Throughout the year 2011, work on establishing standards for the quality of medicines, both in the form of pharmacopoeial monographs and their respective reference standards, to keep the European Pharmacopoeia state-of-the-art was a major focus of the EDQM’s activities. As a follow-up to the international conference on the quality of medicines in October 2010 and a number of other meetings organised to collect feedback from regulatory authorities and stakeholders on their needs as regards the further development of the European Pharmacopoeia, the Ph. Eur. Commission established three new working parties to cover new challenges in the field of biological products. In addition, the importance of stimulating broad feedback from manufacturers worldwide on Ph. Eur. texts published for public consultation was addressed by the decision to allow free access to Pharmeuropa, the European Pharmacopoeia’s forum, via electronic publication.

At the international level, co-operation with the Japanese and United States Pharmacopoeias continued in the Pharmacopoeial Discussion Group (PDG); an informal initiative aimed at international harmonisation of pharmacopoeial requirements. Since its establishment in 1990, the PDG has met twice a year, parallel to the meetings of the International Conference on Harmonisation (ICH). Following the decision of the ICH Steering Committee not to extend in its previous form the mandate of the ICH Expert Working Group Q4B, which was charged with the evaluation of regulatory interchangeability of harmonised pharmacopoeial texts, the three pharmacopoeias now organise their PDG meetings independently from the ICH. The PDG met in June 2011 in Cincinnati, hosted by the USP, and in November 2011 in Strasbourg, hosted by the EDQM. The bilateral, pilot, prospective, API harmonisation initiative with the United States Pharmacopoeia, established in 2008, yielded tangible results, with the adoption of the remaining two monographs by the European Pharmacopoeia Commission and its USP counterpart. In a feedback discussion between the two pharmacopoeias and the manufacturers involved in the pilot project, it was decided to extend the scope of the pilot project to the first revision requests for these monographs before expanding it to new candidate molecules.

Applications for Certification of Suitability to the Monographs of the European Pharmacopoeia (CEP) were processed within
timelines. Monthly statistics on assessment and inspection activities are now published on the EDQM website. For the first time, a larger number of dossiers on herbal drugs and herbal drug preparations were received, numbering eight applications submitted in 2011. In the context of the implementation of the revised Ph. Eur. general chapter 5.2.8 “Minimising the risk for Transmissible Spongiform Encephalopathy” (TSE), a number of CEP applications were reviewed and updated to ensure that all such CEPs were in compliance with the new requirements. As regards policy changes, following discussion with the Joint CHMP/CVMP Quality Working Party, it was decided that information on the container/closure system of a substance would be assessed in the context of a CEP application, regardless of whether a re-test period had been requested by the applicant. All CEPs granted after 01 September 2011 now contain information on the container/closure system. On-site inspections performed in the context of the CEP procedure again identified a number of GMP-non compliant manufacturers. Overall, 18 CEPs were suspended and 14 were withdrawn by the EDQM in 2011.

At its Annual Meeting, the European network of Official Medicines Control Laboratories (OMCLs), co-ordinated by the EDQM, adopted a number of new and revised quality management guidelines. The Network also decided to set up additional working groups on API, counterfeit/illegal medicines, OMCL testing of Unlicensed Pharmaceutical Preparations and on Stockpiled Biologicals. These new groups had their first meetings and discussed their respective work programmes in 2011.

In the field of blood transfusion and organ transplantation, the 16th Guide to the Preparation, Use and Quality Assurance of Blood Components and the 4th Guide to the Safety and Quality Assurance for the Transplantation of Organs, Tissues and Cells were published. In both areas, strengthened collaboration between Council of Europe member states was fostered with, for example, the South-Eastern Europe Health Network (SEEHN) project “Increasing regional self-sufficiency in relation to safer blood and blood components”, led by Romania, and the Black Sea Area project, a three-year collaborative project through which a regional strategy will be developed to promote transplantation activities in the region.

The EDQM contributed to the worldwide fight against falsification/counterfeiting of medical products through a number of activities. Multi-sectorial training sessions for government representatives were continued in 2011 and a live demo of the EDQM’s eTACT project, a traceability system for medicinal products, was presented to stakeholders to solicit comments and feedback. The MEDICRIME Convention, adopted by the Committee of Ministers, the Council of Europe’s governing body, in December 2010, was opened for signature in the context of an international conference on combating counterfeit medical products in Moscow in October 2011. Activities in the field of cosmetics and food contact materials were further progressed.

In 2011, the EDQM organised and participated in a number of international conferences in the US, India, Asia and Africa. Memorandums of Understanding were signed with the World Health Organization, the Russian Federation and Ukraine to allow for exchange of information related to GMP inspections.

Finally, the EDQM is proud that the ISO 9001 audit performed by Afnor, the French certification body, in November 2011 confirmed the ISO 9001 certification of its Certification of Suitability activities (both assessment and inspections) and the market surveillance studies conducted under the auspices of the EDQM, i.e. the activities related to post-marketing surveillance studies for medicinal products authorised by the centralised (CAP) and national (MSS studies) procedures, the mutual recognition (MRP) and decentralised (DCP) procedures and the activities related to the OCABR procedure for the release of batches of human immunological medicinal products (blood and vaccines).

Overall, 2011 was another successful year for the EDQM. I would like to take this opportunity to express our sincere gratitude to the numerous experts appointed by the 36 member states that have signed the Convention on the Elaboration of a European Pharmacopoeia. Their expertise, dedication and support are crucial for the work of the European Pharmacopoeia Commission and its Groups of Experts and Working Parties, the Committees and Expert Groups in the areas of Blood Transfusion, Organ Transplantation, Pharmaceuticals and Pharmaceutical Care, Consumer Protection, the OMCL Network, as well as those involved in assessments and inspections in the context of the Certification Scheme. Without them and the support of the 37 signatory parties of the Convention on the Elaboration of a European Pharmacopoeia, EDQM’s achievements in 2011 would not have been possible.

Susanne Keitel
Director
THE EDQM AT A GLANCE: values, aims, activities

■ The European Directorate for the Quality of Medicines & HealthCare: a Directorate of the Council of Europe

The primary aim of the Council of Europe is to create a common democratic and legal area throughout the whole of the continent, ensuring respect for its fundamental values: human rights, democracy and the rule of law.

Human Rights... Democracy... Rule of Law

These values are the foundations of a tolerant and civilised society and indispensable for European stability, economic growth and social cohesion. On the basis of these fundamental values, we try to find shared solutions to major problems such as terrorism, organised crime and corruption, cybercrime, bioethics and cloning, violence against children and women, and trafficking in human beings. Co-operation between all member states is the only way to solve the major problems facing society today.

Objectives

• to protect human rights, pluralist democracy and the rule of law.

• to promote awareness and encourage the development of Europe’s cultural identity and diversity.

• to find common solutions to the challenges facing European society.

• to consolidate democratic stability in Europe by backing political, legislative and constitutional reform.

■ The mission of the EDQM

The mission of the EDQM is to contribute to the basic human right of access to good quality medicines and healthcare, and to promote and protect human and animal health by:

• establishing quality standards and promoting ethical practices:
  - for the collection, preparation, storage and use of blood components concerning transfusion medicine.
  - for organ transplantation including tissues and cells.

• collaborating with national and international organisations in efforts to eliminate illegal and counterfeit medicinal and medical products.

• providing policies and model approaches for the safe use of medicines in Europe, including guidelines on pharmaceutical care.

• establishing standards and co-ordinating controls for cosmetics and food packaging.

The European Directorate for the Quality of Medicines & HealthCare (EDQM)

The EDQM, whose origins date back to 1964, has over the years become a directorate of the Council of Europe. In 2011, the EDQM employed 240 full-time staff members and was structured into nine administrative entities.

It was set up by virtue of article 9 of the Convention on the Elaboration of a European Pharmacopoeia, which was signed by eight member states of the Council of Europe in 1964 with the vision of creating a common European Pharmacopoeia. Known for many years as the “European Pharmacopoeia Secretariat”, this administrative entity of the Council of Europe has undergone successive name changes, each time to reflect the new missions assigned to it.
1. CORE ACTIVITIES

1.1 The European Pharmacopoeia (Ph. Eur.)

Purpose

The purpose of the European Pharmacopoeia (Ph. Eur.) is to promote public health by the provision of recognised standards ensuring the quality of medicines. Their existence facilitates the free movement of medicinal products in Europe and ensures the quality of medicinal products and their components imported into Europe. Ph. Eur. monographs and texts are designed to be appropriate to the needs of regulatory authorities, manufacturers of starting materials and medicinal products and those engaged in the quality control of medicinal products and their constituents.

The Ph. Eur. is governed by the Ph. Eur. Commission which supervises the work of the more than 70 working parties and groups of experts. The Commission is composed of delegations of the 37 signatory parties and 23 observers to the Convention on the Elaboration of a European Pharmacopoeia.

The European Pharmacopoeia is widely used internationally. The Commission works closely with all users of the Pharmacopoeia in order to better satisfy their needs and facilitate their co-operation.

An official reference to serve public health

Ph. Eur. quality standards are not only part of the requirements for marketing authorisation for a medicinal product, but are legally-binding throughout the entire life-cycle of the product. They guarantee a single common quality standard for medicines throughout Europe.

All producers of medicines and/or substances for pharmaceutical use must, therefore, apply these quality standards in order to market their products in the signatory states of the Convention.

A large scope to cover all public health issues

In its current version, the Ph. Eur. contains 2167 monographs, including general standards that apply to groups of ingredients or dosage forms, and 336 general methods of analysis. As shown below, its scope extends far beyond “classical” chemically-defined medicines.

Officially adopted and implemented by all member states

All standards of the Ph. Eur. are adopted by consensus at the Ph. Eur. Commission. Once adopted, standards become mandatory on the same date in all member states.

The 23 observers from all continents (Albania, Algeria, Argentina, Armenia, Australia, Belarus, Brazil, Canada, China, Georgia, Israel, Kazakhstan, Madagascar, Malaysia, Moldova, Morocco, Russian Federation, Senegal, Syria, Tunisia, Ukraine, United States of America and the World Health Organization) are welcome to participate in the deliberations of the Commission and its Groups of Experts and Working Parties.

% of subscriptions in 2011 to the Eur.Ph. by geographical zone

An on-going process to add and to revise existing quality standards

The Ph. Eur. is maintained by the European Pharmacopoeia Department, composed of scientific officers who act as Secretaries to the groups of experts and working parties that establish the texts of the Ph. Eur. More than 800 experts from all over Europe contribute their expertise and knowledge to the drafting process. As shown in the following figure, there is a continuous need to update monographs, taking account of new developments and requirements arising for scientific, regulatory or other reasons.
Translators in the European Pharmacopoeia Department ensure that the Ph. Eur. is translated into English and French, the two official languages of the Council of Europe. It is also translated into Spanish in co-operation with the Spanish authorities. Translations into other national languages of member states of the Convention, e.g. German, Hungarian and Polish, are performed under the responsibility of the individual member states.

**How quality standards are regularly reviewed and revised to stay state of the art**

- **Scientific/technical evolutions** e.g. Fast LC, HPLC, nano-HPLC, new therapies e.g. CT
- **New risks to Public Health**
- **Ph Eur text update**
- **New working parties**

**New working parties appointed to better cope with emerging topics**

In 2011, the Commission approved the creation of several new working parties:

- **Non-Biological Complexes Working Party**, which will be responsible for the elaboration of monographs on non-biological complexes (e.g. nanoparticle solutions, such as Iron Sucrose Concentrated Solution).

- **Raw Materials for the Production of Cellular and Gene Transfer Products Working Party**, which will elaborate text(s) on such raw materials including antibodies, basal media (for cell culture), serum/serum replacements, growth factors and cytokines.

- **Host-Cell Proteins Working Party**, which will draft recommendations with regard to the development, validation and use of in-house or commercial kits or test methods for the detection and quantification of host-cell derived proteins.

**The European Pharmacopoeia strengthens its interactions**

To optimise the interaction between the European Pharmacopoeia Commission and its users and to allow users to have more time to comment on drafts and ensure broader access to everybody, Pharmeuropa, the European Pharmacopoeia forum, is in the process of becoming paperless.

**Texts will be published on an on-going basis, but the principle of four issues per year and the four comment deadlines will remain unchanged, as will the current channels for providing comments to published draft texts. (see chapter 2.2 Publications activities page 33)**

**Exchanges and discussions with National Pharmacopoeia Authorities (NPA) members of the European Pharmacopoeia Convention**

The annual meeting of the National Pharmacopoeia Authorities of the Ph. Eur. member states took place in Madrid on 9 - 10 May 2011. The meeting, a unique platform for the open exchange of information and discussion between the secretariats of national pharmacopoeia authorities and the Ph. Eur., was hosted by the Agencia española de medicamentos y productos sanitarios (Spanish Agency of Medicines and Health Products). Twenty-six of the thirty-six member states of the Convention on the Elaboration of a European Pharmacopoeia participated in this event.

