDA (CBER) to establish standards either originating from the same batch or with a known ratio to each other if not from the same batch, as common samples that were examined by all participants in the same study. This was particularly the case for 3 major biologicals: diphtheria vaccine, anti-A and anti-B haemagglutinins in IV immunoglobulins, and human coagulation factor IX concentrate. Such efforts contribute to a better harmonisation and facilitate international trade/exchange of these biological pharmaceuticals. EDQM has given a strong support to the WHO/Medicines Quality Assurance Programme Department by engineering, organising and evaluating the results of the external Quality Assurance Assessment

Scheme, phase 4 programme (PTS), which was organised for the WHO network of national control laboratories.

Relations with CEN Advisory Board for Health Standards

During 2008, members of the EDQM and CEN, the European Committee for Standardisation, met in Strasbourg to establish ways of reinforcing the links between the 2 institutions. Efforts will continue in 2009 with the aim of formalising these links.

Relations with the United States

The EDQM participated in a meeting organised by the United States Food and Drug Administration (FDA) in April 2008 to discuss issues concerning the quality of heparins. The FDA had first learned of an increase in the number of heparin adverse effects reported and decided to convene all regulatory authorities to study the problem and share efforts in finding a solution. Further investigations found that a contaminant called over-sulphated chondroitin, a substance that mimics the biological activity of heparin, was present in batches.

The EDQM and FDA worked closely on analytical and GMP strategies that would eliminate the contaminant and at the same time ensure an adequate supply of heparin to meet medical needs. The EDQM also notified its key regulatory international partners of its actions and worked closely with manufacturers and experts to carry out analysis of samples. Representatives of the FDA and United States Pharmacopoeia attended the EDQM heparin workshop organised in Strasbourg in June 2008.

Relations with the Brazilian authorities

The EDQM participated in a seminar organised by the ANVISA in Brasilia, Brazil, in December 2008. The main topic of the seminar was to advise the Brazilian Pharmacopoeia Commission on how to prepare the new edition of the Brazilian Pharmacopoeia. The possibility to develop further international co-operation was also discussed. The seminar was attended by representatives from the Brazilian, Chilean, European and United States pharmacopoeias as well as the WHO.

Relations with the Canadian authorities

In application of the Memorandum of Understanding signed in 2007 by the Therapeutic Products Directorate (TPD) of Health Canada and the EDQM in relation to CEPs, regular collaboration has been established. 4 assessors from Health Canada have been appointed for the Certification procedure and take part in the evaluation of applications for CEPs. Health Canada is moving to accept CEPs in their system for evaluation of the quality of drug substances in the framework of marketing authorisation applications.

Relations with the Chilean authorities

The EDQM met a delegation from the Chilean Pharmacopoeia Project in Strasbourg, France, in October 2008. The Chilean authorities plan to create a new pharmacopoeia authority that will be responsible for setting standards and specifications for pharmaceuticals in Chile. This, the first meeting between the 2 authorities, was an opportunity to exchange views and opinions on how to deal with new public health risks and to learn about the work and organisation of the pharmacopoeia activities.

A tour of the EDQM laboratories and the reference standards facilities was also organised.

Relations with the Chinese authorities

The EDQM participated in a conference on traditional Chinese medicines (TCMs) co-organised by the Chinese Pharmacopoeia and the United States Pharmacopoeia (USP) in Tian Jin, China. The EDQM has a specific programme to draft monographs on herbal preparations and TCMs. The event was an important opportunity to inform participants of the progress being made in this field and a general presentation on EDQM activities was also given.

The EDQM welcomed a trainee from the Institute for the Control of Pharmaceutical and Biological Products (NICBP, Beijing, China) on work experience in the EDQM laboratory.

The EDQM, with the support of the Shanghai Institute for Food and Drug Control (SIFDC), organised a symposium in Shanghai, China, on the European Pharmacopoeia. Over 70 participants attended the 2-day meeting, which was specifically designed to meet the needs of pharmaceutical professionals. A further meeting took place in June 2008 to exchange information and further promote relations.

In the framework of a conference on Quality and Design organised by the Global Cooperation Group (GCP) in December 2008 in Beijing, the EDQM Director met with representatives of the Chinese Food and Drug Administration (SFDA) and the NICBP to discuss further possibilities for co-operation.

Relations with the Indian authorities

The EDQM Director met with the Ministry of Health of India and the Indian Pharmacopoeia Commission in New Delhi, India, in April 2008. During the visit, several areas of potential collaboration were identified including the elaboration of chemical and herbals monographs, the development of joint inspections of manufacturing sites under the framework of the European Pharmacopoeia procedure of certification, the promotion of common training activities in the pharmacopoeial field, scientific co-operation by inviting pharmaceutical scientists to the EDQM, the facilitation of information exchange and the granting of observer status for the European Pharmacopoeia to the Indian Pharmacopoeia Commission. Both parties agreed to continue to work together to strengthen their working relationship in order to improve the quality of medicines in Europe and India.

Relations with the Russian authorities

An international conference on 'Standardisation of Medicines, Harmonisation of Requirements' took place in Moscow, Russian Federation, in October 2008, with the support of the Federal Service for the Supervision of Public Health and Social Development (Roszdravnadzor), the EDQM, the Commonwealth of Independent States (CIS) Executive Committee, and the international project 'Farmsodruzhestvo'.

Roszdravnadzor is a governmental agency responsible for the control and surveillance of healthcare and social development within the Russian Federation. The CIS

groups a number of countries of the former Soviet Union: Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Ukraine, Turkmenistan and Uzbekistan. These countries have decided to work together and use their experience in specific fields such as standardisation and control of pharmaceutical products, with the aim of establishing common working standards, such as a pharmacopoeia.

During the meeting, the leaders of Roszdravnadzor and the EDQM agreed to collaborate to implement the provisions of the Declaration of the international conference 'Europe against Counterfeit Medicines' of October 2006, and to expand scientific and practical co-operation. Roszdravnadzor committed to continue its active and regular participation in the work of the European Pharmacopoeia Commission and its expert groups. Best practice experience of the European Pharmacopoeia Commission will be taken into account when preparing the new edition of the State Pharmacopoeia of the Russian Federation.

