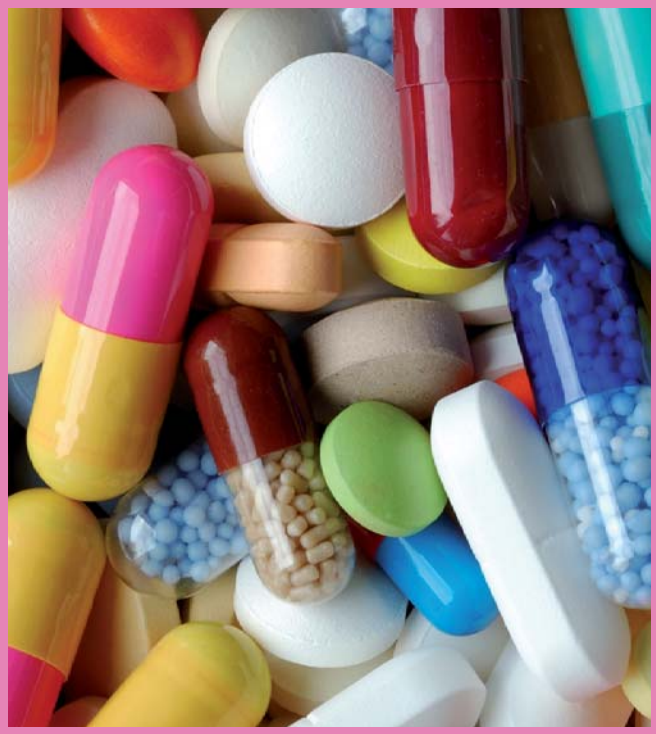
ANNUAL REPORT 2010



edqm
European Directorate for the
Quality of Medicines & HealthCare

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Foreword

Throughout the year 2010, the work in establishing standards for the quality of medicines, both in the form of pharmacopoeial monographs and respective reference standards, to keep the European Pharmacopoeia state-of-the-art was a major focus of the EDQM's activities.

In June 2010, Dr. Marianne Ek of the Swedish Medicines Product Agency succeeded Professor Dr. Hendrik de Jong as Chair of the European Pharmacopoeia Commission. The 7th Edition of the European Pharmacopoeia was published in July 2010 and came into force on January 1, 2011. As a new feature, the "off-line" version is now available as a USB key instead of the previous DVD version to take account of technical developments and make the pharmacopoeia more user-friendly; a decision applauded by users. To mark the publication of the 7th Edition, an international conference on the quality of medicines was organised in Prague to discuss with stakeholders which measures would be necessary to ensure the European Pharmacopoeia remains fit to fulfill its objectives in protecting public health. The new Presidium, consisting of the Chair and the two vice-Chairs, Professor Dr. Jos Hoogmartens (Belgium) and Ms. An Lé (France), has defined the work priorities of the European Pharmacopoeia Commission for the next three years, with a clear commitment to further strengthening international harmonisation and implementing the requirements of the new environmental legislation in the work of the European Pharmacopoeia Commission. The latter will lead to the revision of a number of monographs over the next few years to avoid the use of substances in routine quality control that are classified as of very high concern by the European Chemicals Agency. In its November 2010 session, the European Pharmacopoeia Commission appointed the chairs, experts and specialists of the more than 60 active groups of experts and working parties of the European Pharmacopoeia for a three year mandate. With all these measures, we are convinced the European Pharmacopoeia is well prepared for the challenges of the future and will continue serving as a world-renowned standard to ensure the quality of medicines.

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 in parallel to the meetings of the International Conference on Harmonisation (ICH). In the context of the decision of the ICH Steering Committee not to extend in its previous form the mandate of the ICH Expert Working Group Q4B, charged with the evaluation of regulatory interchangeability of harmonised pharmacopoeial texts, the ICH Steering Committee expressed their gratitude to the PDG for all the work done in the harmonisation of pharmacopoeial texts. As of 2011, the three pharmacopoeias will organise their PDG meetings independently from the ICH, with a first

meeting to discuss future fine-tuning of working procedures to optimise output scheduled to take place in summer 2011. The bilateral, pilot, prospective, API harmonisation initiative with the United States Pharmacopoeia, established in 2008 yielded tangible results, with the first two monographs having been adopted by the European Pharmacopoeia Commission.

Streamlining of the procedure for the Certification of Suitability to the Monographs of the European Pharmacopoeia, initiated in 2008, allowed the EDQM to further reduce handling times of new applications and revisions, which now meet the defined deadlines. As of 2011, monthly statistics on certification of suitability activities and related inspections will be published on the EDQM website.

During the annual meeting of the European network of Official Medicines Control Laboratories (OMCLs), co-ordinated by the EDQM, a technical guideline on monitoring of stockpiled medicines was adopted. In a time when national competent authorities are increasingly debating how best to be prepared for pandemic situations, this document provides guidance on all major elements with respect to the contribution of individual OMCLs and the OMCL Network in supporting decision-making and transparency of results on stockpiled medicines. The OMCL Network also further reflected on how best to contribute to quality monitoring of APIs and combating counterfeit/illegal medicines.

In the field of blood transfusion and organ transplantation, further recommendations to ensure the quality of materials and practices were elaborated, with the revision and updating of the existing "Guide to the preparation, use and quality assurance of blood components" and the "Guide to the safety and quality assurance for the transplantation of organs, tissues and cells" being ready for publication in early 2011.

The EDQM contributed to the world-wide fight against counterfeiting of medical products by continuing multi-sectorial training sessions for government representatives. In 2010, for the first time, government representatives from non-European countries participated in such training. During the Swiss chairmanship of the Council of Europe, the EDQM co-organised an international conference on the practical implementation of the MEDICRIME convention, an international convention on combating counterfeit medical products and similar crimes posing a risk to public health, with Swissmedic, the Swiss Agency for Therapeutical Products, and the Council of Europe's Directorate for Human Rights and Legal Affairs. The MEDICRIME convention was adopted by the Committee of Ministers, the Council of Europe's governing body, in December 2010 and will be open to participation by governments worldwide. In the context of a number of practical activities in combating counterfeited medical products, the EDQM's project for a future traceability system for medicinal products reached its next phase with the development of a pilot system on which input and comments from stakeholders throughout Europe will be solicited in the second half of 2011. The "new" activities acquired in 2009, the Council of Europe's activities in the field of cosmetics and food contact materials, were smoothly integrated into the EDQM's portfolio.

2010 also saw a strengthening of EDQM's international collaboration. In May 2010, the EDQM took over responsibility for the establishment, production and distribution of the World Health Organization's (WHO) International Chemical Reference Standards (ICRS), which are required for the use of the WHO's International Pharmacopoeia. The decision of the WHO to entrust the EDQM with these important activities demonstrates the worldwide reputation of the EDQM in this field. The EDQM also concluded Memorandums of Understanding (MoU) with the National Institute for Food and Drug Safety Evaluation (NIFDS) of Korea and the National Institute for Food and Drug Control (NIFDC) of the People's Republic of China. These MoUs will strengthen the collaboration between the organisations in protecting public health.

The modernisation of EDQM's IT infrastructure and systems saw significant progress with the roll-out of the first part of an Enterprise Resource Planning System (ERP) and the migration to an Electronic Document and Records Management System (EDRMS). The development of a Laboratory Information Management System (LIMS) was finalised and the system will become fully operational in early 2011. These three major IT projects will ensure that the EDQM is technically equipped to meet the challenges that lie ahead.

Finally, EDQM is proud that an ISO 9001 audit performed by Afnor, the French certification body, in November 2010 confirmed the ISO 9001 certification of its Certification of Suitability activities (both assessment and inspections) and extended the certificate to market surveillance studies; with the activities related to the 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, 2010 has been a challenging, but also a very successful year for the EDQM. However, this would not have been possible with the enthusiasm and dedication of the EDQM's staff alone. I would like to take the 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 assessment and inspections in the context of the Certification Scheme.

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 and providing official standards that apply to the manufacture and quality control of medicines in all the signatory states of the Convention for the elaboration of a European Pharmacopoeia and beyond,
- ensuring the application of these official standards to substances used for the production of medicines,
- co-ordinating a network of Official Medicines Control Laboratories (OMCLs) to collaborate and share expertise between member states and effectively use limited resources,
- 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 an administrative directorate of the Council of Europe. In 2010, the EDQM employed 200 full-time staff members and was structured into 9 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 8 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 European Pharmacopoeia is a single reference work for the quality control of medicines in the signatory states of the Convention on its elaboration. The official standards published within it provide a legal and scientific basis for quality control during development, production and marketing processes.

They define the quality and the tests to be carried out on medicines, on the raw materials used in production of medicines or on the intermediates of synthesis.

An official reference to serve public health

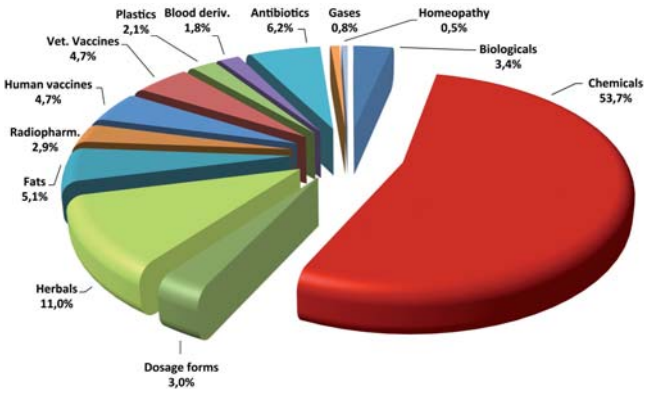
European Pharmacopoeia quality standards are not only part of the requirements for marketing authorisation of a medicinal product, but are legally binding throughout the entire life-cycle of the product. They guarantee a single common quality for medicines throughout Europe.

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

The European Pharmacopoeia contains 2161 monographs, including general standards that apply to groups of ingredients or dosage forms, and 333 general methods of analysis. As shown below, its scope extends far beyond the "classical" chemical medicines:

Scope Ph. Eur. monographs



Officially adopted and implemented by all member states

All standards of the Ph. Eur. are adopted by consensus at the European Pharmacopoeia Commission, consisting of delegates from the 36 member states. Once adopted, standards become mandatory on the same date in all member states of the Convention.

The 23 observers from all continents (e.g. Algeria, Australia, Brazil, Canada, China, Syria, USA) are welcome to participate in the deliberations of the Commission and its Groups of Experts and Working Parties.

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. (comprising more than 60 groups of experts and working parties with more than 800 experts from all over Europe).

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 individual member states.

New Ph. Eur. texts need to be elaborated and existing Ph. Eur. texts need to be regularly reviewed and revised in order to remain state-of-the-art due to the following:

- Developments in the regulatory environment (e.g. new or revised EMA Guidelines, ICH Q8/Q9/Q10/Q11, REACH).
- Scientific/technical developments (e.g. Fast LC, NIR, PAT, new molecules, new therapies such as cell therapy).
- Increased demand for generic and biosimilar products (e.g. new sources of active substances and/or excipients).
- Developments in manufacturing and the effects of globalisation (e.g. continuous manufacturing, changing routes of synthesis).
- New risks to public health (e.g. genotoxic impurities, TSE, contamination/falsification such as occurred with heparins).