Topics discussed included:

- **follow-up to the actions that were proposed and decided upon at**:
  - the international EDQM conference ‘Quality of Medicines in a Globalised World: Dreams and Reality’ organised in Prague in 2010, and
  - the workshop on ‘Future monographs in the field of biological products’ held in Strasbourg in February 2011 with representatives from European competent authorities.
  - a status update on the potential elaboration of a European formula of paediatric formulations.
  - future developments regarding the second series of identification tests, intended to be carried out in pharmacies.

The annual meeting also provided an opportunity for National Pharmacopoeia Authorities to share their best practices, e.g. in supporting the work of the Chairs and experts of the various groups elaborating the Ph. Eur. texts by providing appropriate training and tools.

**International Harmonisation - the Pharmacopoeial Discussion Group (PDG)**

Globalisation and expansion in international trade present a growing need to develop global quality standards for medicines. Standards are a vital instrument for marketing authorisation, market surveillance, and free movement and trade of medicines among regions and countries. Therefore, the European Pharmacopoeia is engaged in a process of harmonisation of general methods and excipient monographs with the Japanese Pharmacopoeia and the United States Pharmacopeia, within an informal structure referred to as the Pharmacopoeial Discussion Group (PDG). Information on the status of harmonised texts is given in general chapter 5.8. Pharmacopoeial harmonisation of the Ph. Eur. and on the International harmonisation page of the EDQM website.
Where harmonisation of general chapters is carried out, the aim is to arrive at inter-changeable methods or requirements so that demonstration of compliance using a general chapter from one of the three pharmacopoeias implies that the same result would be obtained using the general chapter of either of the other two pharmacopoeias. When a formal declaration of inter-changeability has been recommended by ICH, it will be indicated in general chapter 5.8. Pharmacopoeial harmonisation. If residual differences remain in harmonised general chapters, respective information is given in this general chapter.

The PDG considers proposals made by national associations of manufacturers of pharmaceutical products and excipients in order to select general methods of analysis and excipient monographs for addition to its work programme. Each pharmacopoeia is responsible for a programme of international harmonisation.

At present, 28 of the 35 General Chapters and 41 of the 61 excipient monographs of the current work programme have been harmonised. Harmonisation has also been achieved on 9 of the 10 General Chapters identified by the ICH Q6A Guideline. Following consideration of the significantly different types of Glyceryl Monostearate material manufactured in the three regions, PDG decided to remove this item from its work programme.

General chapter sign-offs included the newly-harmonised General Chapter for Microcalorimetry and revision to the General Chapters on Bacterial Endotoxins and Bulk and Tapped Density.

Excipient sign-offs included revisions to the Carmellose, Benzyl Alcohol, Potato Starch, Wheat Starch, Calcium Phosphate Dibasic and Calcium Phosphate Dibasic Anhydrous monographs. The latter four revisions are the outcome of PDG’s review of previously harmonised excipient monographs.

PDG also decided to add the Isomalt monograph to its work programme. In-depth discussions on advanced drafts of certain celluloses and carbohydrate monographs will pave the way for future sign-offs.

Prospective harmonisation of monographs for active substances

As harmonisation of active substances is, thus far, not within the scope of the PDG, the prospective harmonisation of monographs for active substances has been initiated upon request from two manufacturers of active substances. A bilateral pilot project started in 2008 between the Ph. Eur. and the USP. The JP is regularly informed and is observing the process.

Four monographs for active substances are within the scope of the pilot project, namely: Rizatriptan benzoate, Montelukast sodium, Celecoxib and Sildenafil citrate.

All four monographs of the pilot phase have been adopted by the Ph. Eur. Commission: Rizatriptan benzoate (2585) and Montelukast sodium (2583) in 2010 and Celecoxib (2591) and Sildenafil citrate (2270) in 2011.

Following a discussion between the partners involved in the exercise, the pilot phase has been extended to cover the first revision requests on these monographs before expanding it to new candidate molecules.

Key figures for 2011:

During its three sessions, the Commission adopted:

39 new monographs, including:

- monographs on active substances elaborated in close collaboration with the respective manufacturers under the P4 or P4Bio procedures dedicated to substances still under patent: Tadalafil (2606), Nateglinide (2575), Duloxetine hydrochloride (2594), Celecoxib (2591), Sildenafil citrate (2270), Pioglitazone hydrochloride (2601), Nervirpine hemihydrate (2479), Lopinavir (2615), Rivastigmine (2629) and Insulin glargine (2571).

- monographs on herbal drugs and herbal drug preparations and on Traditional Chinese Medicines (TCM): Angelica sinensis root (2558), Atractylodes lancea rhizome (2559), Largehead atractylodes rhizome (2560), Drynaria rhizome (2563), Poria (2475), Niaouli oil, cineole type (2468), Black cohosh (2069), Ginseng dry extract (2356), Pepper (2477), Long pepper (2453), Common selfheal fruit spike (2439), Instant herbal teas (2620), Coix seed (2425), Magnolia officinalis bark (2567) and Orinetvine stem (2450).

- one monograph on homeopathic preparations, Anarmita cocculus (2486).

- one monograph on Water for preparation of extracts (2.2.49).

- three general monographs on Instant herbal teas (2620), Pillules for homeopathic preparations (2153) and on Homoeopathic pillules, impregnated (2079).
177 monographs were revised, amongst them:

• a revised version of the monograph on Human normal immunoglobulin for intravenous administration (918). The production section was modified by adding “The method of preparation also includes a step or steps which have been shown to remove thrombosis generating agents. Emphasis is given to the identification of activated coagulation factors and their zymogens and process steps that may cause their activation. Consideration should also be given to other procoagulant agents which could be introduced by the manufacturing process.” This change was necessary due to recent experience with an immunoglobulin preparation which caused an increased rate of thromboembolic complications. In light of concerns for public health associated with these thromboembolic events, the revised monograph was implemented by the accelerated procedure via a Resolution and the date of implementation will be 01 January 2012.

• the monograph on Vaccines for human use (153): a new paragraph “Test for sterility of intermediates prior to final bulks” will allow for replacement of the sterility test with a test for low bioburden in certain circumstances.

• several individual monographs which were revised to avoid the use of reagents that were proscribed under the REACH regulation.

16 General Chapters,

including a new analytical method for Determination of methanesulfonyl chloride in methanesulfonic acid (2.5.39), a precursor used in the synthesis of methanesulfonic acid, and a general chapter on voltametric titration (2.2.65).

6 general texts (new or revised) were adopted, including:

• A new version of the Technical Guide for the elaboration of monographs and the respective Style Guide. As a major change, the Guides now envisage that new monographs can be drafted by expressing acceptance criteria for related substances using a “quantitative style” instead of expressing them in terms of comparison of peak areas (“not more than the peak due to…”).

• two new versions of the General Notices:

  - Due to the increasing number of fraudulent activities and cases of adulteration, the Commission has decided to add a new section, Potential Adulteration, under § 1.4. MONOGRAPHHS of the General Notices. The appropriateness of including such a section in individual monographs will be decided by the Commission, on a case-by-case basis. The objective of this section will be to make relevant information available to Ph. Eur. users to ensure the proper quality of medicinal products (i.e. active substances, excipients, intermediate products, bulk products and finished products).

  - A new paragraph on “Implementation of pharmacopoeial methods” has been added to raise the awareness of users on measures to be taken when applying Ph. Eur. methods.

• Procedure No. 5 for the Elaboration of Monographs on Homeopathic preparations.

Further progress in the field of harmonised vocabularies

Requests for new Standard Terms are submitted to the EDQM by national authorities, the European Medicines Agency (EMA) or the EU, and are assessed by the Standard Terms Working Party (STWP), which consists of experts appointed by the European Pharmacopoeia Commission following proposals from member states. The STWP meets three times annually to discuss the requests and to propose new terms and definitions or revise existing terms and definitions as necessary. Any new Standard Term that is agreed upon is then sent to the Commission for adoption by correspondence before publication. Approved terms are made available to national authorities in order to allow their experts to provide translations, which are submitted to the
EDQM Secretariat for publication. Terms are currently available in 31 world languages. (see chapter 2.2 Publications activities page 34)

International standards development

The EDQM has been participating in the development of a group of ISO standards that are intended to harmonise the identification of medicinal products (IDMP) from a regulatory perspective. The EDQM has provided particular expertise in the preparation of ISO standard 11239, related to the preparation of controlled vocabularies for pharmaceutical dosage forms, routes of administration and units of presentation and packaging. In 2011, a set of five final draft ISO standards (FDIS) was submitted to the ISO Secretariat for entry into the final balloting stage of the standards development process. In addition to the preparation of the ISO standards, the EDQM has participated in drafting an implementation guide with the M5 expert working group of the ICH, where the IDMP project first originated.

Regular teleconferences were held throughout the year, as well as a number of meetings in Europe and the USA, where collaboration was fostered between regulators and industry representatives from across the globe, in particular with the ICH members (Europe, USA and Japan) and observers (Switzerland, Canada). A training session at the EMA premises in London also took place in September 2011, during which speakers from the EDQM, the EMA and the US FDA provided progress reports on the development of standards and on the implementation guide for the benefit of attendees from regulatory agencies and industry across Europe.

Further contributions of the European Pharmacopoeia Commission to the reduction of animal testing

As a result of an extensive project in the Biological Standardisation Programme of the EDQM, acellular pertussis antigens of combined vaccines can now also be assayed in the guinea-pig model using the same group of animals (guinea-pigs) used for the serological assay of diphtheria and tetanus vaccines, thereby reducing the number of animals required. Nine monographs on combined vaccines have been revised accordingly.

A Symposium on Alternatives to Animal Testing, organised by the EDQM, took place in Strasbourg on 8-9 September 2011, focussing on recent developments in the 3Rs concept with regards to testing on animals. (see chapter 2.3 Communication, landmark events page 35). The three main actions for the European Pharmacopoeia following this workshop are:

• As a consequence of EU Directive 2010/63/EU, Groups of Experts will review all monographs where tests requiring animals are requested to assess whether these tests might be replaced by in vitro alternatives.

• Pyrogen test: Groups of Experts will review all relevant monographs to assess whether the replacement of this test by a bacterial endotoxin test or an in vitro alternative is possible.

• Monocyte activation tests: the Ph. Eur. Working Party dealing with this topic will investigate whether more guidance for the validation is needed in order to encourage users to implement these methods.

Achievements in Biological Standardisation

The Biological Standardisation Programme (BSP), a joint programme with the EU Commission, pursues the following goals in the area of standardisation of biologicals: establishment of Biological Reference Preparations (BRPs), development and validation of new analytical methods, and validation of alternative methods based on the 3Rs concept (i.e. the Refinement, Reduction and Replacement of animal experiments).

To this end, collaborative studies are performed involving all interested partners [e.g. Official Medicines Control Laboratories (OMCLs) and manufacturers]. Whenever possible, such studies are run jointly with the WHO in order to economise the resources of participating laboratories. Since the start of the programme in 1992, 114 BSP projects have been initiated. In 2011, a number of projects were pursued in different fields:

• vaccines for human use: 6 projects
• vaccines for veterinary use: 1 project
• plasma-derived products: 6 projects
• biotechnology products: 5 projects

Of these projects, four were devoted to the establishment of alternatives to animal testing, another four to the development of new or improved assays, and 11 projects concerned the establishment of Biological Reference Preparations (BRPs) (one project focussed on the development of new assay methods and the establishment of BRPs, another was a collaboration with the WHO, and yet another was a collaboration with the WHO and the USP).

The strong efforts to apply the 3Rs concept to the field of quality control of biologicals were continued in 2011. During the symposium on 8-9 September 2011 in Strasbourg (see Chapter 2.3 Communication, landmark events, page 35), the results of three recently concluded BSP 3Rs projects (replacement of the direct challenge potency tests for rabies vaccines for veterinary use, acellular pertussis vaccines and for tetanus immunoglobulin preparations) were presented to the stakeholders. Manufacturers and OMCLs were encouraged to implement the 3Rs methods.

The efforts of the EDQM, and in particular the BSP, to elaborate, validate and implement 3Rs methods are widely acknowledged, for instance by the European Partnership for Alternative Approaches to Animal Testing (EPAA) - a high-level initiative of the EU Commission and the Industry. Consequently, the EDQM is represented on the Steering
Committee of the EPAA Vaccine project as well as in the Technical Committee, and future studies will be run by the BSP.

In 2011, the BSP almost concluded its first project on allergens (BSP090) as a follow-up activity of the CREATE programme, which was sponsored by the 7th EU Framework Programme. The goal of BSP090, which will be concluded in 2012, is to establish the first reference standards for major birch allergens (Bet v 1) and Timothy grass pollen (Phl p 5a), starting from recombinant materials. In addition, ELISA systems for the determination of the two major allergens in allergen extracts will be established and this will allow unequivocal standardisation of such allergen extracts. The results of BSP090 were the theme of a symposium that was held on 24 November in Strasbourg, which was supported by the Paul-Ehrlich-Institut and over 70 participants from 13 countries attended.
1.2 Pharmaceutical Reference Standards

Reference Standards for the European Pharmacopoeia (Ph. Eur.)