The Roszdravnadzor and the EDQM also expressed the need to continue their co-operation for improving the quality of medicines and to develop mechanisms for information exchange. A number of areas and potential projects were discussed including counterfeit medicines, the preparation of the official translation of the European Pharmacopoeia into Russian, the accreditation of the Institute of Standardisation and Control of Medicines of Roszdravnadzor to conform to the requirements of the European Network of Official Medicines Control Laboratories (OMCLs) and the implementation of OMCL Network quality assurance requirements through the centres for quality control of medicines in the different districts of the Russian Federation.

Consultations of partner associations

Annual meeting of the European Network of Official Medicines Control Laboratories (OMCLs), June 2008, Strasbourg, France

The EDQM held its 13th Annual Meeting of the Official Medicines Control Laboratory (OMCL) Network in Strasbourg on 2-6 June 2008. 201 participants from 32 countries, representing 58 OMCLs, attended a general meeting (see section 3 for more information).

Relations with the secretariats of national pharmacopoeias (28-29 April 2008, Dublin, Ireland)

The annual meeting of the national secretariats of pharmacopoeias was attended by 31 participants representing 23 national authorities. The meeting was hosted by the Irish Medicines Board.

PIC/S (Pharmaceutical Inspection Cooperation Scheme)

In 2008 the EDQM started to implement the Memorandum of Understanding signed in July 2007 with the PIC/S. The EDQM inspection team took part in the PIC/S Committee meetings, the seminar on GDP and the API expert circle group. The team had an input in the API aide-memoire and is represented in the working group on the Quality Risk Management (QRM) approach to API inspection triggering. Exchange of information on the outcome of inspections was also initiated by communicating decisions on CEP suspensions in the framework of the inspection programme.

Interactions with Trade Associations

CEFIC/APIC (European Chemical Industry Council/Active Pharmaceutical Ingredients Committee)

As usual each year, the EDQM met with representatives of CEFIC/APIC to exchange views on CEPs and the EDQM Inspection Programme. In 2008, CEFIC/APIC was consulted twice to discuss their views concerning decisions affecting the transparency of CEPs.

EGA (European Generic Medicines Association)

The EDQM held a meeting with the EGA in May 2008 to discuss the progress being made with harmonisation and the P4 programme and measures that would allow more transparency on the Certificate of Suitability (CEP). The EGA provided their feedback on the priorities for monographs elaboration. Both parties agreed to evaluate and discuss progress on an annual basis.

AESGP (Association of the European Self-medication Industry)

The EDQM held a meeting with the AESGP in Strasbourg in October 2008 to follow up on the outcomes of the 2007 conference "New Frontiers in the Quality of Medicines" and to discuss items of mutual interest, e.g. in the area of herbals, homeopathy, the certification scheme and EDQM activities in combating counterfeits.

Professional exhibitions in the pharmaceutical world

Various professional exhibitions provided an opportunity to meet users of the European Pharmacopoeia from Asia and South America. Each time, the EDQM presented the 6th Edition, its publications, its products and its services to visitors, with the use of exhibition stands and, where appropriate, presentations in satellite symposia.

The EDQM participated in the following exhibitions.

CPhI Japan, 9-11 April 2008, Tokyo, Japan

The EDQM participated for the first time in the Congress of Pharmaceutical Ingredients Worldwide (CPhI) fair/exhibition in Japan. The exhibition attracted over 13 000 visitors from 23 different countries and regions. 250 people visited the EDQM stand over 3 days. Brochures and information on the EDQM activities were distributed and visitors were able to obtain answers to their questions on European regulations concerning raw materials for pharmaceutical use.

CPhI China, 24-26 June 2008, Shanghai, China

A total of 26 863 industry professionals visited CPhI China in 2008 confirming the success of this initiative, and the EDQM stand received approximately 600 visitors in 3 days. Visitors came from the Asia region (China, India, Pakistan, Philippines, Vietnam, Thailand, Mongolia), South America (Brazil, Argentina, Venezuela) and the Middle East. Local distributors of EDQM publications were invited to the stand and the presence of the EDQM at this conference was publicised by an extensive mailing campaign.

The opportunity to arrange a private one-to-one consultation was made available to companies holding certificates of suitability of monographs of the European Pharmacopoeia or to those that wish to apply for a certificate.

CPhI South America, 19-21 August 2008, Rio de Janeiro, Brazil

The EDQM participated in the first CPhI South America exhibition in Brazil, one of the world's fastest-growing pharmaceutical markets after China. Approximately 250 visitors from major pharmaceutical companies from across the region visited the EDQM stand. There was particular interest in the Spanish version of the European Pharmacopoeia, the certification procedure and the inspection programme. The EDQM also organised a workshop in which representatives from ANVISA, the Brazilian Pharmacopoeia and the United States Pharmacopoeia attended.

1.7. QUALITY MANAGEMENT SYSTEM

The EDQM continued the development of its Quality Management System based on the ISO 9001 standard (general administration), ISO 17025 (laboratory), ISO Guide 34 (Reference Standards) and ISO Guide 43-1 (Proficiency Testing Scheme), in order to guarantee an optimal service to its interested parties while improving the efficiency of working methods.

The EDQM has decided to go for ISO 9001 certification starting with the procedure on the certification of suitability of monographs of the European Pharmacopoeia. Work has already begun and the certification audit is foreseen in 2009.

The EDQM also completed a full review of its 2063 safety data sheets (SDSs) in order to be compliant with the REACH regulation (1907/2006/EC). All these SDSs are available in English through the EDQM website or upon request. Work has also started to provide these SDSs in other European languages.

2. CERTIFICATION OF SUITABILITY OF MONOGRAPHS OF THE EUROPEAN PHARMACOPOEIA

In 2008, 333 new applications for certificates of suitability (CEPs) and 686 requests for revision were received, in addition to the regular updates following the publication of revised monographs in the supplements of the European Pharmacopoeia. It should be pointed out that although the procedure was extended to herbal drugs and herbal drugs preparations several years ago, the first applications for these substances were only received in 2008.

Over 3700 applications have been received since the procedure was created, and there are currently more than 2350 valid certificates.

This year, the Certification of Substances Division has focused on the improvement of the management of applications for CEPs concerning new applications and revisions. In particular, risk-based assessment principles have been included in the evaluation of the dossiers. This task was conducted in close collaboration with the Licensing Authorities accepting CEPs.