A new Presidium of the European Pharmacopoeia Commission elected for the next 3 years

The Commission elected Dr. Marianne Ek as Chair for a term running from June 2010 to June 2013. Dr. Marianne Ek is head of the Swedish Pharmacopoeia Commission and Deputy Head of the laboratory at the Medical Products Agency (MPA) in Uppsala, Sweden. She is the 16th Chair of the European Pharmacopoeia Commission since 1964 and succeeds Professor Hendrik de Jong who chaired the Commission since June 2007. To continue with the normal process of election, the Commission elected as new Vice-Chairs Professor Dr. Jos Hoogmartens (Belgium) and Ms. An Lé (France). The new Presidium will help the Commission to define its priority areas and achieve its objectives for the next three years.

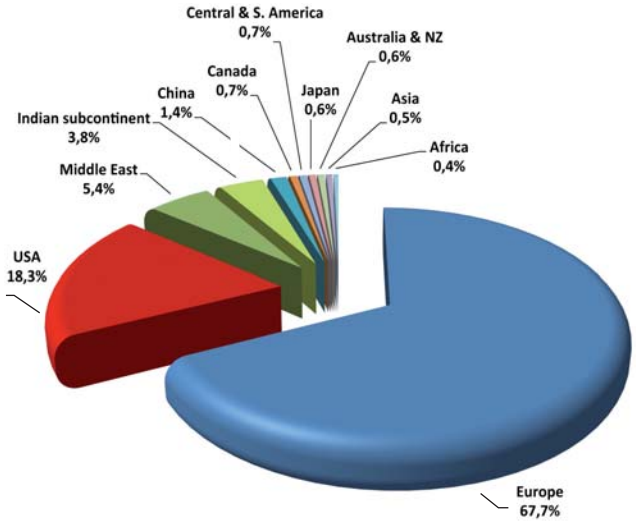
A new 3-year term of office for all chairs and members of Groups of Experts and Working Parties

Following the election of the Chair and Vice Chairs, the Commission, in its November Session, appointed Groups of Experts and Working Parties for a period of three years. Groups of Experts and Working Parties cover the main scientific disciplines of quality control of medicinal products and their constituents. They are comprised of experts that have scientific and technical knowledge in these disciplines. The members of these groups come from regulatory authorities, including official medicines control laboratories, pharmaceutical and chemical manufacturers, universities and research institutions.

Publication of a new edition of the European Pharmacopoeia (7th Edition)

The 7th Edition of the European Pharmacopeia was published in July 2010 and implemented as of 01 January, 2011. The 7th Edition of the Ph. Eur. is available in three formats, in both English and French: print (book version), online and USB stick (with the functionality of the online version).

Subscriptions to 2010 to the Eur. Ph. 7th Edition in 2010 by geographical zone



The Spanish version of the Ph. Eur. now contains the entire 6th Edition and is available to subscribers to the current online version. The translation of the 7th Edition is on-going.

International Harmonisation - the Pharmacopoeial Discussion Group (PDG)

Globalisation and expansion in international trade present a growing need to develop global quality standards for medicines. As standards are a vital instrument for marketing authorisation, market surveillance, and free movement and trade of medicines among as many countries as possible, harmonisation among the world's three major pharmacopoeias, the European Pharmacopoeia (Ph. Eur.), the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP), is an important and challenging task. Within the harmonisation process, the EDQM represents the European Pharmacopoeia. All the relevant groups of experts of the European Pharmacopoeia are involved.

The Pharmacopoeial Discussion Group (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, 27 of the 35 General Chapters and 41 of the 62 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.

General chapter sign-offs included revisions of *Uniformity of Dosage Units and Dissolution*, and corrections to the sign-off of *Capillary Electrophoresis*. The sign-off to the revision on *Uniformity of Dosage Units* represented a resolution of the long-standing concern related to the 2% Relative Standard Deviation exemption in the harmonised *Uniformity of Dosage Unit* text that is not accepted by the United States Food and Drug Administration.

Excipient sign-offs include the newly-harmonised *Crospovidone* monograph and revisions to *Butyl Paraben, Lactose Anhydrous, Cellulose Acetate Phthalate, Citric Acid (Anhydrous)* and *Citric Acid (Monohydrate)*. The three latter revisions are the outcome of the PDG's review of previously harmonised excipient monographs. This exercise is aimed at achieving a higher level of harmonisation of previously signed-off monographs.

Following a meeting of experts from the three regions, the general chapter on *Chromatography* was formally added to the PDG work programme. With representatives from its sister organisations, the Ph. Eur. is also an observer of the ICH Expert Working Group Q3D on Metal Impurities.

Prospective harmonisation of monographs for active substances

As harmonisation of active substances is 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 pilot project started in 2008 with 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* (for the treatment of migraine headaches), *Montelukast sodium* (for the prophylaxis and chronic treatment of asthma), *Celecoxib* (a sulfa non-steroidal anti-inflammatory drug used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation and menstrual symptoms), and *Sildenafil* (used in the treatment of erectile dysfunction and pulmonary arterial hypertension (PAH)).

Where do we stand?

The monographs for *Rizatriptan benzoate* and for *Montelukast sodium* have been adopted by the Ph. Eur. Commission in 2010. The monograph on *Rizatriptan benzoate* was also approved by the corresponding Expert Committee of the USP, with *Montelukast sodium* following in early 2011.

The monograph for *Celecoxib* has been published in Pharmeuropa 22.4 and the one for *Sildenafil citrate* will be published in Pharmeuropa 23.2. Both monographs are also published in the Pharmacopeial Forum.

Key figures for 2010

During its three sessions, the Commission adopted:

- **38 new monographs for ingredients, including:**
  - 8 monographs on active substances elaborated in close collaboration with the respective manufacturers under the P4 procedure dedicated to substances still under patent: *clopidogrel hydrogen sulphate* (antiplatelet agent), *oseltamivir phosphate* (antiviral drug), *atorvastatin calcium* (cholesterol lowering agent), *Rizatriptan benzoate, Montelukast sodium, Voriconazole* (antifungal agent), *Candesartan cilexetil* (angiotensin II inhibitor) and *Fulvestrant* (estrogen receptor antagonist). The monograph on the excipient *Sucralose* was also elaborated under the P4 Procedure.
  - 8 monographs on Traditional Chinese Medicines (TCM): *Acanthopanax bark, Angelica dahurica root, Angelica pubescens root, Isatis root, Kudzuvine root, Thomson kudzuvine root, Baical skullcap root* and *Sophora flower-bud*.

- **143 monographs were revised;** amongst them the ones on *heparin sodium* and *heparin calcium* with a rapid implementation date on 01 August, 2010. The latter have been further revised to ensure appropriate quality control of unfractionated heparin. The style and presentation of all these texts have also been updated in order to bring them in line with the latest version of the Style Guide.

  The *Botulinum toxin type A for injection* monograph was revised in order to add a paragraph stressing the importance of using alternative methods that are preferable in terms of animal welfare. This will further encourage users of the Ph. Eur. to develop and validate suitable alternative methods to *in vivo* assay.

- **17 General Chapters, including 6 new General Chapters;** amongst them:
  - *Determination of methyl, ethyl and isopropyl methanesulfonates in methanesulfonic acid* (2.5.37). The elaboration of this chapter had been requested following an incident related to the appearance of a potentially genotoxic impurity in Nelfinavir mesilate tablets, an anti-retroviral drug used in the treatment of HIV.
  - *Determination of Methyl, Ethyl and Isopropyl methanesulfonate in active substances* (2.5.38)
  - *Preparations For Nebulisation Characterisation* (2.9.44) in response to the requirements of the Ph. Eur. monograph on *Preparations for inhalation* and those of the EMA Note for Guidance: Pharmaceutical Quality of Inhalation and Nasal Products. A methodology was set up for the control of the active substance delivery rate and total active substance delivered, as well as for the aerodynamic assessment of nebulised aerosols.

  The text is based on international efforts to draft a new chapter for both the Ph. Eur. and the USP. The methods have been tested in a number of industrial laboratories and a collaborative study, planned by EPAG (European Pharmaceutical Aerosol Group) members, took place in 2006. The Swedish OMCL participated in this study.

- **Six general texts (new or revised) were adopted, including four technical guides:**
  - Technical guide for the Elaboration of Monographs (5th Edition);
  - Technical guide for radiopharmaceutical preparations;
  - Technical guide for plasma-derived products;
  - Technical guide for the elaboration and use of monographs on immunological veterinary medicinal products (IVMPs).

The latter is aimed at giving more transparency to the interrelationship between different texts of the Ph. Eur. (general monographs, individual monographs, General Chapters, General Notices) and provides further clarification on the mandatory/non-mandatory status of monograph sections in the field of IVMPs. The guide was established by the Ph. Eur. Group of Experts responsible for IVMP monographs, in close collaboration with the Immunologicals Working Party (IWP) of the EMA.

A special revision programme adopted to comply with the EU REACH Regulation

The Commission also approved 184 requests for revision, including one which may affect the compliance of 215 monographs with the EU REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances) Regulation.

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

As part of its continuous efforts to reduce animal testing, the Commission has given a green light to the revision of all monographs on vaccines for veterinary use (i.e. approximately 80 monographs), as a consequence of work at the level of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH). The deletion of the overdose test for inactivated vaccines, following the implementation of VICH GL 44 (Target Animal Safety), had a consequence for the target animal batch safety test (TABST) that is prescribed in inactivated vaccine monographs. Indeed, the overdose test, carried out during development, was previously needed for the definition of suitable criteria in the TABST; a test performed for the release of each batch of vaccine. If the revision of the relevant monographs succeeds, which will consist of the deletion of the TABST in all relevant monographs, this will constitute a major breakthrough in the field of animal welfare, as it will significantly contribute to reducing the number of animal tests.

Achievements in Biological Standardisation

The Biological Standardisation Programme (BSP), a joint effort 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. 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, 112 BSP projects have been initiated. In 2010, a number of projects were pursued in different fields:

- vaccines for human use: 7 projects
- vaccines for veterinary use: 1 project
- plasma-derived products: 5 projects
- biotechnology products: 6 projects.

Amongst these, 3 projects were devoted to the establishment of alternatives to animal experiments, 3 to the development of new assays and 14 projects concerned the establishment of Biological Reference Preparations (BRPs). Two projects were run together with the WHO.

In the field of vaccines for human use, a project had been concluded that aimed at a better standardisation of the serological methods used for clinical evaluation of influenza vaccines during the annual licensing procedure according to the EMA's Committee for Human Medicinal Products (CHMP) guidelines. This project had been requested by the CHMP Biologics Working Party (BWP). The results have been presented to the relevant EMA committees in 2010 and consequences are under discussion at the level of the EMA.

The strong efforts to apply the 3Rs concept to the field of quality control of biologicals were continued in 2010. One project, aimed at replacing the direct challenge potency assay for rabies vaccines (inactivated) for veterinary use by a serological assay, was concluded. Based on this study, the Ph. Eur. Group of Experts 15V started revising the monograph to incorporate the new method. The serological method still uses animals, but approximately 8-10 less compared to the challenge assay. In addition, it is easier to use, more precise and faster than the former method.