Why have reference standards?

Most of the tests and assays described in the Ph. Eur. prescribe the use of official Ph. Eur. reference standards, i.e. carefully characterised specimens of substances intended for quality control.

Ph. Eur. reference standards are established by the EDQM and adopted by the Ph. Eur. Commission.

Chemical Reference Standards (CRS)

In 2011, 254 batches of CRS were established, including 56 assay standards and 69 impurity mixtures. An overview of the establishment of CRS in the period 2006-2011 is given below.

Establishment of CRS

<table>
<thead>
<tr>
<th>Year</th>
<th>New</th>
<th>Replacement</th>
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</thead>
<tbody>
<tr>
<td>2006</td>
<td>142</td>
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<tr>
<td>2007</td>
<td>143</td>
<td></td>
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<td>2008</td>
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<td>2009</td>
<td>131</td>
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<tr>
<td>2010</td>
<td>118</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>133</td>
<td></td>
</tr>
</tbody>
</table>

Portfolio

The collection now consists of 2422 items. The collection is continuously monitored for fitness-for-purpose and 494 batches were examined in 2011.
Careful planning of activities allowed achievement of the objective to have at least 98% of the portfolio available to users at all times.

**Availability of the CRS portfolio in 2011**

The reference standards of the Ph. Eur. are increasingly dispatched outside of the European geographical zone.

**% of Ph. Eur. vials ordered/distributed by world area**

India, USA and China are progressing as non-European users of EDQM reference standards. The overall demand for reference standards increased in 2011.

**Biological Reference Preparations (BRPs)**

In 2011, the international collaborative studies performed by the Biological Standardisation Programme led to the adoption of four BRPs by the Ph. Eur. Commission: Tetanus vaccine BRP (batch 3), Human immunoglobulin BRP for anti-complementary activity and distribution of molecular size (batch 1), Human immunoglobulin BRP for Fc function and distribution of molecular size (batches 1 and 2), and the BRP for human plasma calibrated for coagulation factors V, VIII, XI and XIII (batches 1 and 2).

**EDQM activities for the WHO**

**International Chemical Reference Standards (ICRS)**

Since 2010, the EDQM is responsible for the establishment, monitoring and distribution of the WHO ICRS, which are reference standards used as prescribed by the International Pharmacopoeia edited by the WHO and used worldwide. In 2011, 4 batches of ICRS (α-arthemether, niridazole, niridazole-chloroethylcarboxamide and pyrimethamine) were established and 19 ICRS were monitored for fitness-for-purpose.

**International Standards for Antibiotics (ISA)**

Since May 2006, the EDQM is responsible for the establishment, storage and distribution of ISA. 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 2011, the 2nd International Standard (IS) for Dihydrostreptomycin was established and work on the replacement of the current batches for Neomycin and Neomycin B began.
1.3 Laboratory Activities

Continuous efforts to further improve internal organisation and efficiency

The Laboratory Department (DLab) consists of the Analytical Chemistry Division and the Biology Section. The Analytical Chemistry Division is mainly involved in physico-chemical testing, whereas the Biology section is mainly involved in biochemical and microbiological testing. Both entities operate according to the same process and apply the same Quality Assurance System. This allows sharing of equipment and work, avoidance of duplication and some flexibility in terms of staffing.

This harmonised organisation has facilitated the introduction of a LIMS (Laboratory Information Management System) in the Department.

Positive contributions to the work of the European Pharmacopoeia

The integrated establishment process has enabled the timely adoption of reference standards for the Ph. Eur.

During the year, 104 reports were issued to support the groups of experts or to test the feasibility of CRS production.

Collaboration at international level

In 2011, DLab actively participated in the following joint Ph. Eur. – USP activities:

- Prospective harmonisation of two P4 chemical monographs (Rizatriptan benzoate and Celecoxib). The CRS for rizatriptan benzoate was established. The work on establishing a CRS for celecoxib is nearing completion.

- Establishment of a common insulin aspart CRS, which involved modification of the USP monograph in order to harmonise it with the Ph. Eur. version. This activity was successfully completed.

The EDQM laboratory also provided analytical support to the WHO for the development of a quality guideline on artemisinin as starting material. Two studies were conducted, applying two different compendial LC methods. These studies contributed to the finalisation of the guideline, which is of significant importance to public health as artemisinin is the WHO-recommended therapy against malaria.

Contributions to the permanent process of optimisation

In terms of continuous improvement, initiatives are on-going in the following areas:

- optimising the efficiency of the CRS monitoring programme.
- optimising the workflow for the WHO ICRS programme.
- expanding/advancing laboratory capabilities to better support the three reference standard programmes (CRS, ICRS and ISA) in the EDQM’s portfolio.

Finally, measures were taken to make the contribution of DLab sustainable in the medium- to long-term by:

- introducing new equipment (coulometer with oven, safety balance, fast liquid chromatograph), and
- replacing existing equipment with more modern versions (LC systems, capillary electrophoresis apparatus).
1.4 Certification of Suitability to the Monographs of the European Pharmacopoeia

Purpose of the Certification procedure

The Certification of Suitability to the Monographs of the European Pharmacopoeia (CEP) procedure was established in 1994 and is aimed at:

- ensuring that the quality of substances used in the production of medicines complies with Ph. Eur. standards and, hence, the requirements of the pharmaceutical legislation of the European Union and its member states.

- contributing to keeping the Ph. Eur. continuously up-to-date by assessing whether its quality standards still reflect the quality of substances on the market. Information on the different routes of synthesis and impurity profiles is used to constantly improve the quality of Ph. Eur. standards. This synergy with certification activities is of the utmost importance for the Ph. Eur., as it ensures that Ph. Eur. standards are up-to-date with respect to the products currently on the market.

- facilitating at the European level the management of Marketing Authorisation Applications by a centralised assessment of the quality of substances for pharmaceutical use, which reduces the workload for authorities and the Industry.

Which substances are covered by the Certification procedure?

Under the official procedure described in Resolution AP-CSP (07) 1 and referred to in European Union Directives 2001/83/EC and 2001/82/EC, as amended, and 2003/63/EC, manufacturers or suppliers of active pharmaceutical ingredients or excipients, or of herbal products used in the production or preparation of pharmaceutical products covered by a Ph. Eur. monograph or any substance with a risk of transmissible spongiform encephalopathy (TSE), can apply for a certificate.

Assessment of the quality documentation submitted to the EDQM for certification is complemented by an inspection programme. This inspection programme has been set up to check compliance with both the CEP applications submitted to the EDQM and Good Manufacturing Practices (GMP, as laid down in Volume 4 of the Rules Governing Medicinal Products in the European Union) at the manufacturing/distribution sites covered by CEPs. The EDQM Certification Division is responsible for organising inspections and their follow-up, including taking any subsequent action regarding related CEPs or CEP applications and communicating with the authorities concerned. The annual inspection programme is based on priorities recommended by the EMA/EU, and it is adopted by the Certification Steering Committee following consultation with the authorities in member states and the GMP/GDP Inspectors Working Group of the EMA.

Key figures for 2011

The Certification Division has been receiving an increasing number of applications for CEPs in recent years. In 2011, 372 new applications and about 1200 requests for revision were received. Of these new applications, a record number related to herbal drugs and herbal drug preparations, with 8 dossiers submitted in 2011; a total of 12 such applications were received since the procedure was extended to cover this kind of product in 2003.

When revised monographs are published in the supplements of the Ph. Eur., holders of CEPs are asked to update their relevant CEP applications, and the submitted data are assessed according to the revised official texts.

In 2011, 340 new and 1147 revised CEPs were granted. In addition, 424 requests for revision were approved without issuing a revised CEP, in line with the policy applied to notifications or minor revisions not affecting the quality of the final substance or the content of the CEP.

Key activities in 2011

- Timelines for assessment: In 2011, new dossiers and revision/renewal applications were handled within the official deadlines.

- Update of CEPs for TSE: In the context of the implementation of the revised Ph. Eur. general chapter 5.2.8 “Minimising the risk for Transmissible Spongiform Encephalopathy” (TSE), a number of CEP applications were reviewed and updated to make sure that all such CEPs were in compliance with the new requirements.

- Policy for packaging information on CEPs: In 2011, it was decided that, in all cases, the container/closure system of a substance would be assessed in the context of a CEP application, even if no re-test period was claimed by the...
sites of common interest. The pilot phases ended in 2010, and a report was published in 2011 on the websites of the EMA, FDA, TGA and EDQM. About 100 inspection reports were exchanged and nine joint inspections were performed. The project enhanced contacts between the organisations involved and will be continued on a routine basis.

**The EDQM inspection programme**

The programme for inspections of manufacturing sites covered by CEPs is an important tool to complement the evaluation of the quality of substances for pharmaceutical use. In 2011, 22 on-site inspections were performed, mainly in Asia, with the participation of inspectors from different national agencies. Three sites refused to be inspected following the announcement of an inspection (leading to immediate suspension of the relevant CEPs). Another 25 sites were covered by sharing information with inspectorates of member states and partners. Seven of the inspections carried out led to the suspension or withdrawal of CEPs, or closure of CEP applications, due to non-compliance of the manufacturing sites with GMP or major deviations from the dossiers submitted to obtain the CEPs. In 2011, 18 CEPs were suspended and 14 were withdrawn by the EDQM.

Overall, the EDQM has performed 251 inspections since the inspection programme started in 1999. Of these, 198 were carried out outside the EEA. Since 2003, the vast majority of the inspected sites have been outside the EEA.

**International API inspection programme:**

Since 2008, the EDQM has been involved in the international API inspection pilot programme, initiated by the EMA. This programme involves inspection authorities from the US, Australia and individual European countries, as well as the EDQM, and is aimed at optimising resources through the exchange of information (inspection planning and reports) and the performance of joint inspections for API manufacturing sites. The graph below displays the geographical distribution of manufacturing sites covered by a valid CEP for chemical purity. Excluding European countries, the greatest number of sites covered by chemical CEPs are located in India and China.

**Geographical distribution of manufacturers holding a valid chemical CEP**

The graph below displays the geographical distribution of manufacturing sites covered by a valid CEP for chemical purity. Excluding European countries, the greatest number of sites covered by chemical CEPs are located in India and China.

**Regional location of inspected sites**

- Asia outside China: 8.0%
- North America: 6.6%
- South America: 1.8%
- Middle East: 1.0%
- Africa: 0.5%
- Australasia: 0.2%
- Europe: 40.0%
- China: 20.3%
- India: 21.5%
1.5 Network of Official Medicines Control Laboratories (OMCLs)

Introduction

The network of Official Medicines Control Laboratories (OMCLs), which was created on 26 May 1994 following a decision by the Commission of the European Union (EU) and the Council of Europe (CoE), is open to all countries that have signed the European Pharmacopoeia Convention as well as to observers of the European Pharmacopoeia Commission, provided that the criteria of the network are fulfilled (i.e. independence, public funding, implementation of the Ph. Eur. as a common standard, implementation of the ISO/IEC 17025 standard in the laboratory, etc.). Since 1995, the EDQM is the co-ordinator of this network and responsible for its organisation and further development.

In the context of the OMCLs, ‘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 the competent national authorities, this also means avoidance of duplication of work and access to state-of-the-art technology and selective analytical procedures.

Besides the core activities of the network, over the last few years a number of additional initiatives have been launched, and new programmes have been established in particular in the fields of falsified medicines testing, monitoring of stockpiled medicines, testing of small scale preparations and quality control of active pharmaceutical ingredients (APIs) on the European market.

Quality Management Systems

The following activities, co-ordinated by the EDQM, were carried out in 2011 within the framework of the Quality Management (QM) program of the OMCL network.

- Mutual Joint Audits and Mutual Joint Visits
  During 2011, thirteen Mutual Joint Audits (MJAs) and one Mutual Joint Visit (MJV) were carried out at OMCL sites, corresponding to a more than 50 per cent increase compared to 2010.

- Training activities for the OMCL
  In 2011, one training visit was organised by the EDQM to provide training on biological laboratory methods. In addition, two training courses for auditors were held on our premises, providing training to new auditors for ISO/IEC Standard 17025.

- OMCL Network Quality Management Guidelines
  The following new or updated OMCL Guidelines were adopted at the Annual Meeting in May 2011: 7th Annex of the OMCL Guideline on Qualification of Equipment “Qualification of Mass Spectrometry (MS) instruments”, PA/PH/OMCL (10) 86 2R, and the 1st Annex of the OMCL Guideline on Qualification of Equipment “Qualification of HPLC Equipment”, PA/PH/OMCL (11) 4. Furthermore, recommendation documents were elaborated and distributed during the year, such as “General requirements for infrequently performed techniques” and “Qualification and re-qualification of analysts”.

The existing guideline “Evaluation and Reporting of Results” is currently under review. New guidelines for “Management of Reagents” and “Handling and Use of Reference Standards in OMCLs” are under elaboration.