Operating on the basis of the mandate given by the European Commission, the programme for inspection of manufacturing sites covered by CEPs is an important tool to supplement the evaluation of the quality of substances for pharmaceutical use. As in the previous years, the EDQM inspection program was carried out according to the priorities given by the Certification

Steering Committee. 28 inspections were performed, mainly in Asia, with the participation of inspectors from different national agencies; a number of these inspections led to the suspension of CEPs due to non-compliance of the manufacturing sites with GMP or major deviations compared with the dossier submitted to obtain the CEP. Additionally, 2 companies refused to be inspected and information on 11 manufacturing sites was obtained by exchanging information with the relevant EEA inspectorates. Procedures have been established in collaboration with the EMEA GMP/GDP Inspection Working Group for the management of GMP non-compliance and for potential actions regarding the validity of CEPs in case of negative outcome of inspections. When a suspension of CEP is decided by the Ad Hoc Committee, the relevant national competent supervisory authorities are informed so that any necessary action on related marketing applications/authorisations can be taken.

The EDQM is actively participating in a pilot project of collaboration and information-sharing between Europe, Australia and the USA, for the inspection of manufacturing sites of active substances, and has also been included in the Steering Group for heparin inspection and investigation co-ordinated by the EMEA.

To promote the procedure and communicate better with its partners from authorities and industry, the Certification Division (DCEP) participated in several events (conferences, fairs/exhibitions, one-to-one meetings, technical advice meetings) in particular in Europe, but also in India and China.

3. NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES (OMCLS)

The network of Official Medicines Control Laboratories (OMCLs) was established in 1994 on the initiative of the EDQM in close co-operation with the Commission of the European Union. The network is open to all countries that have signed the European Pharmacopoeia Convention as well as to observers to the European Pharmacopoeia Commission, provided that the criteria of the network are fulfilled.

There are 2 levels of collaboration.

- *General activities* covering all areas of common interest and involving all member states of the network, such as work in the field of quality assurance (QA), the proficiency testing scheme (PTS), market surveillance studies (MSS), and common network strategies (risk-based approach for post-marketing sampling and testing, combating counterfeits and illegal medicines, establishment of centres of expertise, improvement of communication, etc.).
- *Activities restricted to the European Economic Area (EEA)*, in which a number of activities take place within the more restrictive regulatory framework for medicines in the EU/EEA, notably those connected to the Centralised Marketing Authorisation Procedure (CAP), the Mutual Recognition Procedure (MRP) / Decentralised Procedure (DCP) and the Official Control Authority Batch Release (OCABR) of blood and plasma derivatives, human vaccines and veterinary immunobiologicals.

'Networking' means sharing of know-how within a pool of experts, work sharing and mutual recognition of test results based on commonly agreed procedures, and consequently saving of resources and costs in the testing of medicinal products.

For this purpose the implementation and maintenance of harmonised Quality Management Systems (QMSs) (based on ISO/IEC 17025) among the network members and the assessment of established systems, based on commonly agreed procedures, are required. Since 1997 several tools have been put in place to help OMCLs work towards these goals, such as training visits, tutorials, mutual joint visits (MJVs) and mutual joint audits (MJAs).

Good communication is a key element of effective networking. This is strongly facilitated by the annual meetings, which bring together representatives from the entire network to discuss and exchange viewpoints on topics of common interest, such as the independent testing of medicines, to summarise the year's activities and decide on an action plan for the coming year. These meetings are organised by the EDQM and hosted by one of the members of the network on a rotating basis.

Finally, a number of databases with regulated and secured access have been established or are under development to foster information exchange on competences and test results available within the network.

3.1. ACTIVITIES INVOLVING ALL OMCLS OF THE NETWORK

Annual meeting of the plenary network

The 13th annual meeting of the OMCL Network was held on 2-6 June 2008 at the EDQM premises in Strasbourg, France. 201 representatives from 32 countries, representing 58 control laboratories, attended a general meeting and different specialised sessions during which the quality control of medicines was discussed, in particular in the field of pharmaceuticals, biotech products and the official control authority batch release of human vaccines, human blood and plasma derivatives and immunological veterinary medicinal products. As in previous years, issues of particular importance were the exchange of experience and results, policy and guideline development for fostering mutual recognition, quality assurance, risk analysis and combating counterfeit medicines.

The network has continued to fine-tune policy documents and notably adopted updated documents detailing the Terms of Reference of the General European OMCL Network (GEON), the definition of an OMCL and the criteria for membership within the network by clearly defining the obligations and benefits of such a membership. Other highlights of the meeting are discussed in the specific technical chapter of the present report.

OMCL inventory database

One important measure to strengthen the communication within the network and to apply the main principles of the GEON, namely work sharing and sharing of resources and results, is the provision of supportive information and data exchange tools. The OMCL inventory database contributes to this idea. Launched in July 2007, this computer application now

stores general OMCL records (contact points, addresses, QA information, organisational information etc.) from 67 OMCLs and more than 5200 competence records of the network, which are entered and updated on an ongoing basis by the OMCL users, while the EDQM together with an external IT software developer take care of the maintenance and continuous improvement of the technical environment and the stock data. Access to the information is restricted to OMCLs of the network, and several technical measures have been taken to guarantee data security and confidentiality.

During 2008 it was decided, starting from 2008, to distribute the annual reports for non-OCABR activities via this IT tool, which significantly facilitates and speeds up the information exchange on yearly national work programmes between the Network members.

During the summer months of 2008 the OMCLs were invited to send a declaration of conformity in which they confirm in writing that their records in the database are up to date. This exercise will be repeated on a yearly basis and should guarantee the relevance of the datasets.

Finally, some amendments were implemented during 2008 based on feedback received from the users. This work will be continued also in 2009 with the task to make (and keep) the computer application as user-friendly as possible.

Elaboration of an NMR test protocol for the determination of heparin contaminants

On 16 September 2008, the first meeting of a newly founded working group for the establishment of an NMR test protocol for the determination of heparin contaminants took place at the EDQM in Strasbourg. The group consists of 5 representatives from OMCLs and 1 participant from a subcontracted laboratory (University Würzburg) of the German Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM).

The purpose of the group is to complement the work of Ph. Eur. Expert Group 6 in defining a ^1H NMR reference method for the determination of heparin contaminants. As of 1 August 2008, nuclear magnetic resonance spectrometry and capillary electrophoresis are specified in the production section of the European Pharmacopoeia monographs on heparin calcium and heparin sodium (unfractionated heparins) as suitable methods for detecting substances lowering blood pressure and contamination by over-sulphated glycosaminoglycans in heparins. It was the goal of the group to have a suitable reference NMR test protocol available by the beginning of January 2009, which would then be published in *Pharmeuropa* in order to provide additional guidance to users.