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

Once a year, the European Pharmacopoeia Department organises a meeting with NPA representatives of the Contracting Parties. In 2010, the meeting took place in Uppsala on 10-11 May. It is a unique platform for open exchange of information and discussion between the Secretariats of national pharmacopoeia authorities and the Ph. Eur.

Topics discussed included:

- Possible ways to further optimise handling of comments to the draft pharmacopoeia texts that are published in Pharmeuropa and processed by member states and the EDQM;
- Discussion on "hot topics" of the Technical Guide for the Elaboration of Monographs (new version);
- Systematic changes in the 7th Edition of the European Pharmacopoeia published in June 2010;
- Availability of the 7th Edition on USB sticks (instead of DVDs).
- Sharing of best practices in performance measurements, in nominating Chairs and Experts of Groups elaborating the Ph. Eur. texts, and how National Formularies for Paediatric Formulations are elaborated and managed.

1.2 Pharmaceutical Reference Standards

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

Why have reference standards?

The use of reference standards (samples of pure and carefully calibrated substances intended for quality control) is required in most of the tests and assays prescribed by the Ph. Eur. The production and distribution of these standards, therefore, constitute an essential activity of the EDQM for the users of the Ph. Eur.

Chemical Reference Standards (CRS)

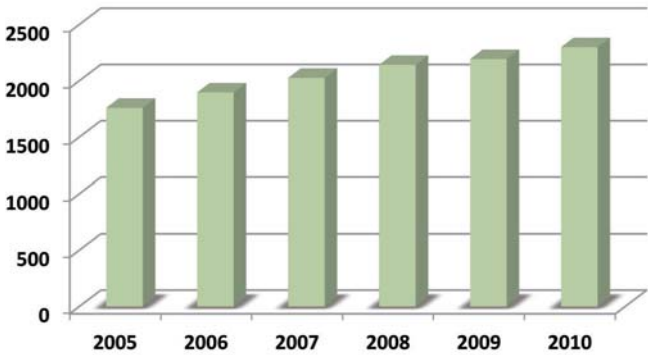
The new integrated establishment process enabled timely establishment of the CRS required by the Ph. Eur. The monographs for *heparin* underwent fast-track revision and required accelerated establishment of four new CRS, which were made available to users in a timely manner.

Portfolio

223 CRS and 3 Herbal Reference Standards (HRS) have been established in 2010, including 36 assay standards, 3 herbal standards and 48 mixtures. 112 new reference standards have been released as well as 96 replacement batches. 461 batches have been produced.

The collection now consists of 2 300 items.

Growth of the CRS portfolio

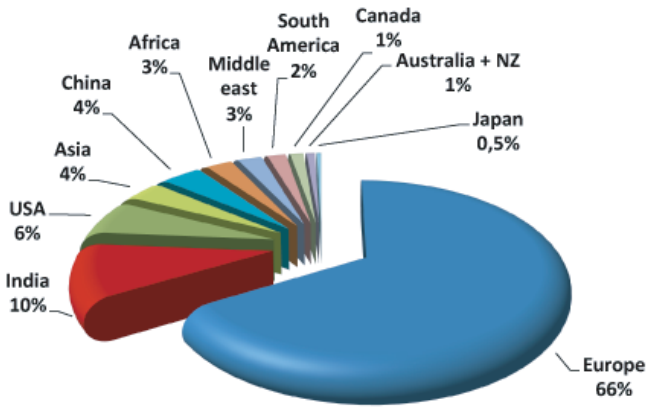


The CRS portfolio is continuously monitored for suitability; 473 batches [20.6%] have been examined in 2010. Careful planning of activities facilitated achievement of the objective to have at least 98% of the portfolio available to users at all times.

Availability of the CRS portforlio in 2010

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

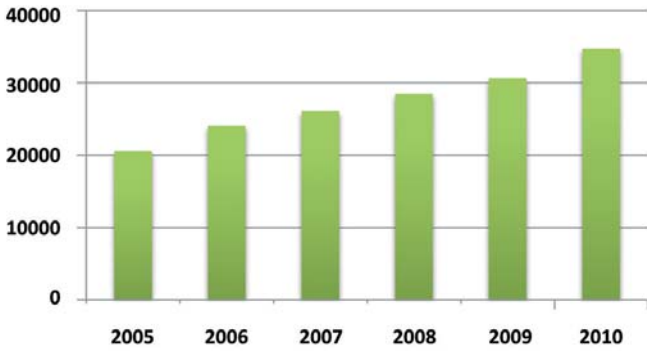
% of Ph. Eur. vials ordered/distributed by world area



India and China are progressing as non-European users of EDQM Reference Standards.

The overall demand for reference standards increased in 2010.

Growth in the number of orders processed/parcels distributed for Ph. Eur. reference standards



Biological Reference Preparations (BRPs)

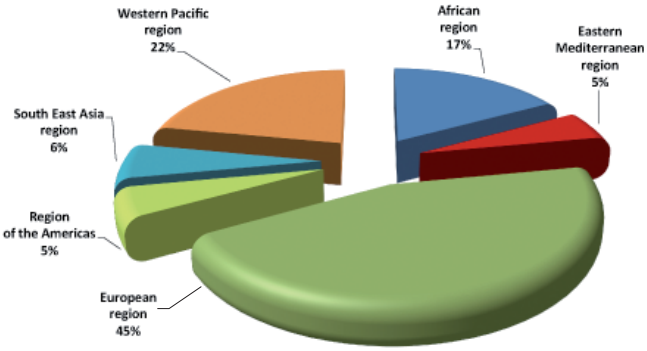
In 2010, the international collaborative studies performed by the Biological Standardisation Programme led to the adoption of two BRPs by the European Pharmacopoeia Commission: *Human coagulation factor VIII BRP* (batch 4) and *heparin, low-molecular-mass BRP* (batches 6, 7 and 8). The *tetanus vaccine BRP* (batch 3), adopted by the European Pharmacopoeia Commission, is envisaged in early 2011.

■ EDQM activities for the WHO

International Chemical Reference Standards (ICRS)

In 2010, the EDQM took over responsibility for the establishment, monitoring and distribution of the WHO ICRS. This represents a portfolio of more than 200 reference standards. ICRS are used worldwide, as prescribed by the International Pharmacopoeia. 14 ICRS have been monitored for suitability in 2010. The distribution of ICRS began in May.

% of ICRS vials ordered/distributed by world area



International Standards for Antibiotics (ISA)

Since May 2006, the EDQM took over from the National Institute for Biological Standards and Control (NIBSC) responsibility for the establishment, storage and distribution of ISA. Batches that were held and distributed by NIBSC have, since then, been distributed by the EDQM.

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

In 2010, the 2nd International Standard (IS) for Vancomycin was established and work on the replacing the 2nd IS for Dihydrostreptomycin began.

1.3 Laboratory Activities

Continuous efforts to further improve internal organisation and efficiency

The Laboratory Department now consists of two organisational entities: the Analytical Chemistry Division and the Biology Section.

A major focus in 2010 has been the establishment of a new organisational structure within the Analytical Chemistry Division and the re-organisation of tasks within the Biological Section.

Positive contributions to the work of the European Pharmacopoeia

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

During the year, 223 Chemical Reference Standards (CRS) have been established, as well as 3 Herbal Reference Standards (HRS). The demand for new impurity reference standards continued to increase.

A total of 48 CRS mixtures (21.5% of the total number of CRS) were established in 2010. Most of these CRS have required modification/compounding of candidate materials.

Collaboration at international level

The Laboratory Department has actively participated in the following joint Ph. Eur. – USP activities:

- Prospective harmonisation of four P4 chemical monographs, two of which have been adopted by the European Pharmacopoeia Commission in November 2010. The establishment of the corresponding common reference standards is underway.
- Establishment of a common glucagon CRS, which involved retrospective harmonisation of the Ph. Eur. and USP monographs. This collaborative study has been completed.
- Establishment of a common insulin aspart CRS, which involved retrospective harmonisation of the USP monograph. The EDQM Laboratory Department leads this project and the collaborative study will be run in 2011.

New responsibilities taken on board: the establishment and monitoring of the WHO International Chemical Reference Substances

In terms of new tasks/responsibilities, during the year the laboratory took over full responsibility for the establishment and monitoring of WHO ICRS.

Contributions to the permanent process of optimisation put in place

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

- improvement of the process of procurement for impurity candidate CRS;
- optimisation of the CRS monitoring programme;
- systematic evaluation of best filling conditions for assay standards.

Finally, several measures were taken to make the Laboratory Department contribution sustainable in the medium to long term:

- the laboratory facilities, especially the clean room area, have been improved;
- the Information Technology (IT) landscape has been modernised by the development of a new IT Laboratory platform, consisting of a **L**aboratory **I**nformation **M**anagement **S**ystem (LIMS) and a **S**cientific **D**ata **M**anagement **S**ystem (SDMS);
- new equipment has been introduced, prioritising automation, to maximise efficiency;
- the network of collaborative laboratories has been consolidated;
- the staff continued to undergo an intensive programme of scientific training.

1.4 Certification of Suitability to the Monographs of the European Pharmacopoeia

Purpose of the Certification procedure

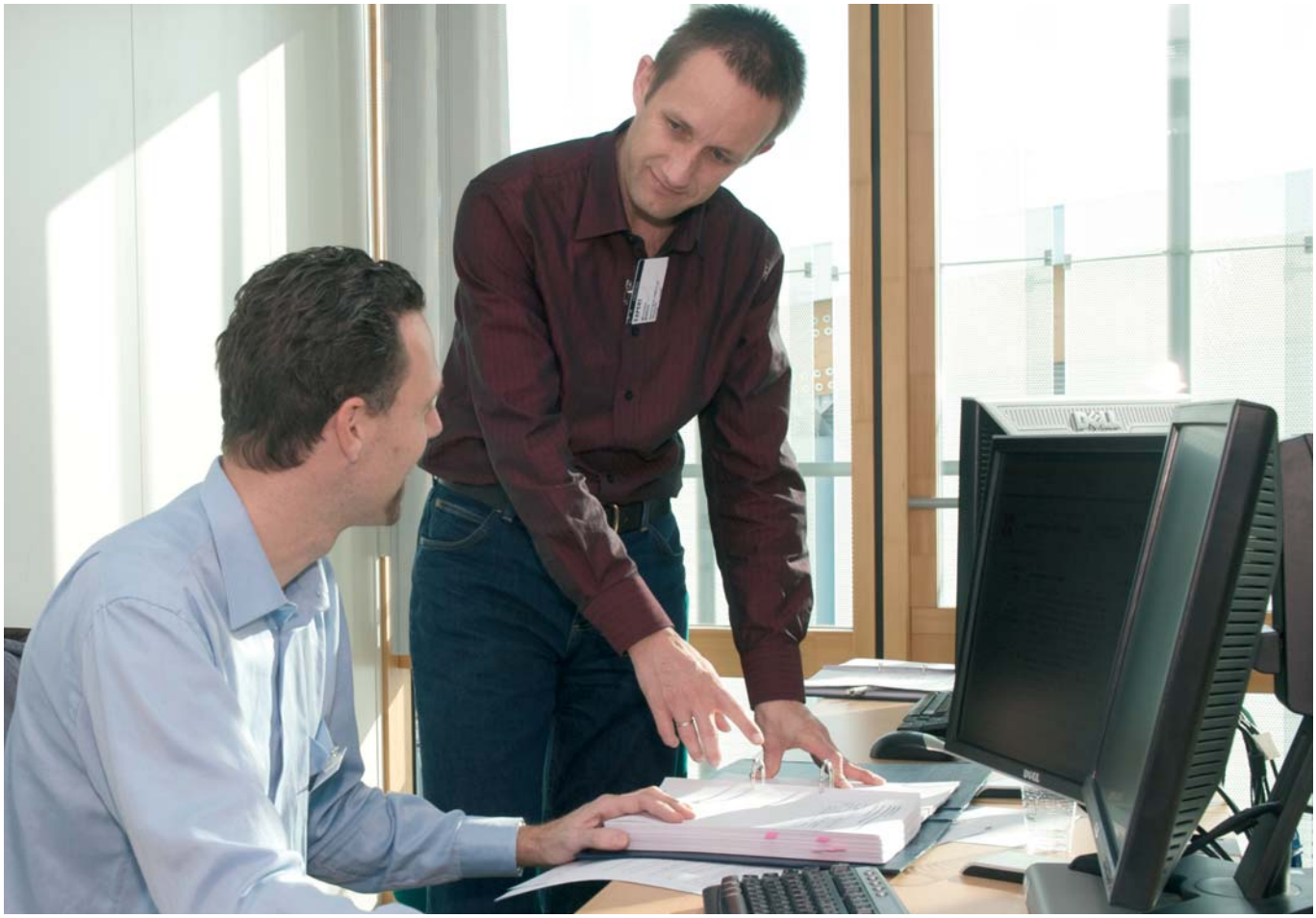
The Certification of Suitability to the Monographs of the European Pharmacopoeia (CEP) procedure was established in 1994 following a two-year pilot phase and is aimed at:

- ensuring that the quality of substances used in the production of medicines complies with Ph. Eur. standards and, hence, the requirements of the European Union's pharmaceutical legislation;
- 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 highest importance for the Ph. Eur., as it ensures that Ph. Eur. standards are up-to-date with respect to the products currently on the world market;
- facilitating at the European level the management of Marketing Authorisation Applications by a centralised assessment, which reduces the workload in all the member states. In addition, CEPs are also recognised in a number of non-European licensing authorities, e.g: Australia, Canada and Singapore.

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 EDQM inspection programme has been set up to check compliance with both the CEP application 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) on the manufacturing/distribution sites covered by CEPs. The EDQM Certification Division is responsible for organising the inspections and their follow-up, including taking any subsequent action regarding related CEPs or CEP applications and communicating with the authorities concerned. The annual



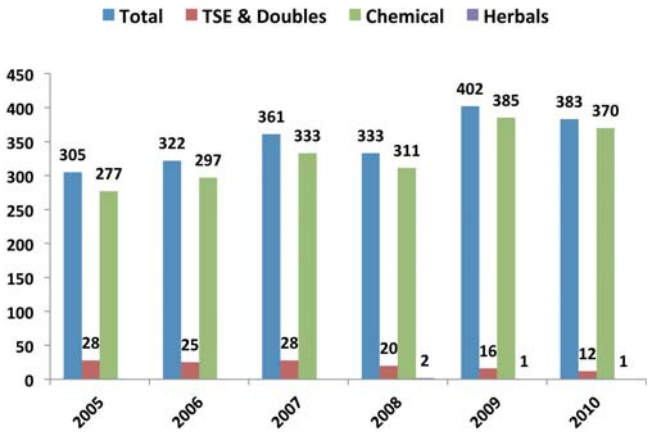
inspection programme is based on priorities recommended by the EMA/EU and it is adopted by the Certification Steering Committee, following consultation with the authorities in member states and the GMP/GDP Inspectors Working Group of the EMA.

Key figures for 2010

The Certification Division has been receiving an increasing number of applications for CEPs in recent years. In 2010, 383 new applications and more than 1000 requests for revision were received. It should be noted that even though the procedure was extended to herbal drugs and herbal drug preparations several years ago, the first applications for these were received in 2009 and only one such application was received in 2010.

In addition, 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.

Number of new applications received



In 2010, 328 new and 955 revised CEPs were granted. In addition, 256 requests for revision were approved without issuing a revised CEP.

Key activities of 2010

In 2010, the Certification Division continued the work initiated some years ago to streamline the management of applications for CEPs (new applications and revisions). This led to a significant reduction of processing times and, since mid-2010, new dossiers and revision/renewal applications have been dealt with within the official deadlines.

To be in line with the revised EU regulation on Variations to Marketing Authorisation Applications, a new system for revisions/renewals of CEPs was implemented at the EDQM in March 2010. The classification of revisions and working procedures were modified accordingly.

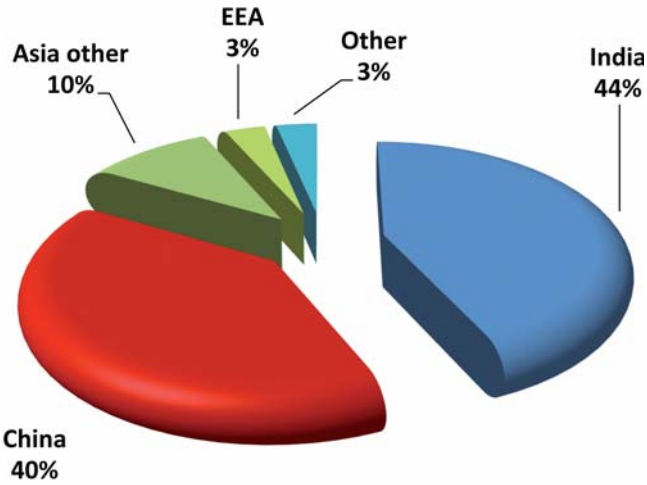
The EDQM is also encouraging electronic submission of CEP applications. Revised guidelines were published in 2010 with the aim of helping applicants to compile electronic dossiers in a flexible way. More than 60% of applications have been submitted to the EDQM in electronic format for new submissions, as well as for requests for revision, and more e-CTDs are being received.

The EDQM inspection programme

The programme for inspection of manufacturing sites covered by CEPs is an important tool to supplement the evaluation of the quality of substances for pharmaceutical use. In 2010, 34 on-site inspections were performed, mainly in Asia, with the participation of inspectors from different national agencies, whilst another 25 sites were covered by sharing information with inspectorates of member states and partners. A number 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 dossier submitted to obtain the CEP. In this context, in 2010, 16 CEPs were suspended and 8 withdrawn by the EDQM. However, 10 CEPs were restored in 2010 after a positive re-inspection was carried out following a suspension.

The EDQM has performed 229 inspections since the inspection programme started in 1999. Of these, 145 were carried out outside the EEA. Since 2003, the vast majority of the inspected sites have been outside the EEA.

Geographic location of inspected sites 2010



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, 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 (e.g. independence, public funding, implementation of the Ph. Eur. as a common standard, implementation of the ISO/IEC 17025 standard). Since 1995, the EDQM is the co-ordinator of this network and responsible for its organisation and further development.

"Networking" here 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.

There are two levels of collaboration within the network: certain activities open to all of the member states or observers of the European Pharmacopoeia take place within the framework of the general network (GEON), while other activities are specific to countries of the European Union (EU) and the European Economic Area (EEA).

The members of the network meet every year to review the results of these activities and discuss plans for future development. The 15th annual meeting took place in Split, Croatia, in May 2010.

Quality Management Systems

The following activities, co-ordinated by the EDQM, were carried out in 2010 within the framework of the Quality Management (QM) Programme of the OMCL Network.

■ Mutual Joint Audits and Mutual Joint Visits

During 2010, nine Mutual Joint Audits (MJAs) were carried out at OMCL sites. Three additional audits were performed in collaboration with the WHO in three Medicine Control Laboratories located in South America, as part of the WHO Pre-Qualification Programme.

■ Training activities for the OMCL Network

In 2010, two Training Visits were organised by the EDQM at two OMCL sites in order to provide technical training on biological laboratory methods. One training course on the use of CombiStats™ was organised.

■ OMCL Network Quality Management Guidelines

The 6th Annex of the OMCL Guideline "Qualification of Equipment", dedicated to the qualification of piston pipettes

was adopted at the OMCL Network annual meeting in May 2010. The 7th Annex, dedicated to the qualification of Mass Spectrometers (GC-EI-MS and LC-MS) is under preparation and will be presented for adoption at the OMCL Network annual meeting in May 2011.

Several Quality Management guidelines are currently under review and various proposals have been received at the EDQM to elaborate new guidelines in the near future.

Key QA documents and guidelines are available on the EDQM website (**http://www.edqm.eu/en/Quality-Management-QM-Guidelines-86.html**).

Reflection Group on Quality Monitoring of Stockpiled Medicines

In October 2008, a Reflection Group on Quality Monitoring of Stockpiled Medicines was established with the secretarial support of the EDQM. This group is composed of representatives of the OMCL Network, as well as one representative from DG-SANCO.

The aim of the Reflection Group, in the first instance, was to elaborate strategies on how to make other stakeholders aware of the competency of OMCLs in contributing to the quality monitoring of nationally stockpiled medicines.

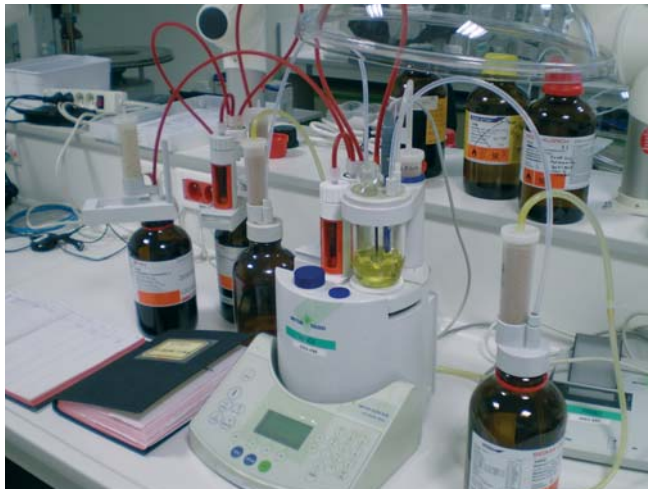
Following the development of a general position paper in 2009, in 2009/2010 the group produced a technical guideline "Monitoring of Stockpiled Medicines – Development of Technical Guidelines", PA/PH/OMCL (09) 94. This guideline, which was adopted at the Annual Meeting of the GEON in May 2010 in Split, Croatia, provides guidance on all major elements with respect to the contribution of individual OMCLs and the OMCL Network in monitoring stockpiled medicines, including aspects such as obtaining and evaluating relevant information, storage of products, sampling, testing and reporting activities, support in decision-making and transparency of results.

This document and the general position paper will be published on the EDQM website in early 2011.

