



European Directorate for the Quality of Medicines (EDQM) Annual Report of Activities - 2005

The activities of the European Directorate for the Quality of Medicines are described in terms of its 3 main areas of responsibility:

1. the European Pharmacopoeia, including publication and communications activities, and international relations,
2. the procedure for Certification of Suitability of monographs of the Pharmacopoeia,
3. the European network of Official Medicines Control Laboratories (OMCLs).

In 2005, pharmacopoeia authorities and licensing authorities all over the world showed growing interest in the work of the European Pharmacopoeia, the Certification of Suitability, and the network of Official Medicines Control Laboratories.

1. THE EUROPEAN PHARMACOPOEIA

PARTIES TO THE CONVENTION AND OBSERVERS

The European Pharmacopoeia convention has been signed by 35 parties including the EU and the following countries: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, The Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Ireland, Iceland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, the Netherlands, Portugal, Serbia and Montenegro (formerly Yugoslavia), Romania, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom.

There are 3 new observer states at the European Pharmacopoeia Commission: Brazil, Israel and Madagascar, bringing the total number to 18, namely: the World Health Organisation (WHO) plus 4 European countries (Albania, Georgia, Poland, Ukraine) and 13 non-European countries (Algeria, Australia, Brazil, Canada, China, Israel, Malaysia, Madagascar, Morocco, Senegal, Syria, Tunisia, United States (FDA)).

GENERAL ACTIVITIES

The European Pharmacopoeia Commission continued its work on the preparation of the supplements of the 5th Edition, which entered into force on 1 January 2005. 3 supplements (5.3, 5.4 and 5.5) were published in 2005 with implementation on 1 January 2006, 1 April 2006 and 1 July 2006.

At its 3 sessions in March, June and November 2005, the European Pharmacopoeia Commission adopted 168 monographs (new and revised). The new procedure (procedure IV) set up for new products based on collaboration with the manufacturers and national control laboratories continued to yield encouraging results: 14 monographs reached at least the public enquiry stage and half were adopted. The number of documents produced (new, revised) was stable: 3025 in 2005 (3190 in 2004). The European Pharmacopoeia's biological standardisation work has been extended to new areas: gene-transfer medicinal products, cell therapy products and required control methods. A new chapter on modern microbiological methods was adopted. A revision of the assay of inactivated poliomyelitis vaccine will considerably reduce the number of animals used.

A total of 203 days were devoted to meetings in 2005. This includes the 3 plenary sessions of the Commission and the corresponding preparatory meetings, the meetings of the Groups of Experts and those of the *ad hoc* Working Parties (76). This total also includes the participation of members of the Secretariat in various other meetings: meetings of the Pharmaceutical Committee (Brussels) on medicines for human and veterinary use, meetings of the various working parties of the Committee for Medicinal Products for Human Use (CHMP) and of the Committee for Veterinary Medicinal Products (CVMP) of the EMEA (nearly 20 meetings such as those of the Quality Working Party, Biotech Working Party, Veterinary Immunological Products Working Party, Inspectors Working Party and Herbal Medicinal Products Working Party). In addition, the EMEA/EDQM meeting of the chairs of these groups (chair of the CHMP, chair of the European Pharmacopoeia Commission) with the participation of the heads of the scientific services of the EMEA/EDQM gave an overview of the subjects of mutual interest and projects that could be set up in the future. Members of the Secretariat also attended meetings of the Pharmacopoeial Discussion Group (PDG) for International Harmonisation with Japan and the United States, preparatory meetings of the Quality Working Party for ICH (Q4B), meetings of VICH working parties and meetings to organise and take part in international scientific conferences and congresses.

INTERNATIONAL HARMONISATION WITH THE PHARMACOPOEIAS OF THE UNITED STATES AND JAPAN

The Pharmacopoeial Discussion Group [European Pharmacopoeia (Ph. Eur.), Japanese Pharmacopoeia (JP) and United States Pharmacopoeia (USP)] met in Brussels (Belgium) on 9-12 May 2005, and in Chicago (United States) on 7-10 November 2005, coinciding with the International Conference on Harmonisation (ICH) meetings, which was useful for exchanging information on the progress of work. These meetings were set up to finalise the harmonisation of a number of general chapters and monographs. The WHO attended as an observer.

Summary of agreements on harmonisation by the PDG

- 3 new monographs signed off: Calcium disodium edetate, Dibasic calcium phosphate dihydrate, and anhydrous dibasic calcium phosphate.
- Revision of 6 monographs: Powdered cellulose, Microcrystalline cellulose, Sodium starch glycolate, Benzyl alcohol, Anhydrous lactose, and Methylcellulose.
- 3 general chapters signed off: Microbial enumeration methods, Tests for specified micro-organisms, and Acceptance criteria for pharmaceutical preparations.