Several OMCL Guidelines were adopted by the European Co-Operation for Accreditation (EA) in September 2011. A new edition of the Quality Management Book containing the latest OMCL guidelines and MJA/MJV/TV instructions/forms was published in 2011.

Key QA documents and guidelines are available on the EDQM website.

**API Working Group**

Globalisation of the manufacture of and trade in API has increased the need for greater control of their quality. On 07 November 2011, a newly formed OMCL working group met for the first time in Strasbourg to discuss strategies with respect to the testing of APIs on the European market. This group consists of OMCL representatives from 13 member states. The goal of this first meeting was to establish a work programme. The major objective of the group is to raise awareness of the valuable contributions of OMCLs in the control of the quality of drug substances on the European market. The tightening of controls on APIs, as previously highlighted at the International Summit of Heads of Medicines Agencies in 2008, to this day remains the focus of national competent authorities and the EMA.

**Combatting Counterfeit and other Illegal Medicines Symposium for OMCLs**

On 29-31 March 2011, the first symposium on combatting counterfeit and other illegal medicines, specifically targeted to OMCLs took place at the EDQM in Strasbourg. In total, 106 participants registered for the event, which included representatives from the General European OMCL Network (GEON), national competent authorities, the EU and the pharmaceutical industry.

The sessions of the first two days of the symposium, which were run as closed sessions restricted to network members and the national competent authorities, focused on the technical aspects of counterfeit medicines testing. The last day was dedicated to general and collaborative aspects in this area and was also open to invited guests from industry.

During the closing discussion, the importance of collaboration involving all stakeholders was emphasised. In addition, a legal loophole with respect to counterfeit dietary supplements and similar “medicines in disguise” was identified, and the role of the OMCLs in tackling this issue was addressed.

**Counterfeit/Illegal Medicines Working Group**

During the “Counterfeit Symposium for OMCLs”, the need to establish an OMCL working group treating all aspects of counterfeit medicines testing was identified and discussed. This idea was brought to the Annual Meeting of the GEON in May 2011, where the plenum agreed on the creation of a Counterfeit/Illegal Medicines Working Group.

Eighteen OMCL representatives from 15 member states have indicated their interest in actively participating in the work of the group. In addition, two OMCLs announced their willingness to contribute to the activities at a later time. The first meeting took place on 02 November 2011 at the INFARMED premises in Lisbon, Portugal, one day prior to the Annual CAP Meeting and was dedicated to the elaboration of a work programme by defining major topics of focus. The group agreed, amongst others, to assist the Secretariat in the establishment of a counterfeit testing database, to foster joint testing programmes in the field of counterfeit medicines and “medicines in disguise”, to support technical training programmes for the network and to offer a technical platform for the exchange of information on new developments. In this respect, so-called designer drugs will be included in the work programme of the group.

**OMCL Testing Group on Unlicensed Pharmaceutical Preparations**

On 07 December 2011, a newly-formed OMCL working group of OMCL representatives from eight member states (initially called the Working Group on Small-Scale Preparations) met for the first time in Strasbourg to discuss strategies with respect to the testing of unlicensed pharmaceutical preparations and with the aim of establishing a work plan for the group. The major objectives of this group are to raise awareness of the significant contributions of the OMCLs in the control of the quality of unlicensed pharmaceutical preparations and to provide guidance on sampling strategies, the selection of testing methods and setting specifications, where needed. The group stressed the importance of monitoring the quality of these types of preparations, and agreed to organise a first market surveillance study within the Network, focused on unlicensed pharmaceutical preparations for paediatric use (capsules and suppositories). The results of the study will be available in the 4th quarter of 2013.

**Stockpiled Biologicals Working Group**

After the elaboration of a first technical guideline in 2009 outlining the contributions of OMCLs in the monitoring of stockpiled medicines (the respective document PA/PH/OMCL (09) 94 3R has been published on the EDQM website, www.edqm.eu), a working group was established in Summer 2011 following a decision made during the Annual Meeting of the OMCL Network in Düsseldorf with the goal of adapting the current document to the particularities of biological products in national stocks (vaccines and anti-sera). In a meeting of the Group on 09 November, the general concept of the revisions was elaborated. The updated version will be tabled for adoption at the Annual Meeting of the OMCL Network in June 2012.
Gene Therapy Products (GTP) Working Group

The OMCL GTP Working Group was set up in 2008 within the OMCL Network in order to prepare the OMCLs for their role in the surveillance of the quality of GTPs. The role of this Working Group is to foster collaboration between OMCLs working in the field of GTPs to save time and resources by sharing knowledge and technologies. Currently, nine OMCLs participate in the Working Group.

During the first meeting in 2008, a work programme for a 5-year period (2008-2013) was established, taking into account the likelihood of the vectors appearing on the market, the clinical trials or requests for scientific advice submitted and the infrastructures and expertise available among the members of the Group. For each vector, a limited number of analytical methods were selected for development and validation. At the meeting of the group in May 2011 at the NIBSC, the work programme was expanded in order to adjust to the most recent developments in the field. The list of vectors now comprises: adeno-associated viruses, plasmids, non-replicative adenoviruses, poxviruses and retro-/lentiviruses.

In 2011, two collaborative studies were completed on plasmids for validation of the determination of DNA concentration by UV photometry and for comparison of HPLC and capillary electrophoresis (CE) for the determination of DNA concentration and topology. The results of the studies will be published in 2012 in Pharmeuropa Bio and Scientific Notes.

The next meeting of the OMCL GTP Working Group is envisaged for Autumn 2012 at the EDQM in Strasbourg.

16th Annual Meeting of the General European Network of Official Medicines Control Laboratories (GEON)

Organised by the EDQM in co-operation with the OMCL of North Rhine-Westphalia, LIGA.NRW, the General European Network of Official Medicines Control Laboratories (GEON) held its 16th Annual Meeting in Düsseldorf, Germany, on 23-27 May 2011. Representing 55 institutions and 34 countries, 204 experts in the field of medicine surveillance and testing came together over the course of this week-long meeting to exchange experiences and to discuss matters of common interest for the co-ordination and harmonisation of their efforts to protect patients’ health in Europe. In different parallel meetings, the results of expert working groups, as well as proposals for future ad hoc working groups, were presented and discussed and common working programmes were established.

OMCL Annual Meeting – General Session / Policy documents

During the General Session of the Annual Meeting, which was open to full and associated members of the Network, the following topics were addressed:

- The concept of a procedure for handling the maintenance of membership to the network was discussed and approved. On the basis of the decisions taken during the meeting, it is planned to provide a document for adoption at the Annual Meeting in 2012.
- Revisions of the Terms of Reference (ToR) of the GEON and its Advisory Group were adopted. In addition a 4th Annex to the core ToR GEON document was approved by the Network, which includes a membership questionnaire. This document is used as an application form for new members to the Network and as a monitoring tool for existing members.
- A detailed analysis of lessons learned from the Heparin crisis for the OMCL Network was presented and discussed. As a follow-up to the discussion, the plenum agreed to commission the Advisory Group to elaborate a crisis management procedure for the GEON.
- A discussion on the outcome of the “Counterfeit Symposium for OMCLs” was held. The Counterfeit/Ilegal Medicines Working Group was established as a follow-up to this event (see above).
- A part of the general session was dedicated to specific topics including API testing initiatives within the Network, analytical activities of OMCLs with respect to stockpiled medicines and, in this context, the testing of stockpiled biologicals and medical devices. The discussion that followed led to the establishment of an API Working Group and to the decision to adapt the current technical guideline on monitoring of stockpiled medicines to the particularities of biologicals (see above).
- In the general part of the programme, amongst others, the activities of the newly-established European Network of Official Cosmetics Control Laboratories (OCCL) was presented. This activity is co-ordinated by the HealthCare group of the EDQM, but there are synergies with the OMCL Network, in particular as a number of OMCLs also have a mandate for the testing of cosmetics.

Proficiency testing scheme studies (PTS)

Over the years, proficiency testing scheme (PTS) studies have become a regular programme within the OMCL Network. In 2011, five studies were organised in the physico-chemical field, with an average participation of 35 national control laboratories and 28 other pharmaceutical control laboratories from the private sector, industry and hospitals. In the biological area, three studies were organised, involving an average of 25 laboratories (12 OMCLs and 13 laboratories from the private sector). The PTS study on radiopharmaceuticals, initiated in 2010, was finalised.

In 2011, two new studies from the 5th PTS agreement with the WHO were organised; a study on dissolution testing and a study on determination of pH and weight per mL. On average, 60 government control laboratories from the
six 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 2011, market surveillance studies (MSSs) aimed at screening the quality of medicinal products on the European market were finalised for simvastatin tablets and for modified-release oral opioid medicinal products. The testing phase was initiated for the MSS on acetylsalicylic acid oral products, clopidogrel APIs and tablets, as well as APIs and medicines containing mesilate salts. Such testing campaigns provide 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 also support the revision of the relevant monographs and/or general chapters and methods of the Ph. Eur., as well as directing specific actions by licensing and supervision authorities.

CombiStats

In 1999, the EDQM initiated the development of a computer program 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 software, developed in-house, which led to a strong demand for a common program 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. The number of users has steadily increased since its public release. A training course was organised in November 2011, which was open to industry and private sector participants. By December 2011, 14 % of the licences were issued to OMCL laboratories in 24 countries and 86 % to non-OMCL users in 40 countries. The pie-chart below shows that roughly half of the non-OMCL licences were issued within the EU and the other half in the rest of the world, including non-European countries such as Argentina, Australia, Brazil, Canada, China, Egypt, India, Indonesia, Israel, Japan, Malaysia, Mexico, South Africa, South Korea, Syria, Taiwan, Tunisia, 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.
In December 2010, the co-ordination activities of the EDQM with respect to the CAP sampling and testing programme successfully underwent ISO9001 certification. A follow-up audit was successfully passed in December 2011.

**Mutual Recognition Procedure (MRP)/Decentralised Procedure (DCP) product testing programme**

The MRP/DCP product market surveillance scheme was initiated on a voluntary basis by members of the OMCL Network from the European Economic Area (EEA) Member States and the EDQM at the end of 2000 and has further developed since then. By avoiding duplicate testing of the same product in different member states, the scheme provides a co-ordinated and cost-saving approach to post-marketing surveillance.

In 2011, the 7th regular programme for the market surveillance of medicinal products authorised in the EEA via the MRP or DCP procedure was conducted. More than 700 product testing projects were allocated to the 2011 programme, which was comparable to the numbers in 2009 and 2010. The number of participants has stabilised over recent years to around 20 OMCLs per programme (24 in 2011). The trend of decreasing numbers of cancelled projects has continued in 2011, which might be an indication that the information on marketing of MRP/DCP products in Europe is more accurate than in former years.

Approximately 3% of the tested products in 2011 were biologicals, which reflects the approximate ratio of biological medicines registered via the MRP and DCP. In 2011, about 15% of the reported tests involved repeated testing of the same products; this is a common ratio for routine post-marketing testing and part of the market surveillance concept.

The general procedure “Co-operation in post-marketing surveillance of Mutual Recognition/Decentralised Procedure
Products”, PA/PH/OMCL (06) 116, was amended to add the aspects of data ownership and confidentiality. The latest version was made available on the EDQM website in February 2011.

For the first time, some key data, representative of the work of the testing groups, was reported to the European Heads of Medicines Agencies and the Heads of OMCLs as part of an awareness-raising campaign for the OMCL Network.

The internal database used for planning, sampling and reporting of MRP/DCP product testing activities within the Network was further developed. A total of 14 database amendments were implemented in 2011, initiated both by the OMCL users of the system and the EDQM Secretariat. In addition, a refreshment training course for core OMCL database users was organised in June.

In December 2011, the co-ordination activities of the EDQM with respect to the MRP/DCP product market surveillance scheme, which are ISO 9001 certified, successfully underwent a re-audit.

Additional information on the MRP/DCP product testing programme can be found on the EDQM website.

Official Control Authority Batch Release (OCABR) of Biologicals for Human Use

The main goal of the OCABR Network is the harmonised application of Article 114 of EU Directive 2001/83/EC, as amended, to foster the mandated mutual recognition of lot release. Network activities include the regular exchange of information and participation in meetings, at which the Network members elaborate and maintain common guidelines. This context provides excellent opportunities for work-sharing. The desire to provide good quality, widely-recognised surveillance of the quality of vaccines and blood-derived medicinal products on the EU market and beyond and to reduce, replace and refine the use of animals in testing are important driving forces for the co-operation between Network members.

The Annual Meeting in Düsseldorf, Germany was attended by almost 70 participants from 24 member states. Parallel sessions were held for blood and vaccine issues, respectively, and a joint session was held to address common points of interest. Participants reviewed activities from the past year and determined strategies for the coming period.