OMCL Annual Meeting – General Session Policy documents

The 15th Annual meeting of the OMCLs took place in Split (Croatia) from 17 to 21 May 2010, with 198 participants from 34 countries. The following topics were addressed:

- An internal procedure for handling new membership applications to the network was adopted.
- The problem of testing of small scale preparations was discussed on the basis of a presentation and a position paper. This led, later in the year, to the launch of a questionnaire and, finally, to the decision to establish a working group.
- The work of the Reflection Group on Quality Monitoring of Stockpiled Medicines was presented and the first technical guideline adopted.
- A document highlighting the principles for mutual recognition of control results and the cost effectiveness of the network has been established by the EU Heads of Medicines Agencies (HMA) Working Group on Product Testing with the participation of the OMCLs. This document was presented and was made available simultaneously on the HMA and EDQM websites in August 2010.
- The contribution of the OMCL Network to quality monitoring of APIs and combating of counterfeit/illegal medicines were two key topics of the General Session. With respect to counterfeit testing, a position paper "The Role of the OMCL Network in the Implementation of the CoE Counterfeit Convention" was adopted. Concerning Active Pharmaceutical Ingredients (API) testing, discussions will also continue in 2011 and strategies will be developed in the near future.
- In terms of QMS topics, improvements of the Mutual Joint Audit/Visit (MJA/MJV) scheme, as a follow-up of feedback received from a meeting of auditors of the MJA/MJV scheme of the OMCL Network, were presented and discussed. In addition, the 6th Annex of the OMCL Guideline "Qualification of Equipment: Qualification of Pipettes", PA/PH/OMCL (09) 64, was adopted, which is now available on the EDQM website.



Proficiency testing scheme (PTS) studies

Over the years, the proficiency testing scheme (PTS) studies have become a regular programme within the OMCL Network. In 2010, five studies were organised in the physico-chemical field, with an average participation of 43 national control laboratories and 29 other pharmaceutical control laboratories from the private sector, industry and hospitals; while in the biological area, four studies were organised, involving an average of 23 laboratories (12 OMCLs and 11 laboratories from the private sector). For the first time, a PTS study on radiopharmaceuticals was also organised.

In 2010, two studies belonging to the 5th PTS agreement with the WHO were organised; a study on assay by titration and a study on determination of water content by the Karl Fischer method. On average, 60 governmental control laboratories belonging to 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 2010, market surveillance studies (MSSs), aimed at screening the quality of medicinal products on the European market, were finalised for levothyroxine tablets and the testing phase was initiated for simvastatin tablets and opioid modified release oral medicinal products. For the studies on acetylsalicylic acid oral preparations and alkyl mesilates in APIs (and medicines presented as mesilate salts) the testing phase will finally take place in 2011. Such a testing campaign provides an overall picture of the quality of products available on the European market for a given class of products. Where pertinent, the results of these studies will also support the revision of the relevant monographs and/or general chapters and methods of the Ph. Eur., as well as specific actions by the licensing and supervisory authorities.

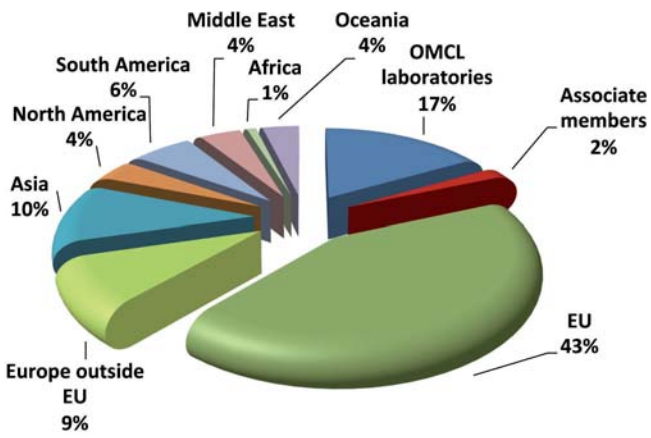
CombiStats™

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 OMCL 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 October 2010 that was open to industry and private sector participants. By December 2010, 16.7% of the licences were issued to OMCL laboratories in 24 countries and 83.3% to non-OMCL users in 35 countries.

The pie-chart shows that approximately 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, Iran, Israel, Japan, Mexico, South Africa, South Korea, Uruguay and the USA. CombiStats™ has thus evolved into a common, internationally-accepted reference in its domain and contributes to mutual recognition of data and results by all interested parties.

CombiStats™ licences per region (in %)



EU/EEA – Specific Activities

Market Surveillance for Centrally Authorised Products (CAP)

The programme for sampling and testing of Centrally Authorised Products (CAP) was successfully continued in 2010 and entered its twelfth consecutive year. The CAP programme is run on the basis of a contract between the European Medicines Agency (EMA), which is the sponsor and has overall responsibility, and the EDQM, which co-ordinates the sampling and testing operations using the information provided by the Marketing Authorisation Holders upon request from the EMA. It covers medicinal products for both human and veterinary use.

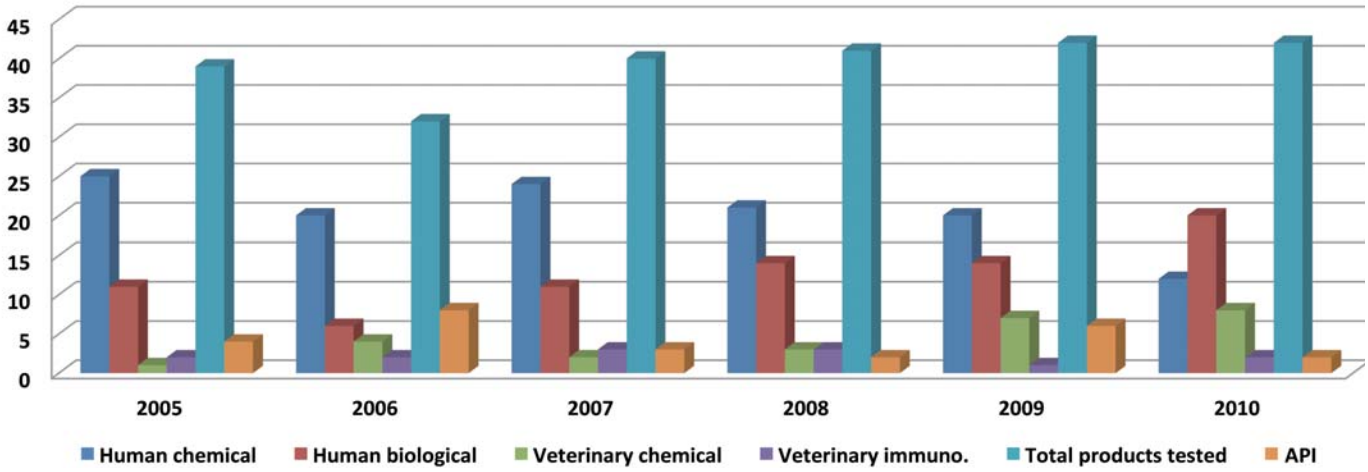
The 2010 work programme included 32 medicinal products for human use (20 biologicals and 12 chemical products) and 10 medicinal products for veterinary use (2 immunobiological products and 8 chemical products). In addition to the finished dosage form, testing of active substances (API) was recommended for two products. The total number of products (42) corresponds to the optimal range, considering the operational capacities of the OMCL Network.

Following the decision at the CAP Annual Meeting in November 2009 in Rome to pursue the plan to check package leaflets and labelling of CAPs, as originally requested by the EMA, a trial phase was set up for the 2010 programme and a revised sampling form including the adopted label checklist was developed for the samplers. At the annual meeting in 2010, it was decided to continue with this exercise in 2011.

The "General Procedure for Sampling and Testing of Centrally Authorised Products" PA/PH/CAP (05) 49, was revised due to the implementation of new forms and streamlining of working processes. The updated version was released in December and is available on the EDQM website.

In November 2010, the CAP Advisory Group members attended a joint meeting with quality assessors and inspectors (QWP

Number of products tested in the CAP Programme 2005-2010



and GMP/GDP IWG) at the EMA in London, which gave representatives from OMCLs the opportunity to address and discuss different topics of common interest for all three groups.

In December 2010, the co-ordination activities of the EDQM with respect to the CAP sampling and testing programme had successfully undergone ISO9001 certification.

In 2011, the CAP programme will include, for the first time, CAP generics (the selected product group will be Clopidogrel film-coated tablets) and preparatory work for a pilot phase began during 2010. The experiences gained during the trial phase will be used to establish a regular CAP generics sampling and testing programme in parallel to the "classical" CAP programme.

Additional information on the CAP programme can be found on the EDQM, as well as on the EMA, website.

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 been further developed since then. By avoiding duplicate testing of the same product in different member states, the scheme provides a co-ordinated and economical approach to post-marketing surveillance.

In 2010, the sixth 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 2010 programme, which is almost identical to the number in 2009. The number of participants has stabilised over recent years to around 20 OMCLs per programme, while the number of cancelled projects due to non-availability of the product on the market, has significantly decreased in 2010, which might be an indication that the information on marketing of MRP/DCP products in Europe is more accurate than in former years.

The general procedure "Co-operation in post-marketing surveillance of Mutual Recognition/Decentralised Procedure Products", PA/PH/OMCL (06) 116, has been further updated and is currently again under revision to add the aspects of data ownership and confidentiality.

The internal database used for planning, sampling and reporting of MRP/DCP product testing activities within the network has been further developed. A total of 20 database amendments were implemented in 2010, initiated both by the OMCL users of the system and the EDQM Secretariat.

In December 2010, the co-ordination activities of the EDQM with respect to the MRP/DCP product market surveillance scheme successfully underwent ISO9001 certification.

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

Harmonised application of Article 114 of EU Directive 2001/83/EC, as amended, is the main goal of the OCABR network, with a focus on ensuring the mandated mutual recognition of lot release. Regular exchange of information and meetings supported by common guidelines elaborated by the network facilitates this. Opportunities for work-sharing and the desire to reduce, replace and refine the use of animals in testing are important driving forces for the co-operation between network members.

Major highlights

The annual meeting in Split, Croatia, was attended by almost 80 participants from 22 member states and provided an opportunity to review activities from the past year and determine strategies for the coming period. Parallel sessions were held for blood and vaccine issues, respectively, and a joint session was held to address common points of interest. The plenary session was an occasion for the election of four (two blood and two vaccine) of the six posts in the OCABR advisory group that were up for renewal. Revisions of the general OCABR administrative procedure and the administrative procedure for OCABR of centrally authorised products to reflect current practice were adopted, as were a number of internal guidelines and procedures related to network functioning. Revisions to two product-specific guidelines for vaccines and one for blood- and plasma-derived medicinal products were also adopted. A number of other product-specific guidelines are in the pipeline for 2011. As usual, the focus was placed on strategies to minimise the use of animals. A review of the first year of operation of the OCABR batch database was very positive and included proposals for improvement and expansion to be pursued. In response to input from the vaccine manufacturers' association, a working group was created to investigate the feasibility of electronic submission of batch release protocols. The first meeting of the group, made up of interested parties from OMCLs and manufacturers from both the blood and vaccine fields, was held in November. The annual workshop for OMCLs, involving testing of bulk batches of oral poliomyelitis vaccine, was successfully held at NIBSC in October.

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)

Annual reports of activities in the VBRN were presented at the Split annual meeting, which was attended by 25 participants from 20 member states. Progress in the harmonised application of Article 81 and Article 82 of EU Directive 2001/82/EU, as amended, for veterinary medicines was noted. Review of the products on the shortlist for application of Article 82 resulted in no changes for 2010. The annual meeting marked the inaugural election of the four-member VBRN advisory group, who held their first meeting in November. Maintenance of competence in specialised techniques and improved communication with other branches of the regulatory network, such as licensing and inspection, were identified as priorities for the work programme of the group. Drafting of a number of guidelines to help codify key procedures was also instigated.