Implementation of harmonised texts

To accelerate the inter-regional implementation of harmonised texts, the JP has introduced a new procedure for the rapid implementation of harmonised general chapters related to the Q6A guideline, since full harmonisation is achieved only when all 3 pharmacopoeias have published and implemented a monograph/general chapter.

Regulatory acceptance of pharmacopoeial interchangeability

To facilitate this recognition, the ICH Steering Committee has set up an Expert Working Group ICH4B. As the 3 pharmacopoeias are made legally binding by the respective legislations, the regulatory authorities have to set up a common procedure to allow official recognition of the 3 pharmacopoeias for texts considered to be harmonised and therefore interchangeable; the authorities must also deliver a clear message to the industries in the 3 regions with a common date for it entering into force.

2 meetings between the PDG and the Q4B group were held on 10 May and November 9 2005, to discuss the regulatory acceptance of harmonised monographs and general chapters, particularly those of relevance to the ICH Q6A guideline; the document detailing the roles and responsibilities of the PDG and Q4B EWG was discussed with further refinement necessary; 5 packages for harmonised general chapters were submitted by the PDG to the Q4B group: dissolution, extractable volume, particulate matter in parenterals, residue on ignition/sulphated ash, and the sterility test.

Examination of the test for residue on ignition/sulphated ash was completed by the Q4B group, and tests, analytical procedures, and acceptance criteria of the 3 pharmacopoeias will be recognised as interchangeable by the regulatory authorities in the 3 regions once the harmonised text has been published and implemented in all 3 regions. This revised text was adopted by the European Pharmacopoeia Commission: it will be included in supplement 5.6. The package for dissolution was submitted to the Q4B group in August 2005. The USP has revised its text for extractable volume and the PDG is awaiting feedback from the Q4B group. Particulate matter was discussed at the meeting of 9 November 2005, and the Q4B group provided a preliminary report outlining a number of issues remaining to be resolved in order to achieve regulatory interchangeability. A number of issues remain to be resolved for the sterility test in order to achieve regulatory interchangeability. Additionally, packages for the PDG harmonised texts on disintegration and uniformity of dosage units are in preparation for submission to the Q4B group.

Relations with industry associations

- 2 meetings with pharmaceutical industry associations were held on 10 May and 8 November 2005 to exchange information on progress with the current work programme and future harmonisation needs. As important stakeholders, industry associations were encouraged to play an active role in the harmonisation process.
- Excipients producers: 2 meetings were held with Tri-PEC (IPEC Americas, IPEC Europe, Japanese Pharmaceutical Excipients Council) on 12 May and 10 November 2005 to discuss the work programme on harmonisation of excipient monographs. Current issues include the policy for functionality-related characteristics, use of additives and processing aids in excipients, co-processed excipients, control of impurities in excipients, and the future of harmonisation.

STANDARD TERMS

The list of standard terms has been translated into 5 more languages (Estonian, Latvian, Lithuanian, Maltese and Romanian), so that these terms are now available in 27 languages, including all of the official languages of the 10 new EU member states. An electronic version of the list of standard terms is available on the EDQM internet site, in a specialised database. The corresponding paper version has been available since the beginning of 2005. Closer collaboration with the EU (EMA) has been initiated, with members of the EDQM participating in EMA meetings and a representative of the EMA participating in EDQM meetings.

COMMUNICATIONS AND PUBLIC RELATIONS

The European Pharmacopoeia Commission reinforced its communications activities by organising the following international scientific conferences, seminars, training sessions and visits of the EDQM or specialised exhibitions for professionals working in the area of quality control of medicines. Events of media interest were organised to commemorate the 10th anniversary of the European Network of Official Medicines Control Laboratories (OMCLs) to convey to the general public the importance of the activities of the EDQM/European Pharmacopoeia in ensuring the quality of all medicines and in the fight against counterfeit products.

Symposia and conferences

Symposium on the quality of homoeopathic products in the new European legislative framework, February 2005, Strasbourg, France

A symposium organised by the EDQM was attended by 83 participants from 15 European countries. Presentations by the European Commission, European regulatory authorities, manufacturers' associations and professional associations focused on the current legislative situation, the practice in different countries in application of the legislation, and future needs for standardisation via the European Pharmacopoeia.