At the plenary session, agreement was reached to further explore interaction with the Biologics and Genetic Therapies Directorate of Health Canada in order to foster co-operative activities in the field of batch release. A mandate was given to draft an appropriate Memorandum of Understanding for future signature. A revision of the EU OCABR administrative procedure to improve the transfer of information to OMCLs was adopted during the same session. A related revision, to be included in section 4 of all product-specific guidelines, was also adopted, leading to the combined revision of 57 guidelines for blood and vaccines. In addition to these latter guideline revisions, two new product-specific guidelines for vaccines were introduced and a number of vaccine guidelines underwent specific revisions to maintain concordance with their respective Ph. Eur. monographs. A number of internal guidelines and procedures related to Network functioning were also revised. An interesting presentation of data on batch consistency, collected through OCABR-testing, provided an excellent example of the contribution of OMCLs to the surveillance of biological medicinal products in real-time and the importance of feedback from these activities.

Other meetings were held throughout the year on specific topics such as the meeting with the manufacturers’ associations for blood- and plasma-derived medicinal products, and the yearly training on testing oral poliomyelitis vaccine bulks, which this year also included participants from relevant manufacturers, all of which proved fruitful and interesting.
Following the successful implementation and use of the OCABR batch database, the Network agreed to an evolution of the database to refine and improve its functioning. The work has since been initiated and should be completed in early 2012.

At its Annual Meeting, the OCABR Network members proposed a follow-up meeting on the batch release testing of influenza vaccines, with a particular focus on available methods. This was realised through a meeting between manufacturers, regulatory authorities (assessors) and OMCLs, jointly co-ordinated by the EDQM and EMA in December 2011 at the EMA in London.

All adopted product-specific guidelines and administrative procedures are available in a book published by the EDQM at the end of each year. They can also be downloaded in their entirety from the EDQM website.

**Official Control Authority Batch Release (OCABR) of Immunological Veterinary Medicinal Products – Veterinary Batch Release Network (VBRN)**

At the Annual Meeting in Düsseldorf, 25 participants from 17 member states took part in the VBRN session. As usual, annual reports of the activities of the different member states were presented. Progress in the harmonised application of Article 81 and Article 82 of EU Directive 2001/82/EU, as amended, for veterinary medicines was noted in most cases. At the meeting in 2011, a new model template for annual reports was adopted in order to further improve and harmonise the reporting of data. Highlights from the annual reports made it apparent that, as already noted in 2010, maintenance of competence in specialised techniques and improved communication with other branches of the regulatory network, such as licensing and inspection, remains an important issue to be followed. The VBRN advisory group has already initiated action in this respect. The advisory group representative from Hungary had the opportunity to raise these issues with the Heads of Medicines Agency at their meeting in April 2011, to encourage their activity towards improvements in these areas.

The VBRN advisory group met with members of the manufacturers’ association IFAH-Europe in February 2011 to discuss items of common interest. The information exchanged there was disseminated to the wider Network at a plenary session of their Annual Meeting.

As mandated by the EU Commission in its recommendation document on batch release for IVMPs, and as endorsed by the Veterinary Pharmaceutical Committee 20/03/2007, the VBRN is reviewing its procedures for the effective release of batches of IVMP to meet the needs of the system. A review of the products on the shortlist for application of Article 82 resulted in no changes in 2011. Items currently being examined for review and improvement are the table proposed for risk assessment during product reviews and the development of a procedure to allow short-term testing of IVMPs not on the restricted list in case of specific needs. These documents will undergo a thorough review process within the Network and with the appropriate external partners before finalisation and adoption.

All adopted administrative procedures and product-specific guidelines, as well as protocol templates, can be downloaded from the EDQM website.
were submitted to the CD-P-TS in Autumn 2011 with a plan for adoption/publication in 2012.

Co-operation with the Russian and Ukrainian blood transfusion societies was initiated in the form of the participation of the EDQM/Council of Europe at meetings held in July (Actual problems of hematology and transfusiology, St Petersburg, Russian Federation) and October 2011 (Current issues in transfusion medicine and blood donation; Collection, processing and usage of blood and blood products, Kiev, Ukraine), respectively.

Collaboration with the South-Eastern Europe Health Network (SEEHN) project on “Increasing regional self-sufficiency in relation to safer blood and blood components”, which is being led by Romania, was started and this facilitated the organisation of a training programme in 2011 on “Increasing trans-national availability of safe blood and blood components for medical emergencies and special circumstances”. An e-learning platform, set up in 2011, will be further developed in the course of 2012.

Inter-institutional co-operation with the EU allowed completion of the pilot phase for a European Programme of External Quality Assessments, with voluntary participation in Proficiency Testing Studies (B-PTS) and commencement of the elaboration of common guidelines for quality management systems (QMS) in blood establishments, which should become an integral part of the Council of Europe’s Guide for the preparation, use and quality assurance of blood components in its forthcoming editions.

The B-PTS activity aims at assessing the performance of laboratories with regard to screening tests used for the qualification of individual blood donations. Since 2010, six B-PTS studies were organised for testing of nucleic acid amplification techniques (Hepatitis C (HCV) – 2 studies, and Human Immunodeficiency (HIV) viruses), serology (Hepatitis B surface antigen (HBsAg) and HIV antibodies) and immunohaematology (ABO grouping and Rhesus phenotyping). The B-PTS activity is being well-received by blood establishments, resulting in an increased interest in participating in the scheme. Steps have been taken to continue the External Quality Assessment schemes and to include a

### 1.6 Blood Transfusion and Organ Transplantation

**Blood transfusion activities**

The European Steering Committee on Blood Transfusion (CD-P-TS) held one meeting at the EDQM in November 2011. The Guide for the preparation, use and quality assurance of blood components represents a key milestone in defining the “standards” for blood transfusion services and forms the basis for many national regulators in Europe and beyond. (see chapter 2.2 Publications activities page 34)

Reporting of data on the collection, testing and use of blood components from European countries and from other regions of the world for the year 2009 has now been completed. A trend analysis on data collected in the years 2001-2008 was performed and will be published in 2012.

A working group on “anti-RhD alloimmunisation immunoprophylaxis and European self-sufficiency of anti-D immunoglobulin” started its activities in 2011.

A survey on quality indicators for optimal clinical use of blood was initiated by the end of 2011.

The ad hoc working groups on Blood Supply Management (working on issues related to the constant shortage in blood and blood components and the subsequent limitation in transfusion therapies, as well as the heterogeneous levels of donation in respective countries) validated a self-assessment questionnaire in a pilot study in the blood banks of four countries and set up an online questionnaire to be completed in 2012 by all observer and member states participating in the activities of the CD-P-TS.

The project on “Risk behaviours having an impact on blood donor management and transfusion safety”, which started in February 2010 with the notable participation of the EU, EMA, ECD (European Centre for Disease Prevention and Control), EBA (European Blood Alliance), US-FDA, Health Canada, TGA and WHO, was completed. The group analysed existing data from epidemiological and risk modeling studies and surveillance programmes, and the implications of moving away from the permanent donor deferral criteria currently applied in relation to risk behaviours. The work was performed in close co-operation with other Council of Europe Steering Committees and expert groups (bioethics, transplantation, blood-derived medicinal products). A draft resolution and a technical memorandum were submitted to the CD-P-TS in Autumn 2011 with a plan for adoption/publication in 2012.

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programme of visits/audits to support implementation of the QMS in testing laboratories of blood establishments in the forthcoming years.

Organ, Tissue and Cell Transplantation

The European Steering Committee on Organ Transplantation (CD-P-TO) met in May 2011 in Strasbourg and in October 2011 in Geneva, preceding the 13th European Organ Donation Day organised by the Council of Europe in this city.

The 4th edition of the Guide to the Safety and Quality Assurance for the Transplantation or Organs, Tissues and Cells was published in 2011. (see chapter 2.2 Publications activities page 34)

The Transplant Newsletter, containing international data on donation and transplantation for 2010, was published in September 2011.

The CD-P-TO, together with the European Committee on Crime Problems (CDPC) and the Steering Committee on Bioethics (CDBI) from the Council of Europe, is involved in an ad hoc group that works on the elaboration of a new legal instrument to fight trafficking in organs, tissues and cells. The first meeting of this Committee of Experts on Trafficking in Human Organs, Tissues and Cells (PC-TO) took place in Strasbourg in December 2011. In addition, the CD-P-TO drafted a Resolution on “Establishing procedures on data collection and dissemination on illicit international transplantation activities” and approved its submission to the Committee of Ministers.

Based on Council of Europe recommendations and the experience gained by the experts from the CD-P-TO in other programmes in the Black Sea area (BSA), the CD-P-TO has now started a 3-year collaborative project through which a strategy will be developed to promote transplantation activities in the region. The Council of Europe member states from the BSA (Armenia, Azerbaijan, Bulgaria, Georgia, Moldova, Romania, Russian Federation, Turkey and Ukraine) will, through this project, start long-term regional co-operation in order to structure, develop and strengthen activities and programmes related to the donation and transplantation of organs, tissues and cells. A start-up meeting, organised regionally in Chisinau (Moldova), launched the project in July 2011. It gathered professionals, nominated by their respective Ministries of Health, from the transplantation and/or organisational services. An Advisory Board of experts from countries with established transplant systems will follow and support the progress of this new project.

Given that no country with established transplant programmes has managed to meet the real demand for kidney transplantations through organs from deceased donors alone, and that the benefits to recipients of live-donor organs are far greater than the risks to consenting and healthy living donors, the CD-P-TO started working on a new legal text on living donors as comparable and equal sources of kidneys for transplantation. Additionally, the CD-P-TO launched a new project aimed at drafting a new recommendation on “Establishing national/supranational living donor registries/databases”. The main goal of this text will be to promote national and supranational registries that will facilitate proper follow-up of living donors in Council of Europe member states. Finally, the CD-P-TO commenced a new project to evaluate the worrisome proliferation throughout Europe of private autologous cord blood banks.
1.7 Pharmaceutical Care and Anti-Counterfeiting Activities

The activities described below (except for the “eTACT” system and the API “fingerprint” database) are overseen by the European Committee on Pharmaceuticals and Pharmaceutical Care (Steering Committee CD-P-PH) and carried out by committees of experts. They aim at developing and promoting best practices in pharmaceutical care and the protection of public health from counterfeit or other illegal and sub-standard medicines.

Based on scientific developments (2008-2010), studies piloting six indicators under real-life conditions were started in seventeen countries. They were carried out by eight academic institutions. A standard procedure was developed to ensure that academic institutions from across Europe could co-operate in the pilot project and in building solid evidence on pharmaceutical care practices.

Safe and appropriate use of medicines

Public authorities and the manufacturing and distribution sectors devote many resources to the quality, safety and efficacy of medicines. The safe and appropriate use of medicines is as important as product quality for the best possible medication outcome in individual patients. Pharmaceutical care is a model concept for the responsible provision of medicine therapy, with the purpose of achieving definite outcomes that improve or maintain a patient’s quality of life (in line with Hepler and Strand). The Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC) has further advanced the development of scientific indicators for measuring the quality of pharmaceutical care in Europe. The indicators cover healthcare delivery by professionals such as doctors, pharmacists and nurses, and are outcome- and patient-oriented. The information derived from the indicators will be of practical use for policy-makers and professional associations in standard-setting.

As medicines prepared by industry do not always satisfy the health needs of patients, the preparation of medicines in pharmacies is important. However, to date, there is wide variability in national quality assurance and preparation requirements. The CD-P-PH/PC drafted a legal instrument in order to prevent the development of gaps in quality assurance between pharmacy-made and industrial medicines. The Council of Europe’s Committee of Ministers adopted Resolution CM/ResAP (2011) on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients on 19 January 2011 and recommended its implementation into the national legislation of its member states. A strategy was developed to support knowledge-transfer among authorities and professionals (e.g. pharmacists) on how to maximise the benefits of the Resolution’s provisions and to assist in its practical implementation.

Responding to the growing demand in Europe for foreign traditional medicines, including Traditional Chinese Medicine (TCM), the CD-P-PH/PC pursued its strategic approach to ensuring safe TCM practices in Europe. Studies were carried out on how to present valid information about TCM practices to patients/consumers in Europe and to meet their needs with due consideration of their varying levels of health literacy. Furthermore, a concept for an education /training curriculum for therapists and pharmacists in Europe was studied.

The Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO) annually issues recommendations to health authorities for the classification of medicines into prescription and non-prescription medicines, which is not harmonised in Europe. Its work promotes patient safety and the accessibility of medicines in Europe. An expert workshop was organised on 8-9 November 2011. Thirty-eight participants from seventeen countries discussed good classification practices, and promoted the role of the CD-P-PH/PHO as a platform for co-operation between member states and the sharing of expertise between national authorities and European institutions.

Public health protection from counterfeit or other illegal and sub-standard medicines

From the outset, the Steering Committee and the Committee of Experts on Minimising Public Health Risks Posed by Counterfeit Medical Products and Similar Crimes (CD-P-PH/CMED) have been significantly involved in the development and adoption process of the Council of Europe Convention on counterfeiting of medical products and similar crimes involving threats to public health (MEDICRIME Convention).