Training within the network through paired exchange between OMCLs in different member states, as part of the OMCL network tutorial programme, was used effectively in 2010 to expand the competencies of the network for better work-sharing.

All adopted administrative procedures and product-specific guidelines, as well as protocol templates, can be downloaded from the EDQM website.

1.6 Blood Transfusion and Organ Transplantation

Blood transfusion activities

The Steering Committee on Blood Transfusion (CD-P-TS) held one meeting under the aegis of the EDQM in November 2010.

The 16th Edition of the "Guide to the preparation, use and quality assurance of blood components" was adopted. The guide represents a key milestone in defining the "standards" for blood transfusion services and forms the basis for many national regulators in Europe and beyond. The 16th Edition of the Guide will be made available in English, French and Russian in 2011, with more languages planned for 2012.

A survey on "Pathogen reduction procedures in 2009" was performed and a symposium on "Pathogen Reduction Technologies for Blood Components" was organised (see chapter 2.4).

Reporting of data on the collection, testing and use of blood components from European countries and from other regions of the world have been completed for the years 2005 to 2008. A trend analysis on data collected in the years 2001-2005 was prepared.

The "Ad hoc" working group on Blood Supply Management (working on the 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 the respective countries) has collected information and generated a self-assessment questionnaire to be distributed in 2011 to blood banks and establishments.

The "Ad hoc" working group responsible for setting up a central database on stocks of frozen blood of rare blood groups, available for international exchange, has been evaluating a pilot database planned for launch in the forthcoming months.

Inter-institutional co-operation has been established with the EU to run a European programme of external quality assessment: voluntary participation in Proficiency Testing Scheme (PTS) studies and audits or visits will be offered to testing laboratories of blood establishments in the forthcoming years. The first PTS study on testing individual blood donations for the presence of hepatitis C virus by nucleic amplification techniques (NAT) has been completed. The second study on testing for hepatitis B surface antigen by serology has started.

Support for the South-East Europe (SEE) Health Network project "Increasing regional self-sufficiency in relation to safer blood and blood components", led by Romania, has resulted in the setting up of a training programme to begin in 2011.

A project on "Risk behaviors having an impact on blood donor management" was started in February 2010 with the participation, notably, of the European Commission (EC), the EMA, the European Centre for Disease Prevention and Control (ECDC), US-FDA, Health Canada, the Australian Therapeutic Goods Administration (TGA) and the WHO. The mandate of the group will be to analyse existing data from epidemiological studies, surveillance programmes and risk modeling and examine the implications of moving away from permanent donor deferral criteria, currently applied to donors showing such risk behaviors.

Organ, Tissue and Cell Transplantation

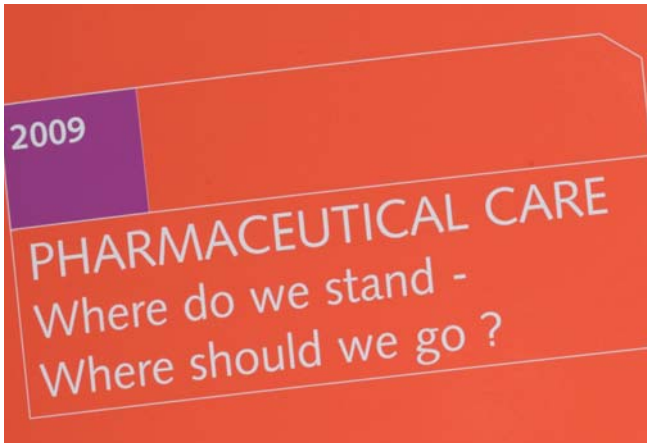
The plenary meeting of the Steering Committee on Organ Transplantation (CD-P-TO) took place in Tbilisi, preceding European Organ Donation Day. The update of the Guide to safety and quality assurance for the transplantation of organs, tissues and cells (that had not been revised since 2007) was approved and was the main topic of the meeting. This 4th Edition will be published in English, French and Russian in 2011.

The chapters on the transplantation of tissues and cells were not revised for the 4th Edition; the revision process will start this year, with France and Italy taking the lead in the responsible "Ad hoc" working group. An initial meeting was held on 22 November 2010 in Rome to define the specifications of the project and the composition of the group. Due to the specificities of the subject, a separate "Ad hoc" working group is necessary for this task. The aim is to finalise the revision by the end of 2011 and either publish it as the 5th Edition of the guide or as a separate booklet.

Several projects reached completion and the results were approved by the CD-P-TO. The outcome of these projects will be published during 2011. The CD-P-TO also focused on studies led by France and Italy in order to estimate the number of patients having been transplanted outside of their own country. These figures provide valuable information. A recommendation by the CD-P-TO to member states to routinely ask for such data is under discussion.

1.7 Pharmaceutical Care

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



Safe and appropriate use of medicines

Public authorities and the manufacturing and distribution sector 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. In line with the acceptance that pharmaceutical care means the responsible provision of medicine therapy for the purpose of achieving definite outcomes that improve or maintain a patient's quality of life (in line with Hepler and Strand[1]), in 2010, the Committee of Experts on quality and safety standards in pharmaceutical practices and pharmaceutical care (CD-P-PH/PC) developed approaches for measuring the quality of pharmaceutical care in Europe through scientific indicators.

Development and testing approaches for 15 indicators were presented to an audience of 40 public health officials and leading scientists from 20 member states at an expert workshop on 10 December 2010. The outcome of the expert workshop was concrete guidance on the further development and testing of indicators, strengthening and expansion of a network of co-operating authorities and scientific institutions, and a plan for mid-term activities.

The scientific indicators use a novel approach based on the application of pharmaceutical care by professionals such as doctors, pharmacists and nurses. They are outcome- and patient-oriented and produce information of practical utility to authorities for policy-making and to professional associations for standard-setting.

As industrial medicines do not always satisfy the health needs of patients, the preparation of medicines in pharmacies is important. However, to date, there is wide variability among national quality assurance and preparation requirements. In order to prevent gaps in quality assurance between industrially-prepared and pharmacy-made medicines, in 2010 the above committee of experts drafted a Council of Europe Resolution on quality and safety assurance requirements for medicinal products prepared in pharmacies for the specific needs of patients. The Committee of Ministers was invited to adopt the resolution and to recommend to member states the implementation of the requirements into national legislation.

Responding to the growing demand in Europe for foreign traditional medicines, including Traditional Chinese Medicine (TCM), the committee of experts studied the risks associated with the use of TCM in a western environment. It organised an expert workshop on 28 October 2010 and an audience of 32 co-operating authorities and experts from 15 member states developed a strategy on how to ensure safe TCM practices based on training and education, safety surveillance and balanced information to patients and practitioners, to be underpinned by legislation as appropriate.

Considering the safety and accessibility of medicines, in 2010 the Committee of Experts on the classification of medicines as regards their supply revised the recommendations addressed to authorities and industry on the classification of medicines into prescription and non-prescription medicines and their relevant supply conditions.

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

Having been significantly involved in the development of the Council of Europe Convention on counterfeiting of medical products and similar crimes (MEDICRIME Convention) involving threats to public health from its outset, in 2010 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) contributed to the finalisation of the convention adopted by the Committee of Ministers on 8 December 2010. (Link: http://conventions.coe.int/Treaty/EN/projets/v3Projets.asp).

An international conference on the practical implementation of the above convention was co-organised in Basel on 15-16 April 2010 with support from the EDQM and its committees,

1. Hepler, D.D. & Strand, L.M, Opportunities and Responsibilities in Pharmaceutical Care, Am.J.Pharm.Educ.,53, 7S-15S(1989)

the Directorate of Human Rights and Legal Affairs, the Directorate of Communication and the Swiss Agency for Therapeutical Products (Swissmedic). In attendance were 145 participants, senior officials from health, law enforcement and judicial authorities from 33 member states and 7 non-member states from Africa, Asia and America and international organisations. The participants expressed political support for the convention and indicated directions for putting it in place.

On 21-22 January 2010, the Committee of Experts co-organised training with the Portuguese Medicines Agency, on how to combat counterfeit medicines and to protect public health. For the first time, training was delivered to participants from Europe and certain countries in Africa and in South America.

Also in 2010, the Committee of Experts started a feasibility study on an inventory of experiences for public health protection obtained from selected cases on counterfeit medical products.

The EDQM made significant progress with other activities to prevent sub-standard and illegal medicines from being placed on the market:

"Track and Traceability system" and the "Fingerprints" databank

Within the anti-counterfeiting framework, the EDQM has elaborated a concept for a system for traceability of medicines. This EDQM initiative consists of developing a state-of-the-art mass serialisation system open to any business stakeholders from the 36 member states of the European Pharmacopeia. Amongst the key assets of this project are:

- its comprehensive coverage of the supply chain from manufacturers to patients, encompassing the distributors, wholesalers, re-packagers and pharmacies;
- coverage of legitimate internet pharmacies operating in countries where this practice is authorised;
- its public governance via the EDQM as a public inter-governmental organisation with a strong reputation in handling procedures involving confidential data.

In 2010, Phase 1 of the project was completed by establishing a Users and Business Requirements document. Phase 2 has started to develop a representation of the future system to be used in workshops with stakeholders in 2011.

Another project has been developed for a databank of "fingerprints" or signatures of active ingredients used for the manufacture of medicines. Resources from a dedicated Task Force of the OMCL Network have been mobilised for this purpose. A number of companies have volunteered and provided samples and methods, allowing the first studies to be completed.

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 materials designed for packaging or other purposes involving contact with foodstuffs or medicines. The work programme has been elaborated by the Consumer Health Protection Committee (CD-P-SC). The CD-P-SC is composed of representatives from national ministries acting in the field of public health.

With the recent appointments made by Finland, Armenia and Sweden for the CD-P-SC and its subordinate bodies, 33 member States of the European Pharmacopoeia Convention in total participate in the work.

Two subordinate Committees of Experts prepare the work for approval 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

Official cosmetics control laboratories in 14 European countries (Austria, Belgium, Cyprus, Czech Republic, France, Germany, Ireland, the Netherlands, Portugal, Romania, Slovenia, Sweden, Switzerland and Turkey) set up a competence network to share work linked to cosmetics surveillance.

This includes inter-laboratory studies, proficiency testing scheme (PTS) studies, market surveillance studies (MSS) and the implementation of harmonised quality management systems. The long-standing experience with the OMCL network has been an asset in the pilot phase.

Cosmetics intended to be used on children under the age of three have been addressed in a draft guidance document for safety assessors. It is intended to finalise and publish this document in 2011.

To implement the recommendations of Resolution AP (2008) 1 on tattoos and permanent make-up, the compilation of safety and documentation requirements for tattoos and permanent make-up are under preparation. This document is expected to be finalised and published in 2011.

Activities were also discussed under the Packaging Materials for Food and Pharmaceutical Products for so-called natural or organic cosmetics and the use of corresponding labels (in some countries labelled "BIO") and related consumer expectations. The Committee decided to schedule specific activities in this area.