As a long-term strategy, an alternative method for the determination of heparin contaminants based on a suitable widely used technique will be developed within the Ph. Eur. Expert Group 6 and included in the heparin monographs. In addition acceptance limits for potential contaminants will be specified. The present working group will also be invited to participate in this future study.

The work of the Heparin NMR Testing Group is a perfect example of the valuable contributions of OMCLs in

establishing and amending monographs of the European Pharmacopoeia.

Gene Therapy Working Group

A working group was established in 2008 including all OMCLs that have activities in the field of gene therapy products. Currently 5 OMCLs participate in this group; participation is open to all OMCLs at any time. The overall goal of the group is to join forces and make optimal use of the OMCL network resources with regard to the quality control of gene therapy products.

The first meeting of the group was hosted by Afssaps in Montpellier, France, on 26-27 May 2008. As a first task, the group reviewed the gene therapy products that are under development and drew up a priority list of products based on their closeness to market introduction. In a second step, a list of the methods and standards needed for control of the products on the priority list was drawn up. The working group will attempt to develop and validate these methods in the coming years. All participating OMCLs have started to add the already-available methods to the OMCL inventory database. They will explore the possibility of carrying out collaborative studies using common test samples provided by potential manufacturers.

Quality management systems

The quality assurance (QA) programme of the OMCL Network, co-ordinated by the EDQM, is aimed at proposing a common tool for OMCLs to implement, maintain, assess and improve their quality management systems in a harmonised way. It also provides assistance to OMCLs willing to increase their technical competence by means of training visits hosted by other OMCLs or tutorials and specific training courses organised by the EDQM.

Mutual joint audits and mutual joint visits

During 2008, 12 mutual joint audits (MJAs) were carried out at OMCL sites: 8 in OMCLs testing medicines for human use (6 with a dual competence in the chemical and biological field, 2 in the chemical field only); 3 in OMCLs testing medicines for veterinary use (2 with a dual competence in the chemical and biological field, 1 in the biological field only); and 1 in an OMCL testing medicines for both human and veterinary use (in the chemical field only).

One of the MJAs was jointly performed with a national accreditation body. This was the second time that the EDQM/OMCL Network carried out a joint audit with a national accreditation body and the outcome was in this case, as in the previous, very promising with respect to future collaboration and optimisation of resources.

A mutual joint visit (MJV) was carried out in an OMCL testing medicines for human use (chemical and biological field).

In 2008, no requests for training visits or tutorials were received by the EDQM.

For 2009, 11 MJAs and 1 training visit are already planned.

Training courses for the OMCL Network

A training course on the use of the computer program CombiStats was organised in 2008. For more details see the section entitled CombiStats.

Other training courses dealing with quality assurance topics will be organised in 2009, depending on requests from the OMCL Network.

OMCL Network quality assurance guidelines

The 4th annex to the OMCL Network guideline 'Qualification of equipment' was adopted at the OMCL Network annual meeting in June 2008, dealing with requirements for the qualification of automatic titrators.

The possibility of developing a new OMCL guideline was explored, dedicated to the validation of computerised systems, addressed to the OMCL environment. The guideline should include several annexes dealing with specific validation requirements for different types of computerised systems.

The issue of a new annex of the guideline 'Qualification of equipment', dedicated to the qualification of pipettes, as well as a new OMCL guideline 'Management of expiry dates of reagents' will be discussed in the near future.

Key QA documents and guidelines are available on the EDQM website (<http://www.edqm.eu/site/Quality-Assurance-Activities-Guidelines-86.html>).

Proficiency testing scheme studies

Over the years, the proficiency testing scheme (PTS) studies have become a regular programme within the Network. In 2008, 5 studies were organised in the physico-chemical field, with an average participation of 37 national control laboratories and 27 other pharmaceutical control laboratories, the private sector, industry and hospitals, while in the biological area 4 studies were organised, involving an average of 21 laboratories (11 OMCLs and 10 laboratories from the private sector.)

The 4th PTS agreement with the WHO covers the period from April 2007 to June 2009. In 2008, 4 out of the 5 studies included in the programme were finalised and the 5th was initiated. On average 50 governmental control laboratories belonging to the 6 different WHO world regions (Africa, Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific) participate in these studies.

General studies on market surveillance

In 2008, market surveillance studies (MSSs) that aimed at screening the quality of medicinal products commercialised on the European market were initiated for the following products: lisinopril dihydrate tablets; intramammary suspensions containing amoxicillin, clavulanic acid and prednisolone; and omeprazole gastro-resistant tablets and capsules; with an average of 15 participating OMCLs. Such a testing campaign provides an overall picture of the quality of products available on the European market for a given class of products. Where pertinent, the results of these studies will also support the revision of the relevant monographs and/or general chapters and methods of the Ph. Eur. The studies on levothyroxine tablets and morphine oral retard products

are still in the preparatory stage and the testing phase will only take place in 2009.

At the Annual Meeting of the OMCL Network in Strasbourg, an MSS on simvastatin tablets was agreed upon. The preparation of the protocol for this study by the scientific advisor was initiated in 2008.

Collaborative study on mesitates

This study was initiated in March 2008 after the recall in June 2007 of several batches of Viracept[®] contaminated with ethyl-methanesulfonate (EMS). The collaborative study, in which 13 OMCLs participated, was carried out on 4 batches of Viracept[®] 250 film-coated tablets containing different levels of EMS and MMS (methyl-methanesulfonate). Identification and quantification of MMS and EMS had to be performed using a GC/MS method. A liquid-liquid extraction procedure had to be applied for sample pre-treatment in order to remove interfering substances. As a follow-up, a market surveillance study on mesilate-containing medicinal products will probably take place in 2009.

Collaborative study on radiopharmaceuticals

A collaborative study on radiopharmaceutical preparations initiated in 2007 was finalised in 2008. A total of 13 laboratories (OMCLs and non-OMCLs) participated in this exercise, which consisted of the determination of the radiochemical purity of a technetium-99m labelled compound by HPLC. The outcome of the study was presented at the meeting of the relevant Group of Experts of the Ph. Eur. in April, where it was agreed that the EDQM would organise a first PTS on radiopharmaceuticals. The PTS initially planned for the end of 2008 had to be postponed to 2009 due to a shortage of samples following the shutdown of 2 nuclear reactors used for the production of medical radioisotopes in Europe.