In May 2011, the Committee of Experts co-organised a regional training session with the Norwegian Medicines Agency on how to combat counterfeit medicines and to protect public health. For the first time, advanced level training was delivered to twenty-five officials from three Baltic States, Finland and Norway.

The CD-P-PH/CMED also co-organised a workshop with the Italian Medicines Agency (AIFA) on 29 November 2011. Sixty-five participants from twenty-five countries discussed key elements of good communication practices on the risks of counterfeit medicines and similar crimes and the practical implementation of the provisions dealing with patient- or consumer-centred awareness-raising included in the MEDICRIME Convention and other recent directives of the European Parliament and of the Council in this field. With significant support from the Italian Medicines Agency (AIFA) in the drafting, production and publication process, the CD-P-PH/CMED published two documents and a training booklet for officials (see chapter 2.3 publication activities page 35).

The CD-P-PH/CMED also started a feasibility study on approaches to identifying and following-up on indications of harm to patients and consumers from counterfeit medical products and similar crimes.

The eTACT service at a glance: interest and added-value to securing medicines in the context of emerging regulations in Europe

As part of its holistic anti-counterfeiting strategy, the Council of Europe/EDQM has further developed the project for an anti-counterfeiting traceability service for medicines. The eTACT service aims to provide a traceability and mass-serialisation system that can be used by authorities and stakeholders (i.e. manufacturers, suppliers, distributors, healthcare professionals and patients) from across the entire pharmaceutical supply-chain, from the 36 member states of the European Pharmacopoeia and beyond.

The eTACT service will help combat counterfeiting and will present several advantages:

- It will use a harmonised approach.
- It will be a flexible system that will improve control of the supply-chain and will give patients the possibility to check the authenticity of their medicines.
- It will be a system under public governance via the EDQM and will, thereby, protect the sensitive commercial data of business stakeholders.

By providing a flexible pan-European system, the EDQM’s eTACT project will enable harmonised, standardised and centralised mass serialisation of products in the legitimate pharmaceutical supply-chain, irrespective of their distribution route.

Allowing patients the possibility of verifying the authenticity of their medication is a unique feature of the EDQM’s project, which will significantly contribute to strengthening the public’s confidence in the legal supply-chain.

Public governance of such a system is vital to ensure effective and proper project development in co-ordination with regulatory authorities and to prevent the misuse of data (e.g. commercial data).

Traceability service

![Image of eTACT service](image)

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In 2011, a live demonstration IT system was developed. The EDQM began presenting the demonstration system to authorities and stakeholders in workshops during the last quarter of 2011. The plan is to hold further workshops and to keep gathering comments from all over Europe. This should allow the EDQM to elaborate a robust users and business requirements document for a real-scale service, to be implemented in line with upcoming national and regional requirements for the traceability of pharmaceuticals in Europe.

The EDQM expects that the on-going debate on the required functionalities of such systems and their governance will result in the different stakeholders converging towards a harmonised and, if possible, unique architecture for the traceability of pharmaceuticals in Europe.

API “Fingerprints” repository

The EDQM has further developed a project for the establishment of a repository of “fingerprints” or signatures of active pharmaceutical ingredients (APIs) used for the manufacture of medicines. The EDQM collaborates with a dedicated task force of the OMCL Network for this purpose. In 2011, as part of a pilot project, the OMCLs involved completed a number of studies, with analyses performed on various methods and samples provided by the companies that had joined the project. In 2012, the EDQM and the OMCL Network plan to finalise the pilot project phase and to review the programme objectives.

1.8 Cosmetics and Packaging for Food and Medicines

Consumer Health Protection

Since 01 January 2009, the EDQM has been engaged in efforts to strengthen consumer health protection in Europe, with a focus on the safe use of cosmetics and packaging or other materials that are intended to be brought in contact with food or medicines.

The work programme was elaborated by the Consumer Health Protection Committee (CD-P-SC, Steering Committee), which is composed of representatives from national ministries acting in the field of public health. So far, 33 member states and observers to the European Pharmacopoeia Convention are involved in the work.

According to the terms of reference, the focus of the work is on the new European network of Official Cosmetics Control Laboratories (OCCL) and on the development of common quality and safety standards for packaging materials that are used for food and medicines.

Two subordinate Committees of Experts implement the work defined by the CD-P-SC: the Committee of Experts on Cosmetic Products (P-SC-COS) and the Committee of Experts on Packaging Materials for Food and Pharmaceutical Products (P-SC-EMB).

Cosmetics testing

The European network of national OCCLs was set up in 2010 with voluntary members to share testing competences and resources and to enhance quality management in each laboratory in accordance with international standards. Under the aegis of the EDQM, collaborative analytical studies and expert meetings are organised, with contributions from several or all participating laboratories. The long-standing experience with the network of Official Medicines Control Laboratories (OMCLs) has been an asset in the start-up phase.
In 2011, a first proficiency testing scheme (PTS) study was carried out on cosmetic products intended for skin bleaching that contained hydroquinone (the use of which is prohibited in the European Union). Analytical results were compared from 16 national laboratories located in Austria, Cyprus, France, Germany, Ireland, the Netherlands, Portugal, Slovenia and Sweden.

A second PTS study was conducted to check the quality of laboratory performances concerning formaldehyde analysis, in which 14 laboratories from 13 European countries participated.

The main task of OCCLs is to check the quality of products on the market. In 2011, several countries collected samples of decorative cosmetics (make-up, eye-shadow, eye liner, lip gloss, etc.) to measure the content of certain metals that may give rise to health concerns, such as antimony, cadmium, chromium, lead, mercury, and nickel. Traces of some of these metals may be unavoidable for technical reasons but, in most countries, maximum tolerable limits have not been set. Results from this study will be available in 2012.

Sun protection products contain substances that filter or block UV light and many products indicate a so-called “sun protection factor, SPF”. Such factors are measured using in vivo and in vitro methods. A seminar on this topic was organised in June 2011 in Montpellier (France), which was hosted by the Agence française de sécurité sanitaire des produits de santé (Afssaps). The presentations focused on analytical developments and approaches to market surveillance in this field. Experts from nine European countries participated and decided to harmonise approaches and further develop methodologies.

**Cosmetics for children under the age of three**

The restriction of cosmetics intended for application on the skin of children up to the age of three is the subject of a draft guidance document for safety assessors. Detailed recommendations for baby creams and lotions were agreed by experts in the field. Products must be safe for the health of babies and should only contain ingredients that are non-toxic; potent allergens or substances with endocrine-disrupting activity should not be present and preservatives should be used at their lowest efficacious concentrations. It is intended to finalise and publish this document in 2012.

To ensure wide application of these recommendations, a Resolution was drafted and its adoption by Council of Europe member states is planned for 2012.

**Tattoos and permanent make-up**

To implement the recommendations of Council of Europe Resolution AP (2008) 1 on tattoos and permanent make-up, the compilation of safety and documentation requirements for tattoos and permanent make-up is under preparation. This document is expected to be finalised and published in 2012.

**Packaging for food and medicines**

A Resolution on metals and alloys used in food contact materials has been finalised, which defines quality requirements for materials such as aluminium foil, kitchen utensils, coffee machines, etc. where no EU regulation exists. The text recommends that Council of Europe member states implement Specific Release Limits (SRL) for metal ions that are released from materials in contact with foodstuffs.

The work programme in the field of Packaging Materials for Food and Pharmaceutical Products includes the elaboration of a Technical Guide on metals and alloys used as food contact materials that supplements the corresponding Resolution (finalisation expected in 2012). Specific limits for the release of metal ions that may be transferred to food from packaging or containers have been agreed. For example, nickel release should not exceed 0.07 mg/kg and lead should not be released in amounts greater than 0.004 mg/kg (concentrations measured in food). Detailed instructions on how to perform laboratory testing are also described.

Furthermore, the Committee of Experts P-SC-EMB decided to entirely review the existing resolutions and technical documents that had been elaborated under the former Council of Europe Partial Agreement in the Social and Public Health Field (dissolved on 31 December 2008) and the work has been assigned to rapporteurs who will prepare draft proposals. This work will be pursued in 2012.

Finally, a new project deals with the use of printing inks for packaging of medicines and food. The aim is to set up a positive list of safe substances to be used by manufacturers and to define general quality criteria and analytical test methods.
The EDQM maintains its ISO 9001 certification

After a comprehensive two-day audit, Afnor Certification (AFAQ) decided to maintain the EDQM’s ISO 9001 certificate. The EDQM is certified as meeting the requirements of ISO 9001:2008 for the following activities:

“Evaluation of applications (initial, revisions and renewals) for certificates of suitability to the monographs of the European Pharmacopoeia, granting of certificates, and management of the inspection programme of manufacturing sites and associated brokers.”

and also:

• Planning, implementation and co-ordination of post-marketing surveillance studies for medicinal products authorised by the centralised (CAP) and national (MSS) procedures;

• Management of the database related to post-marketing surveillance studies of medicinal products authorised by the mutual recognition (MRP) and decentralised (DCP) procedures;

• Co-ordination of the elaboration and issuance of guidelines related to the OCABR procedure for the release of batches of human immunological medicinal products (blood and vaccine);

according to the pharmaceutical legislation, notably directives 2001/82/EC and 2001/83/EC, as amended, and Regulation 726/2004 (EC) for the EU countries.”

The EDQM is committed to extending the scope of its certification in the coming years in order to guarantee an optimal service to its stakeholders, whilst improving the efficiency of its working methods.

The EDQM laboratory (DLab) is audited by the Official Medicines Control Laboratory (OMCL) Network through the Mutual Joint Audit (MJA) scheme.

In order to generate high quality data, DLab operates an ISO/IEC 17025:2005 Quality Management System. This system has been extensively audited by an independent team of four experts from the OMCL Network in preparation for official ISO accreditation in 2012.

2. SUPPORT ACTIVITIES

2.1 Quality and Environmental Management Systems

The EDQM is the first inter-governmental organisation to classify substances for medicinal and primary container use in accordance with the Globally Harmonized System (GHS) of the United Nations Economic Commission for Europe (UNECE) Sub-Committee of Experts and/or Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of substances and mixtures (CLP).
The objective of this classification is to secure the continued availability of the EDQM’s Reference Standards, which are necessary for ensuring the quality of medicines globally. Given the fact that EDQM has no access to applications for marketing authorisations and other safety data, the EDQM published the proposed classifications for consultation. Based on the feedback obtained and in the interest of public health, the EDQM identified the need to reassess the classifications of several substances that had extensive and well-established therapeutic uses; notably, to classify them much as the EU authorities have done with caffeine.

With the objective of addressing hazard classification of pharmacopoeial substances, coherence in GHS implementation and the effective communication of Reference Standards intended for specialised small-volume use in laboratories, the EDQM collaborated with trade associations, the European Commission’s Competent Authorities for the Regulations on the Evaluation, Authorisation and Restriction of Chemicals (REACH) and CLP, the ISO Committee on Reference Materials (ISO REMCO), and the United Nations Economic Commission for Europe (UNECE) Sub-Committee of Experts on GHS (Global Harmonised System).
2.2 Information Technology and Publications activities

A website (www.edqm.eu) continuously progressing in terms of visits

The website, www.edqm.eu, is one of the EDQM’s main means of communication with stakeholders. Over 30,000 monthly visitors (+20%) and 76,000 monthly visits (+7%, statistics obtained using AWSTATS software) were recorded in 2011.

Two new ‘Project’ pages were created covering the latest information on blood transfusion and organ transplantation projects (e.g. Project TS057, the Black Sea Area programme). An audit was also performed to see where improvements could be made to search engine indexing and rankings, and to identify areas that could be made more user-friendly. This work on search engine optimisation will continue into 2012.

An indispensable online user support service (HELPDESK)

The HELPDESK service is the first point of contact for information and support from the EDQM. It provides help with any technical or scientific questions concerning the various activities, products or services of the EDQM. The HELPDESK received 10,624 questions in 2011, which represents an increase of 4% in volume. The HELPDESK Frequently Asked Questions (FAQs) are updated regularly to cover all activities and to respond to changing user needs.

Ambitious IT projects

Enterprise Resource Planning (ERP)

The implementation of standard ERP software was continued in 2011 and will be pursued further in 2012 to better integrate the different business processes used in the EDQM, such as management of the supply-chain, warehouse and customer relations. This integration will help to provide a better and more standardised service to the EDQM’s customers.

Dynamic publication activities in paper and electronic formats

The Publications unit is mainly responsible for all the technical and administrative aspects of publications.

Three supplements of the 7th Edition of the European Pharmacopoeia (7.3 to 7.5) were published in 2011, comprising 982 pages for the English version and 1046 pages for the French version. The 7th edition (including supplement 7.5) consists of 2167 monographs (including those on dosage forms) and 336 general texts (including general monographs and general methods of analysis).

The four issues of Pharmeuropa (paper version) published in 2011 contained 245 texts for enquiry and general information, comprising 760 pages for the English version and 810 pages for the French version. Two issues of Pharmeuropa Bio & Scientific Notes (paper version), containing 10 scientific articles in English, were also published.