Furthermore, it was decided to explore cross-resistance issues linked to the use of antimycotic substances as cosmetic ingredients. A survey has been launched to collect information on such products on the European market.

Packaging for food and medicines

The work programme in the field of Packaging Materials for Food and Pharmaceutical Products includes the elaboration of a draft resolution on metals and alloys used as food contact materials and a supplementary technical guide (due to be finalised in 2011). The text will recommend the implementation of Specific Release Limits (SRL) for metal ions that are released from materials in contact with foodstuffs.

Harmonised analytical test procedures for certain food contact materials are under preparation by a dedicated working group. Regulatory approaches for polymers that are used both in the pharmaceutical and the food sector are the subject of the work of a dedicated working group. Furthermore, the relevant Committee has decided to update existing resolutions and technical documents which had been elaborated under the former Council of Europe Partial Agreement in 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 2011.

2. SUPPORT ACTIVITIES

2.1 Quality and Environmental Management Systems

The EDQM maintains and extends the scope of its ISO 9001 certification

After a comprehensive three-day audit, Afnor Certification (AFAQ) decided to maintain the EDQM ISO 9001 certificate and granted an extension of its scope in the field of the quality control of finished products and human guidelines related to the OCABR procedure.

The EDQM is now certified as meeting the requirements of ISO9001:2008 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 studies) 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 extend the scope of its certification in the coming years in order to guarantee an optimal service to its stakeholders, whilst improving the efficiency of working methods.

Review of safety data sheets

The EDQM has classified the hazards of 2245 Reference Standards in accordance with Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of substances and mixtures (CLP). With the objective of addressing prompt and effective hazard communication of Reference Standards intended for specialised small-volume use in laboratories, the EDQM collaborated with CARACAL, the European Commission's Competent Authorities for Evaluation, Authorisation and Restriction of Chemicals (REACH) and CLP, and the United Nations Economic Commission for Europe (UNECE) Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals.

afaq AFNOR CERTIFICATION

Certificat
Certificate

N° 2009/35920a

AFNOR Certification certifie que le système de management mis en place par :
AFNOR Certification certifies that the management system implemented by:

CONSEIL DE L'EUROPE
DIRECTION EUROPEENNE DE LA QUALITE
DU MEDICAMENT ET SOINS DE SANTE

pour les activités suivantes :
for the following activities:

Evaluation des dossiers de demande (initiale, révision et renouvellement) de certificats de conformité aux monographies de la Pharmacopée européenne, délivrance des certificats, et gestion du programme d'inspection des sites de fabrication et des distributeurs associés.
- Programmation, mise en œuvre et coordination des études de surveillance du marché des médicaments autorisés par les procédures centralisée (CAP) et nationale (études MSS) ;
- Gestion de la base de données associée aux études de surveillance du marché des médicaments autorisés selon les procédures de reconnaissance mutuelle (MRP) et décentralisée (DCP) et gestion des interactions avec ses utilisateurs ;
- Coordination de l'élaboration et de la diffusion des lignes directrices relatives à la procédure OCABR pour la libération de lots de médicaments immunologiques (sang et vaccins) à usage humain ;

en vertu de la réglementation pharmaceutique, notamment les directives 2001/82/CE et 2001/83/CE telles qu'amendées, et le Règlement 726/2004 (CE) pour les pays de l'UE.

(Traduction en anglais en annexe n° 1)
(English translation on appendix n° 1)

a été évalué et jugé conforme aux exigences requises par :
has been assessed and found to meet the requirements of:

ISO 9001 : 2008

et est déployé sur les sites suivants :
and is developed on the following locations:

7, allée Kastner Cs 30026 FR-67081 STRASBOURG CEDEX

Ce certificat est valable à compter du (année/mois/jour) *This certificate is valid from (year/month/day)* **2011-02-08** Jusqu'au* *Until** **2012-12-16**

Directrice Générale d'AFNOR Certification
Managing Director of AFNOR Certification

F. MEAUX

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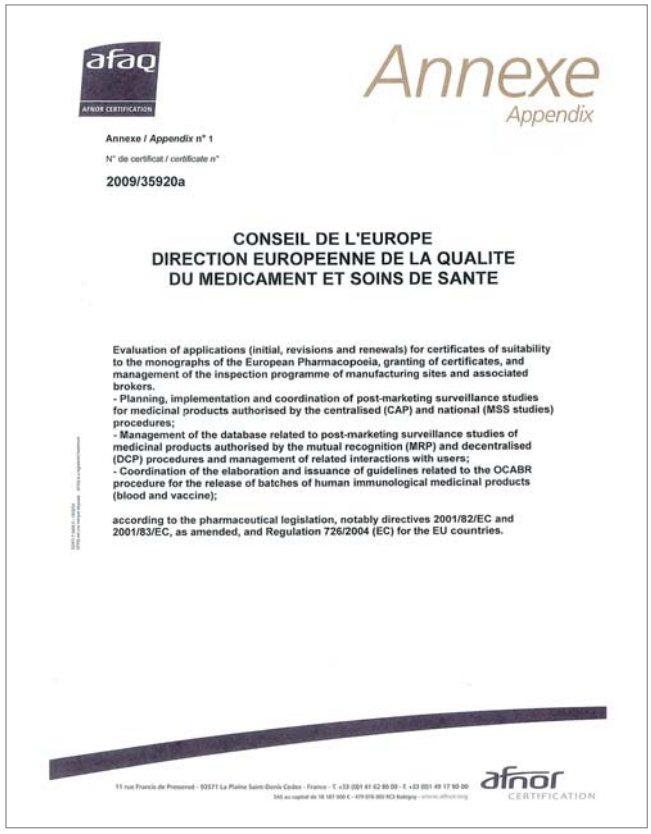

afaq AFNOR CERTIFICATION

Annexe
Appendix

Annexe / *Appendix* n° 1
N° de certificat / *certificate n°*
2009/35920a

CONSEIL DE L'EUROPE
DIRECTION EUROPEENNE DE LA QUALITE
DU MEDICAMENT ET SOINS DE SANTE

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.
- Planning, implementation and coordination of post-marketing surveillance studies for medicinal products authorised by the centralised (CAP) and national (MSS studies) procedures;
- Management of the database related to post-marketing surveillance studies of medicinal products authorised by the mutual recognition (MRP) and decentralised (DCP) procedures and management of related interactions with users;
- Coordination 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.

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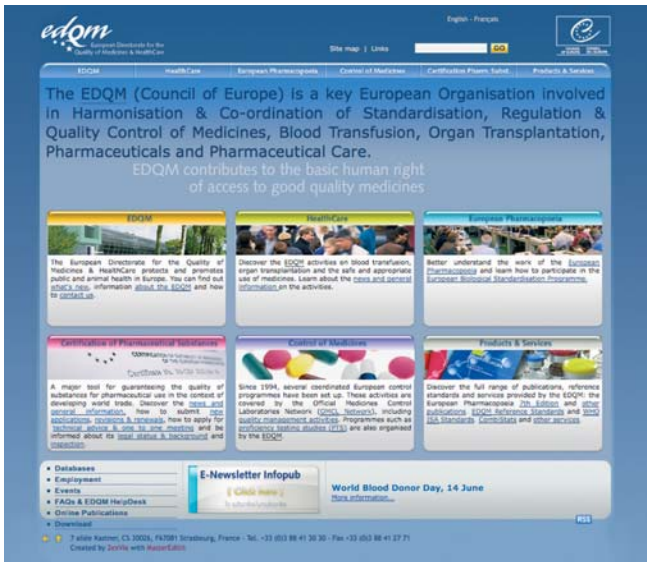
2.2 Information Technology and Publications activities

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. In 2010, the EDQM continued its efforts to improve the quality and user-friendliness of its website layout and presentation.

The number of visitors and visits to the website continued to increase, reaching a monthly average of 25,000 visitors (+14%) and 71,000 visits (+14%, statistics obtained using AWSTATS software) covering more than 100 countries worldwide.

The content on the website was extensively revised to harmonise the presentation of the different activities and it was decided to focus translation efforts on the two official languages of the Council of Europe (English and French). As a consequence, the Chinese language version is no longer available.



An indispensable online user support service (HELPDESK)

The HELPDESK service is the first point of contact for information and support at the EDQM. It provides help with any technical or scientific questions concerning its various activities, products or services. The HELPDESK received 10,155 questions in 2010, which reflects a stabilisation in its volume. The HELPDESK Frequently Asked Questions (FAQs) are updated regularly and new ones are added so that they cover all the EDQM's activities and respond to changing user needs.

Ambitious IT projects

- **Electronic Document & Records Management System (EDRMS): an important milestone achieved**
  Initiated in 2006, the EDQM project aim is to set up an Electronic Document Management and archiving System (EDRMS). In July 2010, the project reached an important milestone: all EDQM staff switched from using a classical file server, organised in silos, to a specific software and repository for managing, filing, sharing and securing all data produced or received by the EDQM.

- **Enterprise Resource Planning (ERP)**
  The implementation of standard ERP software has been continued in 2010 with the roll-off of the first part and will be pursued further in 2011 and 2012 to better integrate the different business processes used in the EDQM, such as supply chain management, warehouse management and customer relationship management. This integration will help to provide a better and more standardised service to the EDQM's customers.

Dynamic publication activities

The Publications unit is mainly responsible for the technical and administrative aspects of the publication of the European Pharmacopoeia, Pharmeuropa and other EDQM publications and technical guides.

The 7th Edition (7.0) and two supplements (7.1 and 7.2) were published in 2010, comprising 3774 pages for the English version and 4038 pages for the French version. The 7th edition (including supplement 7.2) therefore consists of 2161 monographs (including those on dosage forms) and 333 general texts (including general monographs and general methods of analysis).

The four issues of Pharmeuropa published in 2010 contained 174 texts for enquiry and for general information, comprising 632 pages for the English version and 660 pages for the French version. Two issues of Pharmeuropa Bio & Scientific Notes, containing 14 scientific articles in English, were published.

The Publications unit also provides support for the publication of other documents by the EDQM. In 2010, the document "Biological Substances Submitted to the Official Control Authority Batch Release" was prepared in English. In 2010, the electronic catalogue of reference standards was updated in the online database at http://crs.edqm.eu.

In addition, the Publications Unit continued its work on the conversion of monographs to a more concise editorial style and maintained lists of data needed for the publication work. The conversion of the radiopharmaceutical monographs was completed. With regard to herbal drug monographs, the legends found under plant powder illustrations were integrated into the body of Identification B.

An archive version containing all previous editions of the European Pharmacopoeia is now available as a service to subscribers to the current print, on-line and off-line versions.

2.3 Communication: landmark events

Rapid and reactive communication to keep the EDQM's partners better informed

In all, 15 press releases were issued in 2010 highlighting important policy changes, major developments and new collaborations. All were circulated via electronic mail to various media, authorities and partner associations all over the world.

The EDQM's E-Newsletter is a free monthly newsletter summarising the latest information, events and news, with links to retrieve relevant information from its website. The number of subscribers to this service has continued to grow over the past year (8970 subscribers in 2010) and, coupled with the website's RSS feeds, users can easily keep up-to-date with the latest developments and news.