A number of intractable issues have arisen and one aim of the symposium was to work towards consensus on these and to build a relevant work programme for the future orientation of the European Pharmacopoeia Working Party. The question of manufacturing methods and the particular concerns related to raw materials of human, animal and microbiological origin were presented and discussed.

A round-table discussion at the end of the symposium was aimed at compiling recommendations to be made to the European Pharmacopoeia Commission.

After the plenary symposium, a regulatory debriefing session drafted a document to be submitted to the Commission in March 2005, with a view to reviewing the work programme on homeopathic preparations.

The need for input from all interested parties was clearly identified and a strong wish to continue work at the European Pharmacopoeia was evident.

Symposium on alternatives to whole cell pertussis vaccine potency assay, 16 March 2005, Geneva, Switzerland

This symposium was organised by the EDQM, with the support of the European Centre for the Validation of Alternative Methods (ECVAM, JRC, European Commission) and the participation of the WHO (World Health Organisation).

The aim of the symposium was to determine whether a replacement test – more acceptable in terms of animal welfare – for the current whole cell pertussis vaccine potency assay could be evaluated within the Biological Standardisation Programme. 40 participants from 21 countries took part in the meeting. The significant steps in whole cell pertussis vaccine development and control were outlined, as well as an overview of the work performed to develop humane and science-based improvements of whole cell pertussis vaccine quality control methods.

Information day of the European OMCLs and 10th anniversary (1995-2005), 27 May 2005, Rome, Italy

An information day was organised on 27 May in Rome to celebrate the 10th Anniversary of the European network of OMCLs. Participants in this event, which was open to all, were able to learn more about all of the activities and structures of the network. Representatives of the licensing authorities, inspection and various industrial associations (EFPIA, APIC-COFIC, AESGP, EGA, EVM) took part in the programme. 2 round-tables for prospective topics were also set up: the first concerned the construction of a partnership between the network of OMCLs and industry to fight more effectively against counterfeit medicines, and the second concerned the development of future activities in the network. Nearly 300 participants from 33 countries attended this event. For further details, see the section on Biological Standardisation.

Certification of suitability of monographs of the European Pharmacopoeia. Implementation of the 5th Edition - New procedures for revision and renewal of certificates, 27-28 October 2005, Istanbul, Turkey

2 days of exchanges and lively discussions confirmed that the procedure for the certification of monographs of the European Pharmacopoeia is a major tool of growing importance for guaranteeing the quality of constantly developing world trade. The procedure also plays an important role in the implementation of the revised European Directives (2001/83/EEC as amended by 2004/27/EEC and 2001/82/EEC as amended by 2004/28/EEC).

The objectives of this conference were particularly important since they involved reviewing the results obtained since the last conference (4 years earlier), and sharing points of view and experiences with the principal users. The programme facilitated dialogue with users, and indeed 12 workshops sessions (covering the procedure for renewals and revisions, deficiencies in dossiers, sterile products and inspections, respectively) and 56 individual consultations (or One-to-One sessions) were organised, giving each attendee the opportunity to express and exchange views with European authority representatives and the assessors who evaluate the certification dossiers.

Over 180 representatives involved in the quality of medicines, from 32 countries including Canada, India, China, South Korea, Israel and the United States, participated in this international conference organised by the EDQM. The success of the conference reflected the dynamism of international activities surrounding the quality of medicines, and the importance of co-operation between the different partners involved (EDQM, European Commission, EMEA, national licensing authorities, inspection and industries).

Training sessions

The EDQM organised 3 training sessions in 2005: in London (March 2005), Strasbourg (December 2005), and its first training session in the United States (April 2005). This latter session was organised at the request and with the support of the New Jersey Pharmaceutical Quality Control Association (NJPQCA), and was attended by more than 100 delegates from the East Coast of the United States.

Other training sessions organised at the invitation of the national authorities also took place in Belgrade, Serbia (150 attendees, April 2005), Hang Zhou, China (100 attendees, June 2005), Seoul, South Korea (150 attendees, August 2005) and Beijing, China (150 attendees, September 2005).

Official visits to the EDQM

As part of its regular exchanges with its partners, the EDQM welcomed the following groups to its premises.

Permanent representatives at the Council of Europe (January and February 2005)

South Korean delegation (July 2005)

The purpose of this visit was to initiate relations between the EDQM/European Pharmacopoeia and the Korean authorities. The programme and the presentations aimed to describe the role and responsibilities of the EDQM and the European Pharmacopoeia Commission to the visitors, and to give an overview of European procedures and standards. The visit also included a tour of the EDQM laboratories.