Analysis of suspicious unknown products

The first study of the testing phase on the analysis of suspicious unknown products started in January 2008 with the participation of 19 OMCLs. The laboratories were provided with 4 tablets from an 'unknown' medicinal product taken from a commercial batch and had to analyse the sample using the method of their choice. All the participants correctly identified the active ingredient in the tablets. A second similar study was organised in the last trimester of the year with 31 participating OMCLs. The results will be analysed in 2009.

CombiStats

In 1999, the EDQM initiated the development of a computer programme for the statistical evaluation of biological dilution assays in accordance with chapter 5.3 of the Ph. Eur. At that time, most laboratories of the OMCL network used their own in-house-developed software, which led to a strong demand for a common programme to harmonise the presentation of assay data and the analysis thereof. The lack of availability of suitable commercial software resulted in the development of CombiStats, which has been used to the general satisfaction of the network since 2000.

Initially the software was only available to OMCLs, but as of November 2005, non-OMCL laboratories can also

obtain a user licence. Together with the public release of the software, an official website was launched (<http://www.combistats.eu>), on which an online manual, a tutorial, examples and background information can be found. A free demonstration version of CombiStats can also be downloaded. The software has been advertised in Pharmeuropa and flyers are distributed to make the software better known to potential users. An important update was released in May 2008 adding new features and methods of analysis. A training course for OMCLs was organised at the EDQM in November 2008 and more training courses will follow in 2009. They will progressively be opened to industry and private sector participants.

By the end of 2008, a significant number of licences have been issued, 28.5 % of which were to OMCL laboratories in 23 countries and 71.5 % to non-OMCL users in 30 countries. As of 20 November 2008, CombiStats is used in 19 countries of the EU and 18 countries outside the EU, including non-European countries such as Argentina, Australia, Brazil, Canada, India, Japan, Mexico, South Africa, South Korea, Taiwan, Uruguay and the USA. CombiStats has thus evolved into a common internationally agreed reference in its domain and contributes to mutual recognition of data and results by all interested parties.

3.2. EU/EEA-SPECIFIC ACTIVITIES

Official Control Authority Batch Release (OCABR) of biologicals for human use

Major highlights

At the annual meeting of the OMCLs in Strasbourg, representatives from the 27 EU member states, the EEA member states and Switzerland were invited to take part in the annual plenary session for OCABR network activity. More than 65 participants from 22 member states attended. In addition to the combined plenary session, parallel sessions were held to focus on activities related to OCABR for either human blood and plasma derivatives or human vaccines.

As part of an ongoing initiative to apply the 3R principles to OCABR an important meeting was organised in January 2008. The meeting involved an exchange between OMCLs and a number of representatives from vaccine manufacturers as part of a reflection on ongoing and future strategies for replacing, reducing and refining (3Rs) the use of animals during OCABR.

A separate meeting was held in January with representatives from IPFA and PPTA manufacturers' association of human blood and plasma derivatives to address issues specifically relevant to them.

A practical workshop for OMCLs involved in testing of oral poliomyelitis vaccine monovalent bulks was held successfully in March 2008 at the NIBSC. This important workshop provides an opportunity for hands-on training and maintenance of competence and encourages the open exchange of experience for improved harmonisation related to a critical technique.

Significant progress was made in 2008 on the development of a real-time database of batches having undergone OCABR. A small group of OMCLs involved in OCABR have taken part in a test phase of the database which is expected to be launched in 2009.

Annual meeting summary

OMCLs provided a review of their activities during the reporting period for batch release of both blood derivatives and vaccines and specific scientific presentations were given at the annual meeting.

2008 was an election year for the OCABR advisory group, which consists of 6 members (3 for blood- and plasma-derived medicinal products and 3 for vaccines). 2 new representatives (France and Belgium) and 1 re-elected representative (UK) completed the group, which also includes representatives from the Czech Republic, Germany and Italy.

Other issues of interest included the evolution and need for the involvement of EU OMCLs in the testing of human biologicals as part of the EU OMCL procedure for application of Article 58 of Council Regulation 726/2004. This has involved the development of additional guidance documents in co-operation with the WHO.

Application of the 3R principles was a big topic at the annual meeting. The evaluation of strategies to be applied for *in vivo* reduction schemes, based on sound scientific reasoning and experience with existing products, was highlighted.

New strategies for work-sharing to streamline release procedures were also brought to the forefront.

Adopted guidelines/procedures

• Common procedures for OCABR

Adopted revisions to the EC Administrative Procedure for OCABR include the addition of a new annex VIII (for nullification of OCABR certificates for batches that were released but subsequently withdrawn from the market for reasons that may be independent of the batch release) and a revision to annex IIf (certificate for ancillary medicinal products derived from human blood or plasma in a medical device).

An OCABR network practical guideline on the procedures to be followed for appearance testing was also adopted.

A reflection paper on OCABR in the global regulatory context was finalised and endorsed by the OCABR network. The paper has been communicated to the regulatory authorities at Heads of Medicines Agencies and the EMEA to underline the role of the OCABR network in the global surveillance system of medicines in the EU and to foresee possible routes for evolution while encouraging more interaction with the different regulatory branches.

• Guidelines for human blood and plasma derivative products

3 revised product-specific guidelines were adopted for:

- clotting factor concentrates, plasma inhibitor concentrates and fibrin sealants;
- human immunoglobulins;
- human plasma (pooled and treated for virus inactivation).

• Guidelines for human vaccines

1 new product-specific guideline and 5 revised guidelines were adopted for:

- cell-cultured influenza vaccine (surface antigen, inactivated) (new guideline);
- influenza vaccine;
- influenza vaccine (surface antigen, inactivated, virosome);
- pandemic influenza vaccine;
- poliomyelitis vaccine (inactivated);
- rabies vaccine.

All adopted product-specific guidelines and administrative procedures are available in the book published by EDQM at the end of December 2008. They can also be downloaded in their entirety from the EDQM website (http://www.edqm.eu/site/Human_Biologicals_OCABR-611.html).

Official Control Authority Batch Release (OCABR) of immunological veterinary medicinal products (IVMPs)

22 representatives from 15 member states and a representative from the EU Commission participated in the veterinary session of the annual meeting of 2008. This occasion marked the first full reporting period following the implementation of procedures and guidelines, developed through the course of 2006/2007 by the IVMP OCABR network in co-operation with the EU Commission and with industry consultation and adopted by the Veterinary Pharmaceutical Committee in March 2007.