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

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

At European level, one technical workshop was organised on the *"Guide for the elaboration and use of monographs on immunological veterinary medicinal products (IVMPs)"* (Strasbourg, France, March 2010). The guide was drafted to facilitate the interpretation and use of European Pharmacopoeia monographs and general chapters in the field of veterinary vaccines. The objectives of the workshop were to provide clarification on the inter-relationship between the different sections of the pharmacopoeia and give the participants an opportunity to meet, exchange ideas and share information.

An international conference on the "Quality of medicines in a globalised world: Dreams and reality" (Prague, Czech Republic, October 2010) was organised to discuss the challenges and opportunities stemming from globalisation in the trade of medicines and to mark the launch of the 7th Edition of the European Pharmacopoeia. The conference was opened by Dr. Leoš Heger, Minister for Health in the Czech Republic, who expressed his country's support to the invaluable work of the EDQM in protecting public health. Interactive workshops were organised to stimulate discussion and debate around five specific themes: the characterisation of biological molecules; the impact of new technologies on the European Pharmacopoeia; the control of impurities; the application of 3Rs principles; and the need for changes in the European Pharmacopoeia.

Regulators from around the world, including the European Commission, the EU Heads of Medicines Agencies, the European Medicines Agency, the US Food and Drug Administration and Japan's National Institute for Health Sciences, provided insights during the plenary session on the challenges and the opportunities for collaboration in a globalised market for medicines. The WHO, pharmacopoeias (US, Japan, China, India and Brazil) and key industry associations were invited to present their views. Over 250 delegates and experts from 32 countries attended the conference.

Training organised at European level to strengthen links with European Pharmacopoeia users

The EDQM organised training sessions in Strasbourg, France (July 2010) and Istanbul, Turkey (December 2010). These training sessions aim not only at giving delegates a basic understanding of the European Pharmacopoeia, but also to present some of the more significant and relevant issues under broad discussion. In addition, case study groups, workshops and individual "one-to-one" meetings were arranged with the speakers.

Finally, at the request of users, a training session on "Combi-Stats™", a computer program used for the statistical analysis of data from biological dilution assays or potency assays, was organised (Strasbourg, France, November 2010).

Partnership at international level

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

An IPA-EDQM-IPC technical conference, entitled "Towards new challenges in global regulatory perspective", was organised in Mumbai (India, January 2010). This conference was very successful and confirms that there is a high level of interest and a strong demand for information and expertise at a worldwide level.

The EDQM was happy to participate in a symposium in Pretoria, South Africa (April 2010) organised with the support of the South African Association of Pharmacists in Industry (SAAPI). The programme was especially designed to meet the expectations and educational needs of the audience, with a particular focus on pharmaceutical reference substances.

Further afield, the EDQM collaborated with the China Chamber of Commerce for Import & Export of Medicines & Health Products (CCCMHPIE), a national trade association, and the Chinese Ministry of Commerce (Anji, China, May 2010). The training session was organised for pharmaceutical health product manufacturers and the programme focused on the EDQM's Certification procedure and inspections programme.

In May and September 2010, the EDQM and the 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 European Pharmacopoeia and the EDQM's Certification of Suitability procedure with European regulatory authorities and the WHO.

The EDQM worked closely with the New Jersey Pharmaceutical Quality Control Association (NJPQCA) to organise a training session on the 7th Edition of the European Pharmacopoeia in the United States (Iselin, USA, September 2010). Again, the highly participative programme enabled delegates to learn more about the changes taking place in Europe, at the EDQM and the European Pharmacopoeia, and the hot topics currently under debate.

In addition, the EDQM participated in the WHO Inter-regional Seminar for Quality Control Laboratories (South Africa, November 2010). This seminar brought together laboratory representatives from different regions and aimed at presenting new WHO pre-qualification guidelines and improvements in the sharing of information and technical expertise. In this context, the EDQM was invited to present its major achievement in the field of official medicines control laboratory networking (OMCL Network) that could be used as a model for WHO pre-qualified laboratories.

The EDQM co-organised with the Paul-Ehrlich-Institut an international conference on "Potency testing of veterinary vaccines for animals: the way from *in vivo* to *in vitro*" (December 2010, Germany) in line with the EDQM's efforts to reduce the use of animals in routine quality control, where possible. In attendance were 130 participants from industry, regulatory authorities and academia.

Participation in international fairs to promote the 7th Edition of the European Pharmacopoeia

The EDQM actively participates in international trade shows every year, such as the Congress of Pharmaceutical Ingredients (CPhI) China trade exhibition (Shanghai, China, June 2010). The EDQM stand received many visitors during the 3-day fair and people were able to obtain answers to their questions on European regulations on the use of raw materials for pharmaceutical products and the EDQM's publications and services. Information brochures and catalogues were available in Chinese to facilitate understanding.

Another important opportunity for the EDQM to meet Indian manufacturers in person was at CPhI India (Mumbai, India, December 2010). This trade fair attracted over 10,000 visitors and the EDQM stand received an unprecedentedly large number of visitors during the three days. The local distributors of EDQM publications were invited to the stand and the EDQM's presence at this trade fair was publicised via an extensive mailing campaign. In addition, free technical consultations were made available to companies holding Certificates of Suitability of monographs of the European Pharmacopoeia and to those intending to apply for a certificate.

Active support in terms of communicating blood transfusion activities

A technical symposium on the "Implementation of pathogen reduction technologies for blood components" (Strasbourg, France, September 2010) involved representatives from blood establishments and services and regulatory authorities, as well as recognised specialists and manufacturers of pathogen reduction systems. Participants from Australia, Canada, Japan, New Zealand, the USA and the WHO joined European professionals from 39 countries for this event.

In addition to the events mentioned above, the EDQM also supported the World Blood Donor Day, celebrated on the

14th June every year, to raise global awareness about the need for safe blood and regular voluntary blood donation.

The World Blood Donor Day provides a unique occasion to pay tribute to the millions of people whose selfless acts allow lives to be saved. The theme for the 2010 Day was "New blood for the world".

The Council of Europe supported several European initiatives, including those of the *Etablissement Français du Sang* (EFS) and its Alsace section, and the German Red Cross *(Deutsches Rotes Kreuz,* DRK) responsible for blood transfusion activities in Germany. An event-specific media kit was created and it comprised posters, pamphlets, stickers and various gadgets. This kit is on offer to all member states to accompany their own local campaigns.

The EDQM participated in the XXXIst International Congress of the International Society of Blood Transfusion (ISBT) (Berlin, Germany, July 2010). The congress was jointly organised with the German Society for Transfusion Medicine and Immunohematology (DGTI). Visitors to the EDQM stand came from all regions of the world (Africa, Asia, Australia, Europe and North and South America) and it was a great opportunity to meet and present the Guide to nurses, scientists, physicians and personnel working in the field of transfusion medicine.

As well as for organ transplantation activities

Council of Europe celebrations for the 12th European Day for Organ Donation and Transplantation took place in Tbilisi, Georgia (October 2010). The Day was hosted by the Georgian Health Ministry and the Georgian Association of Transplantologists (GAT). The aim of this celebration is to help a different member state each year to raise awareness of the importance of organ donation and transplantation. The slogan for the Day was "Transplanted Organ - Saved Life".

Along with various street activities, stands and entertainment, a "Walk for Life" took place to raise awareness for organ donation and a symbolic declaration was signed to mark the occasion. A conference and press conference was also organised.

Campaign materials and an information kit were made available to all European countries to support and add to their local efforts.

Satellite events were held by several partners from the Balkan area under the leadership of *Slovenia Transplant*, aimed at designing a model for the organisation of the European Donation Day in smaller member states.

Visits

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

2.4 International collaboration

Memorandums of Understanding

In 2010, the EDQM has further strengthened collaboration with international partners. Bilateral Memorandums of Understanding (MoU) were signed with the Korean National Institute for Food and Drugs Safety (NIFDS) in November and with the Chinese National Institute for Food and Drug Control (NIFDC, formerly known as NICPBP) in December 2010. These MoUs demonstrate the wish of these partners to reinforce their collaboration with the EDQM in their activities in protecting public health.

International collaboration in GMP Inspections

The EDQM continued its active role in the EU/USA/Australia pilot project for collaboration on GMP inspections of APIs, 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 in the same company, and therefore saved resources and money for all parties. A review of the results of this pilot project in 2010 clearly identified the need to continue this exercise.

In addition, an EDQM inspector visited the Australian Therapeutic Goods Administration (TGA) in order to share knowledge concerning the evaluation of the need and frequency of re-inspections for manufacturers of APIs, with the view of optimising the resources dedicated to on-site inspections.

IRMM-EDQM Workshop

A joint workshop of the EU Joint Research Council's (JRC) Institute for Reference Material and Measurements (IRMM) and the EDQM took place in December 2010. The aim was to exchange information and enhance mutual understanding. Each organisation presented its key activities, processes, challenges and needs in the area of reference standards and reference materials.

As an outcome, the following actions were agreed:

- to join forces in order to better address regulatory issues (Reach, GHS);
- to increase mutual understanding by exchanging participants in the training sessions;
- to open a line of communication/exchange in areas of common interest (laboratory networking, ISO standards, future conferences etc).

A visit of EDQM officers to the new IRMM facilities in Geel, Belgium is envisaged in 2011.

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 2010, 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 48 "Ad hoc" working parties have been set up by the Commission to carry out the Ph. Eur. work programme. Already, 2140 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 Ph. Eur., 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 refer to it constantly.

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 the continuity of operations in the interval between 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. MONOGRAPHS Steering Committee

The activities associated with the procedure for suitability to Ph. Eur. monographs are guided by a Steering Committee and 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 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, for example:

- European Database of Frozen Blood of Rare Groups,
- Blood Donor Management,
- *Ad-hoc* Working Group "Guide to the Preparation, Use and Quality Assurance of Blood Components",
- Risk behaviours having an impact on blood donor management.

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

The Steering committee supervises the activities of a number of individual projects on topics such as "Non-heart-beating donors", "Double listing on transplantation waiting lists" and "Co-operation of states from the Black Sea Area in organ transplantation" which need to be developed. The *"Guide to Safety and Quality Assurance for the Transplantation of Organs, Tissues and Cells"* has been revised in 2010. The Committee now supervises the work of an "Ad hoc" group dedicated to the revision of the tissue and cells part of the transplantation guide.

The Committee is also involved in an "Ad hoc" group, together with experts of the European Committee on Crime Problems

(CDPC) and the Steering Committee on Bioethics (CDBI), in order to "identify the main elements that could form part of a binding legal instrument and report back to the Rapporteur Group on Legal Co-operation (GR-J) by next April. This follows the recommendations made in the *Joint Council of Europe - United Nations Study on trafficking in human beings for the purpose of the removal of organs* and, in particular, on the elaboration of an international legal instrument setting out a definition of trafficking in organs, tissues and cells and the measures to prevent such trafficking and protect the victims, as well as the criminal law measures to punish the crime.

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

The 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)

The Committee is responsible for managing the work programme and decision-making. It has two subordinate bodies that examine health-related issues and evaluate the risks, draft reports and recommendations for regulatory approaches:

- Committee of Experts on Packaging Materials for Food and Pharmaceutical Products (P-SC-EMB),
- Committee of Experts on Cosmetic Products (P-SC-COS).

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