Chinese delegation (September 2005)

Exchanges with the Chinese authorities continued to be developed, and the EDQM received a visit from a delegation of representatives of the Chinese Pharmacopoeia and the State Food and Drug Administration (SFDA). The presentations and discussions mainly concerned the work of the EDQM and the European Pharmacopoeia, and the role of the European network of OMCL. In September 2005, the EDQM also went to Beijing to be received by the heads of the SFDA, the Chinese Pharmacopoeia and the Chinese National Institute for the Control of Pharmaceutical and Biological Products (NICPB).

Russian delegation (September and December 2005)

In September, the EDQM welcomed a delegation of Russian representatives of industry and of the Ministry of Health, interested in the activities of the EDQM and the European Pharmacopoeia. The permanent representation of Russia at the Council of Europe was also received in December. Possible rapprochement was discussed.

Brazilian delegation (November 2005)

Following a request for observer status from Brazil, an official delegation visited the EDQM in November 2005 in Strasbourg, and was able to participate for the first time in a session of the European Pharmacopoeia Commission.

Association of Southeast Asian Nations (ASEAN)

The EDQM participated in 2 training sessions under a work programme initiated by the European Committee for Standardisation (CEN) and commissioned by the EU to evaluate and train control laboratories for the testing of pharmaceutical products on the markets of the various ASEAN countries.

A delegation of national control laboratories of ASEAN member states participated in the first training session organised by the EDQM on its premises (December 2005).

Student visits (March, May and September 2005)

The EDQM welcomed 2 groups of Dutch students in March and May 2005. The first group, consisting of 40 pharmacy students at the University of Utrecht, visited the EDQM as part of a programme of scientific visits organised to familiarise students with pharmaceutical science in other European countries. The second group consisted of 40 students in international relations from the University of Groningen.

In September 2005, a group of students studying for a Master's degree from the Institut des Hautes Études Européennes in Strasbourg came to learn about the activities of the Council of Europe that are carried out in the EDQM.

Exhibitions and professional meetings

These exhibitions and professional meetings provided an opportunity to meet users of the European Pharmacopoeia from Europe and Asia. The EDQM presented the 5th Edition, its publications and its services to visitors through stands, presentations and training sessions adapted to the needs of associations or authorities.

The EDQM participated in the following events.

Pharmaceutical Sciences Fair and Exhibition, 12-17 June 2005, Nice, France

This fair was organised by the European Federation for Pharmaceutical Sciences (EUFEPS), with several EUFEPS Member Societies and other proactive scientific organisations. It was attended by over 3000 participants from all over Europe. The EDQM was one of the partners in creating this new type of event that brings together students, lecturers, young professionals and representatives of the pharmaceutical industries. The main theme of the event was the interaction between education, research and practical applications.

CPhI, June 2005, Shanghai, China

The EDQM participated in the Congress of Pharmaceutical Ingredients (CPhI) exhibition for the 3rd consecutive year. It was attended by nearly 10 000 visitors in 2005. The EDQM stand received many visits by participants (1200 visitors in 3 days) who were able to obtain answers to their questions on European regulations concerning raw materials for pharmaceutical use, and the publications and services of the EDQM. The brochures and catalogues were translated into Chinese to facilitate understanding.

XpoPharm, September 2005, Seoul, South Korea

At the request of the Korean Food and Drug Association (KFDA) and the Korean Pharmaceutical Trade Association (KPTA), the EDQM participated in the XpoPharm 2005 exhibition during its first official visit to South Korea.

Indian Pharmaceutical Congress (IPC), December 2005, Hyderabad, India

The EDQM was invited to participate in this event by the organisers. The attendees were mainly academics, but also included representatives of the authorities and industries.

European Pharmacopoeia exhibition for the general public

At the time of the 40th anniversary of the European Pharmacopoeia, it had been decided to organise an exhibition aimed at members of the general public, who often find the concept of medicines to be mysterious. This exhibition, entitled ‘Find out about the European Pharmacopoeia and Medicines’, consisted of panels that explained what a pharmacopoeia was, how it guaranteed the quality of our medicines, and the history of the European Pharmacopoeia and its work. The exhibition content is available, in both English and French, to authorities, universities, institutions etc. and to anyone who wishes to use it as an educational tool for a particular event.

During 2005, the exhibition was presented in several different locations:

- Faculty of Pharmacy, Louis Pasteur University, Illkirch, Strasbourg (19-29 April);
- Administrative centre, Place de l’Etoile, Strasbourg (30 April-26 May) and in the main building of the Council of Europe as part of the ‘Fête de l’Europe’;
- Meeting of the national pharmacopoeias, Danish Medicines Agency, Copenhagen, Denmark (30-31 May);

— Pharmaceutical Sciences Fair and Exhibition, Nice (12-17 June).