The following documents were adopted:

- the procedure for application of Article 81 (Official Batch Protocol Review (OBPR));
- the procedure for application of Article 82 (Official Control Authority Batch Release (OCABR));
- 15 product-specific guidelines for products on a shortlist for OCABR as determined through risk assessment;
- 5 model templates for manufacturers' protocols to be submitted for OCABR and OBPR.

All adopted documents can be downloaded from the EDQM website (http://www.edqm.eu/site/Veterinary_Biologicals_OCABROBPR-634.html).

Member states provided a summary of their activity over the reporting period and their progress in application of Article 81 and Article 82 procedures. This also allowed an update to determine the state of application of both Article 81 and Article 82 in the different member states since OCABR is a 'may' clause, and OBPR is a voluntary procedure applied through goodwill and mutual understanding. There was a strong message from the EU Commission to encourage member states to phase out as quickly as possible their national systems and adhere to the agreed EU system.

A drafting group made up of experts from the network was created to prepare different key documents such as the terms of reference for the future running of the network, including the creation of an advisory group and a procedure for evaluation of products on the shortlist of products to undergo OCABR to see if they could be eligible for test-reduction schemes.

An open session was also held to allow representatives from the manufacturers' association IFAH-Europe to provide their input on the progress made with the new system.

An entire session was dedicated to the challenges faced for potency testing of inactivated rabies vaccines for veterinary use. The difficulties linked to validation of this assay and the need to reduce animal use were highlighted in a presentation from France. A promising example of a validated alternative assay developed at the Paul-Ehrlich-Institut in Germany was also presented. It was greeted by considerable interest from network members and has led to the instigation of a collaborative study to establish the method as part of the EDQM Biological Standardisation Programme (see above).

Market surveillance for products with a centralised marketing authorisation

The programme for sampling and testing of centrally authorised products (CAPs) was successfully continued in 2008 and entered its 10th consecutive year. Since its implementation the programme has been continuously improved thanks to the collaboration between all stakeholders:

- the European Medicines Agency (EMA), which is the sponsor and has the overall responsibility for the programme;
- the EDQM, which co-ordinates the sampling and testing operations on the basis of the information provided by the marketing authorisation (MA) holders upon request from the EMA, and reports to the EMA the outcome of the sampling and testing operations with proposals for follow-up actions where necessary;
- the national inspection services, which perform product sampling on the market;
- the OMCLs of the EU/EEA OMCL Network, which perform analytical testing of products.

The CAP programme covers medicinal products for both human and veterinary use. In 2008 it covered a total of 42 medicinal products, corresponding to 36 medicinal products for human use (15 biologicals and 21 chemical/pharmaceutical/radiopharmaceutical products) and as 6 medicinal products for veterinary use (3 immunobiological and 3 chemical products). In 2008 the programme included the examination of the active substances (APIs) of 2 different products. This makes 2008 the sampling and testing programme with the lowest number of APIs tested since 2002. With regard to the total number of medicinal products included in the programme, an increase of 5 % compared to the 2007 CAP programme could be observed. The agreement established between the EMA and EDQM stated that the number of products included in the yearly programmes would be fixed at at least 40 as of 2007. Products to be included in the 2008 programme were selected by EMA expert committees from those authorised in 2005 (year n-3), thus guaranteeing that the selected products have been launched and manufactured on a large scale. In addition to these products the list was complemented with 13 products that had already been in one of the previous yearly programmes; these products were selected on the basis of proposals from OMCLs. This subsequent testing of products already tested highlights the willingness of the EMA, EDQM and OMCLs to make sure that products are checked several times in their lifetime and not only once, 3 years after granting of the

MA. The major reasons leading to a repeat testing were either major changes in manufacturing process of the concerned products since initial testing or a high number of variations in the quality field.

In accordance with the procedure PA/PH/CAP (05) 96 DEF 'Procedure for ad-hoc testing of centrally authorised products', one product for which a variation of its MA had been submitted to the EMEA (substitution of a former batch of the reference standard by a newly qualified batch) was added to the 2008 programme in April 2008 upon request from the CHMP. The purpose of this testing was to assess the calibration of the new reference standard performed by the MAH and ensure it was consistent with the former reference standard.

In general, market samples were collected in 3 EU/EEA countries for each product in order to have an overview of the actual product quality of distributed batches. This sampling pattern was customised for products with a low volume of distribution such as orphan medicines and for products where different dosage strengths were investigated. Overall, 110 sampling operations have been carried out by national inspection services in 27 EU/EEA member states. The proportion of samples drawn from hospitals and retail pharmacies has significantly increased since 2007 to approximately 20 % of the total sampling operations, in comparison with the sampling operations carried out at wholesalers. The application of the new 1-OMCL-only testing scheme for all chemical products tested since the 2007 programme may have contributed to this positive trend by reducing the overall number of pharmaceutical units to be sampled for chemical products. Even though more than 80 % of the samples still originate from MA-holder warehouses or wholesalers, the trend towards sampling further down in the distribution chain that seems to emerge from this data should be regarded as a promising first step. Market samples, non-commercially available standards and specific reagents provided by the manufacturers represented approximately 450 items. Collection of these materials, storage, coding and dispatching to OMCLs for testing was dealt with by the EDQM.

As planned, the new testing scheme for chemical products, gradually introduced since 2005, was applied to all chemical products for the second time during the 2008 programme. All chemical products were tested by a single OMCL, with the possibility of involving a second OMCL at a second stage only in the case of analytical or compliance issues necessitating an independent evaluation.

Testing of biological products continues to be performed by 2 OMCLs in parallel. It is intended in the future to move towards a similar approach for biological products. However, testing of biological products is a complex issue and reduction of the number of testing OMCLs should be considered cautiously. Nevertheless, it was decided at the 2008 annual CAP meeting that, as of the 2010 programme, insulin analogues would be tested only in a single OMCL like chemical products, as it implies physico-chemical and biochemical methods only. This decision was taken further to a review of data gathered throughout the last 10 years of the programme showing no added benefit for the testing of this group of products in 2 OMCLs. This data review for biological products will be updated regularly and will steer the decision to

apply (or not) the testing scheme for chemical products to other groups of biological products with the objective of freeing testing capacities, allowing the testing of an increased number of products per yearly programme.