Support was also provided for the publication of other EDQM publications in the fields of:

- Blood components:
  - The 16th edition of the Guide to the preparation, use and quality assurance of blood components was published in English and Russian. The 16th edition of this Guide is currently being translated by the national authorities, in co-operation with their respective blood services, of many countries. Preparation of the 17th edition (for publication in 2013) is on-going.

Webinars

In November 2011, the first ‘webinar’ took place, a web-based conference conducted over the Internet. This new conference technology has many advantages, ranging from flexibility to cost-effectiveness, and will be used to conduct more intensive and focused lectures to stakeholders anywhere in the world. The first webinar was on ‘e-Submissions for CEP Applications’. Two sessions at different times were organised in order to facilitate participation from outside Europe. Questions were answered ‘live’ and the slides were sent out to participants afterwards. A recording was also made available if the attendees wished to listen to the talk again.
- Individual Reports for 2005 through to 2008 and a Trend Analysis 2001-2005 for the collection, testing and use of blood and blood components in Europe.

- An Executive Summary on the implementation of pathogen reduction technologies.

• Transplantation of organs, tissues and cells:

- The 4th Edition of the Guide to the safety and quality assurance for the transplantation of organs, tissues and cells was published in English, French, Russian and Spanish. The chapters on the transplantation of tissues and cells were revised independently by an ad hoc working group and published online in December 2011. During this revision process, it became evident that, due to the specificities of organ transplantation and that of tissues and cells, both areas needed to be dealt with separately by different groups of experts. Therefore, the revision process for the 5th edition of the Guide will entail the generation of two distinct guides; one specific to organ transplantation and the other to that of tissues and cells. This revision process started in 2011 and will continue throughout 2012.

- A first compilation of the Council of Europe’s resolutions, recommendations and several relevant reports on safety, quality and ethical matters concerning the procurement, storage and transplantation of organs, tissues and cells was also published.

• Counterfeit medical products and similar crimes:

- Risk Communication about Counterfeit Medical Products and Similar crimes (2011).


- Technical guide for the elaboration of monographs and a guide for monographs on human plasma-derived products.

- Biological substances submitted to the Official Control Authority Batch Release.

- Quality management documents for the OMCL network.

In addition, the Publications Unit continued its work on keeping a harmonised editorial style throughout all publications and maintained lists of data needed for publication work.

■ From paper to online publications: new services launched in 2011

- In March 2011, publications on Blood Transfusion and Organ Transplantation were published online, providing electronic access to book subscribers. The online edition features multiple languages, and some translations that are only available online. The site is available to subscribers at http://tots.edqm.eu/.

- Pharmeuropa successfully transited from a paper publication to an online publication in 2011. After an initial trial period, the online version became official with the publication of Pharmeuropa 24.1. The homepage provides links to public inquiries on draft European texts or on matters of general policy, the latest official announcements on newly-adopted monographs, the latest news on Pharmacopoeial harmonisation, a readers’ forum and access to three databases. It is possible to sign up for email notifications when draft comments on texts are added to the site. Access to Pharmeuropa online is free, but it is necessary to register to receive full access to the content of the site. National authorities have privileged access to a commenting tool, making it possible for them to submit comments directly in the ‘Texts for Comment’ database. The site is available at: http://pharmeuropa.edqm.eu.

■ Standard Terms database

The lists of Standard Terms were drawn up in response to a request from the European Commission, and cover dosage forms, routes and/or methods of administration, and containers, closures and delivery devices used for medicines for human and veterinary use. Standard Terms are used in the European Union Marketing Authorisation application forms, the Summary of Product Characteristics (SmPC), product labelling, and electronic communications.

Terms are currently available in 31 world languages (Albanian, Bulgarian, Chinese, Croatian, Czech, Danish, Dutch, English, Estonian, Finnish, French, German, Greek, Hungarian, Icelandic, Italian, Kazakh, Latvian, Lithuanian, Macedonian, Maltese, Norwegian, Polish, Portuguese, Romanian, Serbian, Slovak, Slovenian, Spanish, Swedish and Turkish).

Since its launch in 2008, the increasing number of terms necessitated a review of the structure of the database itself. In 2011, work began on the development of a new database, based on a forthcoming international standard (prEn ISO 11239, Health Informatics – Identification of medicinal products – Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging).

At the end of 2011, the Standard Terms database held 743 unique terms, with 48 new terms having been added during the year.
2.3 Communication, Landmark events

Communication with stakeholders, partners and the general public

Communication plays a strategic role within the regulatory environment. The EDQM aims to disseminate important announcements, changes in policy, product releases and new collaborations by releasing regular press communications. In 2011, 19 press releases were issued and circulated via electronic mail to various media, authorities and partner associations all over the world.

The EDQM’s free, monthly E-Newsletter summarises the latest information, events and news, with links for retrieving that information from its website. The number of subscribers grew to over 10,700 and, along with the RSS feeds, new web content was quickly delivered to subscribers, with all major headlines summarised in a single email.

A year dedicated to consultations on topical subjects to allow feedback and better prepare users for Quality challenges

Various events took place on technical and scientific subjects related to EDQM activities.

The EDQM organised a technical workshop restricted to representatives from authorities on ‘Future Monographs in the Field of Biologicals’ in Strasbourg, France in February 2011, providing the opportunity to discuss with European competent authorities how this area should be developed in the future.

In September 2011, a symposium was organised on ‘Alternatives to Animal Testing’ in Strasbourg, France, to share information and experiences on the recent changes that have occurred in this field, to discuss new developments and trends, and to take a closer look at new methods that could be explored in the future. An initial session on the regulatory background provided the opportunity to discuss the new Directive 2010/63/EU on the “Protection of Animals used for Scientific Purposes”. The Directive, to be implemented on 01 January 2013, will have a significant impact on monographs, OMCLs and manufacturers. The most recent achievements of the BSP programme with regard to activities on the 3Rs concept were also discussed. The meeting was attended by officials and experts from 19 countries, as well as representatives from European and national institutions and authorities.

In October 2011, an international high-level conference was hosted and co-organised by the Russian Federation’s Ministry of Public Health and Social Development and the Federal Service on Surveillance in Healthcare and Social Development (Roszdravnadzor), the Council of Europe’s Directorate General of Human Rights and Legal Affairs (DG-HL) and the EDQM in Moscow. The conference aimed to significantly advance the fight against counterfeit medical products and similar crimes at an international level and involved 230 participants, including senior officials from health, law enforcement and judicial authorities from Council of Europe member and non-member states.

On 28 October 2011, during an official Ceremony, the Council of Europe’s ‘Medicrime’ Convention was opened for signature to member states, with twelve countries paving the way for implementation of the Medicrime Convention.

The EDQM’s European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and its Committee of Experts on Minimising the Public Health Risks Posed by Counterfeiting of Medical Products and Related Crimes (CD-P-PH/CMED) both contributed significantly to the programme and supported the signature of the Convention at national levels.

In November 2011, an expert workshop ‘European Formulary for Paediatric Formulations’ took place in Strasbourg to discuss the needs and scope of a harmonised European formulary for paediatric formulations in community and hospital pharmacies, and debate what approaches and criteria should be considered.

Training sessions – strengthening knowledge and sharing know-how

Training sessions were organised in Strasbourg in July 2011 and Bratislava, Slovakia in December 2011. These courses aimed at increasing and refreshing users’ knowledge of the European Pharmacopoeia and focused on providing delegates with a good grounding of its basic themes and topics. These programmes are frequently updated and the workshops and case study groups are tailored to reflect the most current regulatory realities.

A training session on ‘CombiStats™’, a computer programme used for the statistical analysis of data from biological dilution assays or potency assays, was organised in Strasbourg, France, in November 2011.

Partnerships at international level

To help national authorities and professionals worldwide, the EDQM co-organised a number of events; namely, in chronological order:

A workshop was organised jointly with the Korea Food and Drug Administration (KFDA) on “Establishment and Management of Reference Standards for Pharmaceutical and Biopharmaceutical Products”. The workshop took place in Osong, South Korea, in April 2011. This workshop was attended by representatives of the Korean health authorities and industry who had the opportunity to learn about the
European Pharmacopoeia and the EDQM’s reference standards. By increasing mutual understanding, this workshop is expected to strengthen co-operation between the EDQM and the KFDA on subjects of common interest.

In May and September 2011, the EDQM and the World Health Organization (WHO) jointly organised two conferences on the quality of active pharmaceutical ingredients (APIs) in India and China respectively; the former co-organised by the Drug Information Association (DIA), the latter in collaboration with the Chinese State Food and Drug Administration (SFDA). These conferences highlighted important aspects relevant to the quality of APIs, dossier assessment, inspections and pharmacopoeial requirements, and emphasised the close collaboration of the EDQM with European and international regulatory authorities and the WHO.

Within the framework of the French-African Network of the National Laboratories of Drugs Quality Control (LNCQ) and under the auspices of the French Agency for Sanitary Safety of Health Products (ANSM, formerly AFSAPPS), the EDQM contributed to a training session entitled, ‘Formation Centralisée 2011 AFSAPPS-OMS-DEQM’ which was held in Dakar, Senegal, in September 2011. The World Health Organization (WHO) was also involved. The training focused on two important general aspects: establishment of reference standards and co-operation among official medicines control laboratories. The programme also included practical training on two important tests, i.e. the dissolution test and Karl-Fischer determination of water.

The EDQM was invited to participate in a round-table meeting on ‘A Joint Action against Fake Medicine in West Africa’ which took place in Ouagadougou, Burkina-Faso (September 2011). This meeting was held under the high patronage of His Excellency, Mr Blaise Compaoré, President of Burkina Faso and Head of the Council of Ministers. Many ministries and regional and international organisations were involved, such as the French Ministry of Foreign and European Affairs, the Ministry of Health of Burkina Faso, the West African Health Organisation (WAHO) and the West African Economic and Monetary Union (WAEMU). The EDQM contributed to discussions on counterfeit drug control and strongly encouraged countries to sign the Council of Europe’s Medicrime Convention.

In September 2011, the EDQM was invited to participate in the APEC ‘Life-Sciences Innovation Forum: Drug Safety and Detection Workshop’ which brought together about 200 participants from APEC economies, including 100 Chinese officials from all over the country. Participants mostly came from authorities, with few industry representatives. The workshop covered a number of issues related to combating falsified/counterfeit medicines, such as rapid detection technologies, the MEDICRIME Convention and mass serialisation technologies and projects and the outcome of the discussions were compiled in a recommendation to the APEC Regulatory Harmonisation Steering Committee for further action.

In October 2011, the EDQM and the Ministry of Health of Ukraine jointly supported the organisation of the ‘Ukrainian International Transfusion Medicine Congress and Exhibition’ which took place in Kiev, Ukraine. The conference, entitled ‘Current issues in Transfusion Medicine and Blood Donation: Collection, Processing and Usage of Blood and Blood Products’, aimed to share information on significant areas of transfusion medicine such as the management of blood preparation and supply, blood donor management, quality control and patient safety. The activities and role of the EDQM in the field of blood transfusion were presented.
Together with the China Chamber of Commerce for Import & Export of Medicines & Health Products (CCCMHPIE), a national trade association, and the Chinese Ministry of Commerce, the EDQM organised a conference which took place in Xian, China, in November 2011. Over 100 participants from industry attended and the programme highlighted important aspects relating to dossier requirements for drug substances in Europe, the preparation of CEP applications, the EDQM’s inspections programme and highlighted important aspects relevant to the quality of APIs.

The EDQM also participated in the 2nd International Forum on Rapid Drug Testing and the 3rd China-US Joint Symposium on Pharmaceutical Analytical Technology and Compendial Methods in Hangzhou on 15-16 November 2011 by making a presentation on the establishment of Ph. Eur. standards and its Quality Management System. This meeting was an excellent opportunity to meet international partners mainly involved in pharmacopoeial standards.

International trade fairs are an important way to promote the activities and work of the EDQM. Participating in fairs such as the Congress of Pharmaceutical Ingredients (CPhI) that took place in Shanghai, China, in June 2011 and Mumbai, India, in December 2011, are important to keep users of the European Pharmacopoeia up-to-date with the regulatory changes in Europe and permit the EDQM to meet in person with users of the Pharmacopoeia. Visitors at these fairs could also benefit from one-to-one technical consultations on the EDQM’s Certification procedure and received brochures and catalogues. Materials were available in Chinese and local distributors of EDQM publications were also invited to the stand.

Promoting communication in blood transfusion activities

On 14 June 2011, countries around the world again celebrated World Blood Donor Day. The 2011 global event was hosted in Argentina under the theme ‘More blood. More life’. This day is an annual event to recognise and thank the millions of people around the world who donate their blood on a voluntary basis to help save lives.

The Council of Europe supported several European initiatives, including the Etablissement Français du Sang (EFS) and its Alsace section, the German Red Cross (Deutsches Rotes Kreuz, DRK) and the Swedish Blood Centre by providing the EDQM’s media kit to organisers. This kit is available to all member states for use during their own local campaigns.