INTERNET SITE - <http://www.pheur.org>

Online services continued to be developed for users, with access through the internet site of the EDQM. 2005 saw a number of very helpful new services being made available.

— Online access to electronic versions of the publication *Pharmeuropa* and to the List of Standard Terms.

— Direct registration for conferences, symposia and training sessions.

— The *Frequently Asked Questions* (FAQ) page was updated for all of the activities of the EDQM. New questions and answers were included and user feedback was used to revise answers.

— A new HELPDESK service was set up in June 2005, to deal with a growing number of requests for information on technical and scientific aspects of European Pharmacopoeia texts, and to provide user support online. This service can be accessed from the internet site of the EDQM. After identifying themselves or opening a personal account, users can submit their questions. They will then receive an acknowledgment of receipt which will include a reference number and a link to a personal message box. This message box will show the status of the response to the user's question by the EDQM and finally the reply itself. A record of the questions and the answers to these questions will be kept for one year by the system. This new system will improve the traceability of questions sent to the EDQM and speed up the response time.

— The KNOWLEDGE database continues to be the central repository of technical and regulatory information for the texts of the European Pharmacopoeia. The KNOWLEDGE database is now connected to the 2 other specialised databases for reference substances and Certification. For a given substance, users of the KNOWLEDGE database have direct access to the list of reference substances or preparations used in the monograph and the Certificates of Suitability that have been granted.

PROVIDING REFERENCE SUBSTANCES AND PREPARATIONS

106 new chemical reference substances (or spectra) and biological reference preparations were adopted during the year, bringing the number of substances available to users of the European Pharmacopoeia to 1761. Extensive collaborative studies were required for 52 of these substances to determine the content of the substances used in the assays. In addition, 118 substances were replaced and the European Pharmacopoeia laboratory regularly monitored 405 substances and carried out quality control tests during the production of 506 batches. The number of chemical reference substances and biological reference preparations distributed to users continued to climb (from 135 431 vials in 2004 to 152 983 in 2005), and the number of orders increased from 17 903 to 20 535. From bulk substances selected by the European Pharmacopoeia Commission for use as reference substances, the Production Unit of the EDQM prepared 512 batches (filling 277 404 vials), and 8 batches by lyophilisation (filling 15 627 vials).

PREPARATION AND DISTRIBUTION OF SAMPLES

2773 new samples (compared with 2651 in 2004) were received by the EDQM this year. The total number of samples in stock was about 20 000. 403 studies were carried out by the European Pharmacopoeia laboratory to compare or check the analytical methods proposed for new monographs or for revisions of monographs at the request of the groups of experts of the Commission. The Production Unit had to prepare 3128 samples for these laboratory studies to check the quality of the substances available on the market (multisource substances) or to check the robustness of draft European monographs. In addition, 9264 samples were prepared for distribution to the various experts of the EDQM (for the elaboration of monographs and the organisation of collaborative studies, market surveillance studies, biological standardisation projects, etc.).

BIOLOGICAL STANDARDISATION

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

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

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

Since its start in 1992, 86 BSP projects have been initiated and 80 BRPs or replacement batches have been established.

In the year 2005, the following projects were pursued.

In the field of vaccines for human use

- Feasibility study for establishment of common *in vitro* potency assay for inactivated poliomyelitis vaccine (IPV)
- Validation of alternatives to Auszyme ELISA kits for *in vitro* potency assay of rDNA hepatitis B vaccines
- Validation of serological method for potency assay of acellular pertussis vaccine
- Standardisation of assay for residual pertussis toxin
- Standardisation of test on molecular size distribution of haemophilus type b conjugate vaccine
- Standardisation of human influenza vaccine serology
- Establishment of BRP and validation of methods for vaccinia immunoglobulin

- Validation of NMR methods for quality control of polysaccharide vaccines
- Establishment of replacement batches for hepatitis A vaccine BRP

In the field of vaccines for veterinary use

- Establishment of mycoplasma reference strains BRPs
- Establishment of equine influenza antiserum BRP batch 2

In the field of blood and plasma products

- Establishment of BRP for normal human plasma for assay of SD-plasma and fibrin sealant kits
- Establishment of human coagulation factor VII concentrate BRP
- Establishment of replacement batches for human normal immunoglobulin BRP
- Establishment of immunoglobulin panel for anti-D antibodies test BRP
- Validation of *in vitro* assay method for tetanus immunoglobulin

In the field of biotechnology products

- Establishment of somatropin CRS batch 2
- Establishment of heparin sodium BRP batch 3
- Establishment of an HPLC potency assay for interferon alfa2
- Establishment of low molecular mass heparin for calibration BRP batch 2

The studies led to the adoption of the following reference preparations in 2005.