On the whole, 36 OMCLs from 27 EU/EEA countries took part in the 2008 programme, which consisted of a total of 66 testing operations. In 2008, only 1 product did not meet the authorised specifications: concerns regarding the suitability of the analytical method used by the MA holder for routine investigation of a powder for oral suspension were brought up by out-of-specification results obtained during the testing. This finding was not considered a threat to public health and no recall was initiated. Nevertheless, the issue was reported to the EMEA who initiated appropriate follow-up actions.

All other products tested complied with their authorised specifications; for some of them minor issues, mainly related to the quality of the analytical documentation (MA dossier and/or Standard Operating Procedures for QC), were reported. Difficulties were also encountered during method setting-up, e.g. for automated methods or techniques requiring unusual and very specialised equipment.

For all products, individual product reports were issued by the EDQM and distributed to all parties (EMEA, OMCL Network, involved sampling contact persons). All issues were thus reported to the EMEA and their scientific experts, together with the proposals for necessary follow-up actions on the registration dossier and/or on analytical testing methods. The individual product reports are distributed to the MA holder via the EMEA whenever concerns arise from the testing operations.

Thanks to the work of the Advisory Group of the CAP programme and the collaboration with the EMEA, a risk-based approach (RBA) for the selection of human products to be tested was established. This will replace the 'n-3' rule for inclusion of centrally authorised products in a yearly programme. A similar RBA is under finalisation for veterinary products. The RBA will be used to select the human products included in the 2010 programme; regarding veterinary products, it is expected that the RBA will also be implemented as soon as possible.

Discussions about harmonisation of the selection of parameters to be tested for each product continued in 2008 within the CAP Advisory Group. A document intended to help assessors selecting the different parameters to be investigated was prepared and included as a recommendation to the template used by assessors for each individual product at the time of the file evaluation.

Post-marketing surveillance of products with a marketing authorisation according to the Mutual Recognition Procedure (MRP) and the Decentralised Procedure (DCP)

In 2008, the 4th regular programme of post-marketing surveillance of MRP and DCP products was carried out. For the first time the whole programme – from the planning to the reporting phase – was steered by the MRP/DCP product testing database, which was launched in July 2007. This IT tool allows a better co-ordination of the planning, sampling and reporting activities, and

also provides a platform for information exchange about follow-up actions taken on the basis of test results. Access to the data is at the moment restricted to OMCLs of the Network actively involved in the programme, and several technical measures have been taken to guarantee data security and confidentiality. In the near future, read-only access will be granted to users of the Communication and Tracking System (CTS), the regulators of national competent authorities and other concerned parties (inspectorates and pharmacovigilance departments), which have shown their interest in getting user rights.

During 2008 more than 20 OMCLs participated actively (or passively by sending test samples) in the programme and more than 300 projects could be finalised. The secretariat has also taken care to enter retrospectively into the database test results on the basis of standardised Summary Reporting Sheets received between 2004 and mid-2007 from OMCLs, which completes the picture of the work carried out so far by the group since the start of the enlarged trial phase.

The MRP/DCP product testing database now allows more in-depth analyses of the programme due to a powerful statistics tool integrated in the system. The generated figures and charts will be a good basis for the strategic discussion within the newly founded HMA Working Group on Product Testing, which will start to operate at the beginning of 2009.

4. HEALTHCARE ACTIVITIES

4.1. BLOOD TRANSFUSION (TS) AND ORGAN TRANSPLANTATION (TO)

Within the context of intergovernmental co-operation in the field of health, the Council of Europe has consistently selected ethical problems for study. One of the most important ethical issues relates to the non-commercialisation of human substances, i.e. blood, organs and tissues.

With regard to blood transfusion, co-operation among member states started in the 1950s. From the outset, the activities were inspired by the following guiding principles: promotion of voluntary, non-remunerated blood donation; mutual assistance of member states (e.g. in the exchange of blood-typing reagents and access to rare blood donations); optimal use of blood and blood products; and protection of the donor and the recipient.

Later, activities in the field of organ transplantation were initiated according to the leading principles of ensuring the dignity of the human being, maintaining and promoting human rights and fundamental freedom, non-commercialisation of substances of human origin and protection of donors and recipients.

Around its first agreements in the 1950s and 1970s, the Council of Europe has established pan-European programmes on blood transfusion and transplantation. Since February 2007, these programmes have been run by the EDQM under the aegis of 2 new steering committees (the European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS) and the European Committee (Partial Agreement) on Organ Transplantation (CD-P-TO)) that were created by the Council of Europe.

Major achievements in 2008

Meetings, events, communication

In 2008 each of the committees met twice to elaborate their respective work programmes and to initiate activities. Financial assistance was granted to support the participation of a number of delegates from far eastern Europe to these plenary meetings.

The 10th European Organ Donation and Transplantation Day was hosted by the Slovenija Transplant Institute on 18 October 2008 in Ljubljana (Slovenia).

A 'Healthcare' section was included on the EDQM website.

Projects and publications

The 14th edition of the Council of Europe 'Guide for preparation, testing and use of blood components' was published in French and English in January 2008.

The follow-up of the reporting from Council of Europe member states on the collection, testing and use of blood components was organised, and the 2004 survey was completed and published. Reports on the 2005 and 2006 surveys and on trend analysis on data from the years 2001-2006 are currently under preparation.

The addendum to the 3rd edition of the Council of Europe 'Guide to safety and quality assurance for the transplantation of organs, tissues and cells' was finalised for publication in early 2009.

International surveys on critical issues (e.g. transplant tourism) and drafting of state-of-the-art position papers (e.g. on international organ exchanges) were initiated.

Resolutions

3 resolutions that were elaborated in collaboration with the Bioethics Committee of the Council of Europe (CDBI) on donor responsibility and limitation of donation of blood and components, living donor kidney transplantation and living donor liver transplantation were adopted by the Committee of Ministers in 2008 (12 March 2008 and 26 March 2008).

The full text is available on the EDQM website (http://www.edqm.eu/site/News_and_General_Information-44.html).

4.2. PHARMACEUTICALS AND PHARMACEUTICAL CARE

The quality of medicines and the quality of healthcare is of ever-increasing importance to the quality of life and well-being of individuals. The most frequent healthcare intervention is a prescribed medicine, which is subject to strict regulatory control in Europe. Yet, less than half of the prescribed medicines are used correctly and as prescribed: medication errors and overmedication being as harmful as a lack of adequate treatment. Counterfeiting of medicines, healthcare products and other crimes involving pharmaceuticals bypassing all regulatory controls are on the rise in Europe and worldwide. Healthcare systems have to satisfy public health needs as regards medico-technological progress in a challenging environment of socio-demographic change and restricted budget resources.