The EDQM participated in the 21st Regional Congress of the International Society of Blood Transfusion (ISBT) in Lisbon, Portugal, in June 2011 and promoted the new edition of the Guide to the Preparation, Use and Quality Assurance of Blood Components (16th Edition 2010) to all professionals working within the field of transfusion medicine. Information on the role of the EDQM in ensuring the quality and safety of blood transfusion and the projects it is involved in at a European level, as well as on Council of Europe recommendations and resolutions, was provided.

Organ transplantation activities

Since 1998, the Council of Europe organises a European Day for Organ Donation and Transplantation to promote organ donation and transplantation in its member states. Each year it is hosted in a different member state, with the aim to raise awareness of the importance of organ donation and transplantation.

In October 2011, the event took place in Geneva, Switzerland and was organised and co-ordinated by the Fairtransplant foundation. Other foundations, including Swiss Transplant, AGIR, the Hôpitaux Universitaires de Genève (HUG), and the association ‘Footballers sans Frontières’ were all involved in the preparations. The 2011 European Day for Organ Donation and Transplantation also coincided with the 40th anniversary of transplantation in Geneva.

Various street activities, information stands and a football match, with the participation of some of soccer’s great legends and famous personalities, were organised in support of organ donation, as well as a conference and press conference.

Over 300 EDQM and Council of Europe staff participated in a photo shoot in front of the ‘Palais de l’Europe’ to highlight organ donation. The photo was widely distributed to the media for use in their press releases and articles. Campaign materials and an information kit were made available to all European countries to support and add to their local efforts.

Visits

The EDQM continued to open its doors to various groups of visitors as part of its policy of openness and transparency.
2.4 International collaboration

Memorandums of Understanding

In an era of globalisation, international collaboration is of paramount importance for the EDQM to fulfill its mission of protecting public health. Harmonisation of standards, exchange of information and work-sharing are just a few examples of the EDQM’s activities in working closely with its partners and stakeholders at an international level.

Bilateral meetings and visits

Australia

A representative of the Australian Therapeutic Goods Administration (TGA) visited the EDQM in October 2011 to discuss laboratory testing programmes and experience with the official batch release procedure. The risk-based selection procedure for products to be included in the testing program was of special interest.

China

To further strengthen its collaboration with the Chinese Pharmacopoeia, the EDQM Director met with the Deputy Commissioner of SFDA and Secretary General of the Chinese Pharmacopoeia Commission (ChPC) and the Deputy Secretary General of the ChPC and other Commission members in Beijing in May 2011. The discussion focused on strengthening collaboration in the field of monograph development, with a focus on TCM, the possibility of exchanging scientists and organising joint training sessions and conferences.

The EDQM also participated in a workshop on clinical trials, the quality of API and inspections in Brussels in May 2011, which was organised and funded by the EU/China Trade Project. Participants included representatives of the EU Commission, DG Sanco, the European Medicines Agency, the Chinese Food and Drug Administration (SFDA) and European trade associations.

The EDQM signed a trilateral Memorandum of Understanding (MoU) with the State Administration of Traditional Chinese Medicine of the People’s Republic of China (SATCM) and its National Key Laboratory of TCM Quality Control (NKL-TCM) in June 2011. The SATCM is the state organisation of the Chinese Ministry of Health responsible for the development of TCM and ethnic medicines. The NKL-TCM is a key Chinese national research laboratory, established with the full support of the SATCM. The MoU sets out the basis upon which the parties will provide mutual assistance and exchange of information in the elaboration of quality standards for TCM herbal drugs.

The productive co-operation with the National Institute for Food and Drug Control (NIFDC) continued in 2011 with visits of NIFDC delegations to the EDQM in May and November 2011. The discussions focused on experience in the development of reference standards and collaborative studies, as well as quality management systems and the activities of the OMCL network. The EDQM’s laboratory and reference standard production facilities were also visited. In the framework of its collaboration with the WHO, the EDQM was also requested to present and explain its Quality Management System to the NIFDC, including the Mutual Joint Audit scheme.

Korea

Following a Memorandum of Understanding signed with the Korean Food and Drug Administration (KFDA) in 2010, a KFDA delegation visited the EDQM in June 2011 to discuss quality management systems, topics related to the establishment and production of reference standards, and laboratory activities. In addition, the two partners co-organised a workshop on “Establishment and Management of Reference Standards for Pharmaceutical and Biopharmaceutical Products” in South Korea in April 2011. (see chapter 2.3 Communication, landmark events page 35)

Singapore

An official delegation from the Singapore Health Sciences Authority (HSA) was welcomed in March 2011. Discussions focused on the EDQM’s Reference Standards and Quality Management System. As a follow-up to this visit and with the view to further strengthening the collaboration between the two organisations, Singapore requested observer status to the European Pharmacopoeia Commission in October 2011.

United States of America

Following the signature of a confidentiality agreement with the US Food and Drug Administration (FDA), the FDA’s European liaison officer visited the EDQM to get a more detailed understanding of all of the EDQM’s activities and to discuss activities in the field of combatting falsified/counterfeit medical products and the certification of suitability procedure, with a focus on inspections. Both the FDA and EDQM have participated in the international API inspection program from the outset of the pilot phase.

WHO

In addition to its activities relating to International Chemical Reference Standards (ICRS) and International Standards for Antibiotics (ISA) described in chapter 1.2, the EDQM has supported the WHO’s standard-setting activities by
active contributions to the work of the Expert Committee on Specifications and the Expert Committee on Biological Standardization.

International collaboration on GMP Inspections

The EDQM continued its active role in the EU/USA/Australia project for collaboration on GMP inspections of API manufacturers by exchanging information or by performing joint inspections for sites of common interest. This helped to reduce the rate of duplicate inspections by different authorities of the same company and, therefore, saved resources and money for all parties. A review of the results of the pilot phase at the end of 2010 clearly identified the need to continue this exercise and to extend its scope to other authorities.

As an observer to the Pharmaceutical Inspection Co-operation Scheme (PIC/S), the EDQM participated at the annual seminar of the Committee of Officials, as well as at a meeting of the Expert Circle on APIs, during which a training session on cases of falsification during inspections of API manufacturers was organised.

In addition, the EDQM signed bilateral confidentiality arrangements with the World Health Organization, the Russian Federation and Ukraine to enable exchange of information on GMP inspections for sites of common interest.

Development of international standards

In addition to its activities at the level of the Pharmacopoeial Discussion Group (PDG) – see chapter 1.1 - the EDQM has been participating in the development of a group of ISO standards that are intended to harmonise the identification of medicinal products (IDMP) from a regulatory perspective. The EDQM has provided particular expertise in the preparation of ISO standard 11239, related to the preparation of controlled vocabularies for pharmaceutical dosage forms, routes of administration, units of presentation and packaging. In 2011, the set of five standards was submitted to the ISO Secretariat for entry into the final balloting stage of the standards development process, as final draft ISO standards (FDIS). In addition to the preparation of the ISO standards, the EDQM has participated in the drafting of an implementation guide within the M5 expert working group of the ICH, where the IDMP project first originated.

Regular teleconferences were held throughout the year, as well as a number of meetings in Europe and the USA, where collaboration was fostered between regulators and industry representatives from across the globe, in particular the ICH members (Europe, USA, Japan) and observers (Switzerland, Canada). A training session at the EMA premises in London also took place in September 2011, during which speakers from the EDQM, the EMA and the US FDA provided progress reports on the development of standards and on a guide to implementation for the benefit of attendees from regulatory agencies and industry across Europe.

Conferences and workshops

Information on international conferences and workshops organised by the EDQM or in which the EDQM participated is provided in section 2.3 Communication and Landmark events.
List of EDQM committees

THE EUROPEAN PHARMACOPOEIA COMMISSION

The Commission was set up in 1964 in accordance with the Convention on the Elaboration of a European Pharmacopoeia. In 2011, its membership comprised the 37 signatory parties to the Convention (36 states and the European Union). The Commission sets the work programme and defines the quality standards for all our medicines and their components by appointing national experts authorised to work on the elaboration of these standards. Twenty permanent groups of experts and 51 “Ad hoc” working parties have been set up by the Commission to carry out the Ph. Eur. work programme. Already, 2167 texts containing quality standards have been elaborated, adopted and implemented. These texts are constantly being revised to keep pace with technical and scientific progress in production and quality control. The European Pharmacopoeia, which is now in its 7th Edition, is essential to the protection of public health. It is intended for professionals working in the area of medicines, who constantly refer to it.

THE BIOLOGICAL STANDARDISATION PROGRAMME (BSP) Steering Committee

The BSP focuses on the standardisation of the methods and tools for the quality control of biologicals by establishing reference standards and validating new methods; in particular, such methods where the use of animals is reduced, refined or replaced (3Rs initiative). These activities are supervised by the BSP Steering Committee.

NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES (OMCL) Advisory Groups

About 35 countries have been participating in the activities of the OMCL Network since 1994; these activities are co-ordinated by the EDQM. The role of this Network is to ensure the consistent quality of medicines marketed in the member states and to contribute to the mutual recognition of the results of quality control testing of medicines by these states. Major decisions are taken by the annual plenary meetings of the OMCL Network. Advisory groups prepare and ensure the implementation of the annual work programme. There are two levels of collaboration within the network:

- general activities involving all of the member states of the Convention and the observer states. These general activities cover work in the area of quality management systems, such as audits and proficiency testing studies (PTS) as well as market surveillance studies (MSS). These activities are prepared and followed by the General OMCL Advisory Group (AdGEON);
- activities restricted to the EU and the European Economic Area (EEA) concerning products with a centralised marketing authorisation (CAP), products authorised according to the mutual recognition or the decentralised procedure (MRP/DCP) and the Official Control Authority Batch Release (OCABR) system for biological products (human and veterinary). This latter activity also involves Switzerland. For the CAP and the OCABR activities, advisory groups ensure continuity of operations in the interval between the annual meetings of each specific network.

These activities involve the European and national authorities. The OMCL Network also participates in investigations into fraudulent medicines.

CERTIFICATION OF SUITABILITY TO PH. EUR. MONOPHYS Steering Committee

The activities associated with the procedure for certification of suitability to Ph. Eur. monographs are guided by a Steering Committee and, currently, two Technical Advisory Boards (TAB). The Steering Committee is composed of representatives of European licensing authorities and inspectorates. It takes decisions on general policy, examines and comments on matters brought to its attention by the Technical Advisory Boards, adopts guidelines and the inspection programme and co-ordinates questions amongst the represented parties. It is also responsible for appointing assessors as well as the members of the Technical Advisory Boards and their Chairs.

A network of about 80 assessors and 30 national inspectors participate in the work required for the evaluation of files and the inspection of manufacturing sites.

EUROPEAN COMMITTEE ON BLOOD TRANSFUSION (CD-P-TS)

This Steering Committee supervises the work of a number of individual projects and Working Groups, e.g. the European Database of Frozen Blood of Rare Groups. Blood Donor Management, the Ad-hoc Working Groups on the “Guide to the Preparation, Use and Quality Assurance of Blood Components” and “Risk behaviours having an impact on blood donor management”.

EUROPEAN COMMITTEE ON ORGAN TRANSPLANTATION (CD-P-TO)

This Steering Committee focuses on elaborating and promoting the principle of non-commercialisation of organ donation, strengthening measures to avoid organ trafficking and elaborating high ethical, quality and safety standards in the field of organ transplantation. It supervises the elaboration of the guides in the transplantation field as well as the activities of a number of individual projects on topics such as “living donation”, “transplantation for non-residents”, “multiple listing on transplantation waiting lists”, “autologous cord blood banks” and “co-operation of states from the Black Sea Area in organ transplantation”.

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EUROPEAN COMMITTEE ON PHARMACEUTICALS AND PHARMACEUTICAL CARE (CD-P-PH)

This Steering Committee supervises the programmes of activities of its subordinate committees:

• Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO).

• Committee of Experts on Quality and Safety Standards for Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC).

• Committee of Experts on Minimising Public Health Risks Posed by Counterfeiting of Medical Products and Related Crimes (CD-P-PH/CMED).

CONSUMER HEALTH PROTECTION COMMITTEE (CD-P-SC)

Product safety and quality are critical to the protection of consumer health. The CD-P-SC is responsible for managing the work programme and decision-making process in the areas of cosmetics and packaging for food and medicines. Health authorities in the 36 European countries that signed the Convention on the Elaboration of a European Pharmacopoeia are eligible to contribute to the work.

The Committee has two subordinate bodies that examine health-related issues and evaluate the risks, and draft reports and recommendations for regulatory approaches:

• Committee of Experts on Packaging Materials for Food and Pharmaceutical Products (P-SC-EMB). The P-SC-EMB has working groups dedicated to migration testing, metals and alloys, polymers and printing inks.

• Committee of Experts on Cosmetic Products (P-SC-COS). The P-SC-COS co-ordinates the work of the network of Official Cosmetics Control Laboratories (OCCL). Besides cosmetics, the P-SC-COS also has a working group that addresses health issues related to tattoos and permanent make-up.
Notes