- Newcastle disease vaccine (inactivated) BRPs for the *in vitro* potency assay
- Immunoglobulin panel for anti-D antibodies test BRP
- Vaccinia immunoglobulin BRP
- Human immunoglobulin BRP batch 3
- Human immunoglobulin (molecular size) BRP batch 1

The full reports on the concluded collaborative studies were published or will be published in *Pharmeuropa Bio* 2005-1 or 2006-1, respectively.

In 2005, significant progress was made towards the establishment of mycoplasma reference strains. The technically demanding production of a sufficient number of vials of reference strains for *Mycoplasma hyorhinis*, *M. synoviae*, *M. orale*, *M. fermentans* and *Acholeplasma laidlawii* has been completed. Depending on the results of final suitability checks, it is assumed that the reference preparations will be made available in mid-2006. It is intended to make them globally available in the context of both European and international harmonisation efforts (VICH).

Strong efforts were made to apply the 3R concept to the field of quality control of biologicals. The *in vitro* potency assay for Newcastle disease vaccine (inactivated) that had been validated in a collaborative study in 2004 was

presented to the Ph. Eur. Expert Group 15V and led to a revision of the monograph; the revised monograph was adopted by the Ph. Eur. Commission in November 2005. Furthermore, an international symposium was organised together with the European Centre for Validation of Alternative Methods (ECVAM) and with the support of the WHO in Geneva on 16 March 2005, in order to evaluate possibilities for replacement of the *in vivo* potency test for whole cell pertussis vaccine (Kendrick test). The proceedings of the symposium have been published and follow-up activities have been initiated. 3 new projects were initiated in 2005 in the context of the 3R concept: one projects aims to replace the challenge assay for tetanus immunoglobulin with an *in vitro* assay; the second attempts to better standardise the assay for residual pertussis toxin and ultimately replace the *in vivo* histamine challenge test with an *in vitro* assay; the third extends previous projects on the development of serological assays to replace the *in vivo* challenge as the batch potency test for vaccines containing diphtheria and tetanus components to acellular pertussis vaccine. The goal is to enable the potency assay for vaccines containing all of these components to be carried out using serum from the same animals. This will enormously reduce the number of animals needed for these assays. As in previous years, co-operation with international partners continued; projects to establish common standards were set up whenever possible with the WHO Expert Committee on Biological Standardisation (ECBS); an example includes the establishment of a standard for low molecular mass heparin for calibration. The project for the establishment of the immunoglobulin panel for anti-D antibodies test BRP was run together with the FDA/CBER.

TRANSLATIONS AND PUBLICATIONS

It should be noted that the European Pharmacopoeia is published in both official languages of the Council of Europe, namely English and French. The EDQM therefore has its own specialised translation service. In 2005, 258 texts were translated from English to French (equivalent to 1246 pages with 300 words per page) and 186 from French to English (equivalent to 907 pages with 300 words per page).

In the area of publications, the year 2005 issues of *Pharmeuropa* comprised a total of 554 pages in French and 532 pages in English, *Pharmeuropa Bio* (issues in English only) comprised 54 pages, *Pharmeuropa Scientific Notes*, a new publication in English only, comprised 66 pages and the 5th Edition of the European Pharmacopoeia comprised 4642 pages in French and 4370 in English. The 3 supplements for 2005 of the 5th Edition comprised 1102 pages in French and 1034 in English.

The 5th edition consists of 1920 monographs, 293 general texts and 2297 descriptions of reagents, and is published in both electronic and printed form.

A 'Certificate of Authenticity' for the EDQM publications was developed to protect against unauthorised copying. This certificate contains open and hidden security features. In addition, these certificates contain a unique 'EDQM Publication ID', which serves for registration of the electronic versions and allows users to verify their genuine EDQM publication using an online registration.

The cumulative electronic edition of the European Pharmacopoeia is available in 3 different formats: a CDROM version for individual use, an intranet version for use within company networks, and an online version accessible through the internet. All 3 electronic editions are based on browser technology and feature a powerful search engine, hyperlinks between monographs, general methods and reagents, and a direct link to the online database for reference substances and the knowledge database. The online version uses an improved interface with some added features, such as displaying the number of hits in the table of contents, and improved hitlist presentation. All 3 electronic formats contain printable Acrobat PDF files of the texts that are identical to those of the paper version.