The key approach towards promoting the good use of medicines at all stages of the medication chain to the

end user is the responsible provision of medication for the direct benefit of the patient. The principles of pharmaceutical care are a necessary element of healthcare based on the fundamental relationship between the patient and the provider mutually giving and accepting competence and responsibility.

The above-mentioned area covers a programme of activities of great relevance for the quality of healthcare and healthcare practice in Europe, in particular:

- patient-oriented, intergovernmental co-operation as regards pharmaceutical practice, focusing on the safe and effective use of medicines in society;
- model approaches for risk management, prevention and improved co-operation among public and private sectors in the field of public health protection from counterfeit medical products and related crimes;
- the harmonisation of provisions and practice as regards the legal classification of medicines as prescription and non-prescription medicines, with a view to patient safety, the accessibility of medicines and responsible management of healthcare expenditure.

This programme is co-ordinated by the EDQM.

On 6 February 2008, the Committee of Ministers adopted the revised terms of reference of the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH), entrusting it with overseeing the above programme of activities including those of the former Public Health Committee (CD-P-SP) set out in the Convention on the Elaboration of a European Pharmacopoeia (ETS No. 50), as amended by Protocol ETS No. 134.

At its first meeting on 2-3 April 2008, the CD-P-PH adopted the draft revised terms of reference of the Committee of Experts on the classification of medicines as regards their supply (CD-P-PH/PHO), the Committee of Experts on the quality and safety of standards in pharmaceutical practices and pharmaceutical care (CD-P-PH/PC), and the Committee of Experts on minimising public health risks posed by counterfeiting of medical products and related crimes (CD-P-PH/CMED), taking account of and in continuity with the former Committees under the aegis of the Partial Agreement in the Social and Public Health Field.

Quality and safety standards in pharmaceutical practice and pharmaceutical care

In 2008, the Committee of Experts CD-P-PH/PC met twice to carry out the programme of activities included in its terms of reference. The CD-P-PH/PC:

- launched a survey in the interested member states on key concepts in pharmaceutical care, quality indicators, and existing sources for relevant data/information (October-December 2008) as a basis for its activity on the implementation of quality assessment in pharmaceutical practice and care in Europe through quality indicators; the recipients include public health authorities, national associations of medical doctors, pharmacists, nurses and patients in the signatory states and other Council of Europe member states;

- finalised the survey on the status of traditional Chinese medicine (TCM) in the signatory states and other Council of Europe member states with a view to presenting to the CD-P-PH proposals for follow-up to the findings of the survey, including the analysis of gaps in legislation as regards risks for public health;
- finalised a survey on quality and safety standards in pharmacy preparations with a view to possible harmonisation of quality and safety standards for small-scale preparations in pharmacies in Europe; this activity is complementary to the survey on an inventory of officinal preparations being carried out by the European Pharmacopoeia Department.

Minimising public health risks posed by counterfeiting of medical products and related crimes

In 2008, the Committee of Experts CD-P-PH/CMED met twice to carry out the programme of activities included in its terms of reference. The CD-P-PH/CMED:

- organised 2 training courses on how to combat counterfeit medicines and how to protect public health in Strasbourg, France, on 26-27 June 2008 and in Larnaca, Cyprus, on 18-19 November 2008, respectively; the June 2008 training was opened by Mr Bernard Marquet, Chairman of the Sub-Committee on the European Social Charter and Employment of the Social, Health and Family Affairs Committee of the Council of Europe Parliamentary Assembly (PACE), and received much media attention;
- finalised the manuscript for the book 'Counterfeit medicines: facts and practical advice' and its supplement 'Counterfeit medicines. Part II Exercises';
- started an outcome-focused pilot study on different modes of implementation of a network of Single Points of Contact (SPOCs) in the interested member states, as had been proposed in the past by the Council of Europe Ad hoc Group on Counterfeit Medicines and endorsed at the 2nd General Meeting of the WHO IMPACT, Lisbon, December 2007;
- adopted the model procedure 'Counterfeit medicines in Europe: risk communication strategies for Drug Regulatory Authorities', which was endorsed by the WHO IMPACT at its 3rd General Meeting on 3-5 December 2008 in Hammamet, Tunisia;
- discussed a basic concept for a multisectorial knowledge-base for the management, prevention and follow-up of risks by the involved public sectors (health and law enforcement); the technical feasibility of the knowledge-base ('KnowX') will be examined in 2009.

Classification of medicines as regards their supply

In 2008, the Committee of Experts CD-P-PH/PHO met twice to carry out the programme of activities included in its terms of reference: the information on the classification of medicines as regards their supply as prescription and non-prescription medicines was updated to reflect the recent status of medicines classification in the signatory states. The recommendations about the classification of medicines as regards their supply, which takes into account patient safety, and the accessibility of

medicines were prepared and are available on the EDQM website (<http://www.edqm.eu/site/CD-P-PHO-Committee-of-Experts-on-the-classification-of-medicines-as-regard-their-supply-CD-P-PHPC-1328.html>).

Draft Convention against counterfeiting of medical products and similar crimes that involve threats to public health

The Secretariat of the sector Healthcare: Pharmaceuticals and Pharmaceutical Care ensured the inter-secretariat co-operation and liaison with the DG Human Rights and Legal Affairs, Directorate for Standard Setting, Department of Law Reform, as regards the preparation of a possible Council of Europe Convention against counterfeiting of medical products and similar crimes that involve threats to public health. It ensured the co-secretariat for the Group of Specialists on Counterfeit

Pharmaceutical Products (PC-S-CP) entrusted in 2008 with preparing a preliminary draft convention text.

United Nations Internet Governance Forum

The Council of Europe is a stakeholder at the United Nations Internet Governance Forum (UN IGF): the Secretariat of the sector Healthcare: Pharmaceuticals and Pharmaceutical Care participated in the preparation of the workshop 'Medicines on the Web – Risks and Benefits', at the UN IGF 2008 Conference, which took place in Hyderabad, India, on 3-6 December 2008. The objective of the workshop was to raise awareness on risks and benefits associated with buying medicines via the internet, to facilitate multi-stakeholder discussion about the needs of consumers and patients as regards medicines on the internet, and on whether and how the safety of medicines marketed on the internet can be guaranteed.