Pharmeuropa (including Pharmeuropa Bio and Pharmeuropa Scientific Notes) is now also available online. All issues stretching back to Volume 10 (1998) have been indexed and are available as searchable Acrobat PDF files. The online access is included for subscribers to the printed version of Volume 18 (2006). The necessary access code can be generated using the information from the Certificate of Authenticity on the inside-front cover of Pharmeuropa 18.1.

Access to the online version of Standard Terms has now been included in the subscription to the printed version, and the access is handled in the same way as for Pharmeuropa, using the EPID number on the Certificate of Authenticity on the inside-front cover.

2. CERTIFICATION OF SUITABILITY OF MONOGRAPHS OF THE EUROPEAN PHARMACOPOEIA

286 new applications (including 19 for products with TSE risk) and 465 requests for revision were received, in addition to the regular updates following the publication of revised monographs in the supplements of the European Pharmacopoeia. 780 (new or revised) certificates were granted after assessment; a further 350 certificates were revised automatically to refer to the 5th Edition of the European Pharmacopoeia.

In total, over 2700 applications have been received and 1900 certificates have been granted since the procedure became operational, and these are regularly updated.

Requests for revision or renewal of certificates, which increased by 50% compared with 2004, are now dealt with according to a procedure that has been brought into line with the procedure for marketing authorisation of medicines. In particular, the deadlines for examination of dossiers have been shortened according to well-defined evaluation criteria based on the Community regulations classification.

The 4th International Conference on Certification successfully took place at the end of October 2005 (in Istanbul). Presentations were made by the various partners (industrial associations, national and European authorities), and the conference was attended by 180 participants.

The procedure illustrates the exemplary collaboration between the partners, namely the working parties of the CHMP, CVMP, and the European Pharmacopoeia Commission, which, while consulting Industry (EFPIA, AESGP, CEFIC/APIC, IFHA, EGA, EAPPI, IPEC), worked together to find practical solutions to improve quality assurance without complicating the administrative procedures for evaluation. The licensing authorities have clearly expressed their preference for the Certification Procedure when there is a European Pharmacopoeia monograph (guideline on Requirements in relation to active substances, and implementation of directives 2001/82/EC, 2001/83/EC and 2003/63/EC, as amended).

The 3 Cs (Consultation, Co-ordination, Co-operation) that characterise the procedure are implemented by a Steering Committee consisting of the Chairs of the European Pharmacopoeia Commission, the Joint CHMP/CVMP Quality Working Party, the CHMP Biotech Working Party, the CVMP Immunological Products Working Party, the Herbal Medicinal Products Working Party, the Inspection Working Party, and representatives of the European Commission, authorities of non-EU member states of the European Pharmacopoeia, the EMEA and the EDQM. The Steering Committee met twice in 2005, thus ensuring that decisions involving licensing, pharmacopoeia and certification are taken in a coherent manner.

In addition to the Steering Committee, which is responsible for decisions on general policy, 2 technical advisory boards have been set up, one for chemical substances and the other for TSE risk substances. They consist of expert rapporteurs who participate in the evaluation of dossiers. These boards deal with any technical or scientific questions raised by the rapporteurs.

3. NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES (OMCLs)

The network was established in 1995 by an initiative of EDQM in close co-operation with the Commission of the European Union and is open to all countries that have signed the European Pharmacopoeia Convention, as well as to observers at the European Pharmacopoeia Commission, provided that the criteria of the network are fulfilled.

There are two levels of collaboration:

- *General activities* involving all member states of the network: all the OMCLs are invited to meetings and are asked to participate in collaborative studies in all the areas of general interest;
- *Activities restricted to the European Economic Area (EEA)*: a number of activities take place within the more restrictive regulatory framework for medicines in the EU, notably those connected to the Centralised Marketing Authorisation Procedure, the Mutual Recognition Procedure (MRP), and the Official Control Authority Batch Release (OCABR) of blood and plasma derivatives, human vaccines and veterinary immunobiologicals.

‘Networking’ means sharing of know-how within a pool of experts, work-sharing, and the mutual recognition of test results based on commonly agreed procedures, which consequently saves resources and costs in testing of medicinal products. For that purpose, the implementation and maintenance of harmonised quality management systems (QMSs) (based on ISO/IEC 17025) among the network members and the assessment of established systems based on commonly agreed procedures are required. Since 1997, several instruments have been in place to help OMCLs work towards these goals, such as training visits (staff members of an OMCL visit the facilities of another OMCL to learn about quality assurance (QA) topics or specific analytical techniques), tutorials (tutors visit an OMCL to coach the personnel on QA subjects), mutual joint visits (to observe and give advice on the implementation of a QMS), and mutual joint audits (to assess the technical competence and the level of compliance of an OMCL). Annual meetings also contribute towards networking, bringing together representatives from the whole network to discuss and exchange viewpoints on common interests, such as the independent testing of medicines, and to summarise the year’s activities and decide on an action plan for the coming year. These meetings are organised by the EDQM and hosted by one of the members of the network on a rotating basis.

ACTIVITIES INVOLVING ALL OMCLS OF THE NETWORK

Annual meeting of the plenary network

The 10th annual meeting of the plenary network was held on 23-26 May 2005 at the Istituto Superiore di Sanità in Rome, Italy, and was attended by almost 200 representatives from 31 countries. For the first time, a satellite symposium to the annual meeting, dedicated to the activities of the OMCL Network, was organised by EDQM (the OMCL Information Day). The symposium took place at the University La Sapienza, Rome, on 27 May 2005, and was attended by about 300 participants from industry and public health services from 33 countries. In plenary lectures and 2 round-table discussions the broad spectrum of activities of the network was presented to a large group of stakeholders. In particular, the activities in the area of counterfeits of medicinal products were discussed.

Quality management systems

The quality assurance (QA) programme of the OMCL Network covers 4 different domains:

- educational (tutorials, training courses);
- assistance (training visits);
- implementation of the quality management systems (QMS) (mutual joint visits);
- surveillance of the QMS (mutual joint audits).

During 2005, the following activities were carried out within the OMCL Network as part of the QA programme, coordinated by the EDQM Division IV:

- 5 mutual joint audits: 2 in OMCLs testing human and veterinary medicines (chemical), and 3 in OMCLs testing human medicines (1 biological, 2 chemical + biological);

- 7 mutual joint visits: 3 in OMCLs testing human medicines (1 biological, 1 chemical, 1 chemical + biological), 3 in OMCLs testing veterinary medicines (1 biological, 2 chemical + biological) and 1 in an OMCL testing human and veterinary medicines (chemical + biological);
- 8 training visits organised for members of 2 OMCLs (1 EU and 1 non EU);
- 1 tutorial carried out in an OMCL testing human medicines (biological).

In total, since the beginning of the QA programme (Dec 1997), 30 mutual joint audits, 44 mutual joint visits, 2 tutorials and 9 training visits have been carried out within the OMCL Network. These figures show the strong commitment of the OMCL Network towards installing a common approach for upgrading their quality system to a harmonised high standard and to benefit from each other's experience.

In 2005, the QA programme was specially focused on the OMCLs of the new EU member states that had not yet been visited, as a pre-assessment in preparation for the mutual recognition visit by the Canadian authorities.

Training visits are coordinated and supported by the EDQM Division IV. In 2005 this programme was fully developed and actively promoted. The following training subjects were covered in 2005: chromogenic assay, ELISA, LC-MS, potency assay and purity tests for certain vaccines, PCR and molecular size distribution of haemophilus type b vaccines.

Training courses

Division IV of the EDQM organised 2 training courses in 2005, open to all scientific and technical staff of the OMCL Network. The training session on QA general issues took place at the EDQM on 19-21 April 2005, with 54 participants from 26 countries. Another, more technique-oriented training session in the chemicalpharmaceutical field took place at the EDQM on 24-27 October 2005, with 92 participants from 35 countries (5 participants from 4 African countries and 2 from Ukraine were sponsored by the WHO). Both sessions were very positively rated by the participants and the possibility of exchanging experiences with other colleagues of the network was highly appreciated.

Another technical training session focusing on methods used in the biological field was held on 6-9 February 2006 at the EDQM. A training course for auditors participating in the mutual joint audits/visits scheme is foreseen later in 2006.

OMCL Network guidelines

The OMCL Network guideline ‘Qualification of equipment’ was adopted at the annual meeting in May 2005. It essentially deals with requirements for HPLC equipment. Further annexes related to other equipment such as gas chromatography are under development.

Collaboration with the European co-operation for Accreditation (EA)

Discussions with representatives of the EA concerning the recognition of the contribution of OMCLs in setting up QMSs within their domain are progressing. In particular, the following guidelines/documents were approved by the EA as recommendation documents to be used in the context of quality system audits of OMCLs and are now also available from the EA website:

- Validation of analytical procedures;
- Scope of accreditation of Official Medicines Control Laboratories;
- Uncertainty of measurement: Policy on the estimation and application of uncertainty in analytical measurement (compliance testing).

Proficiency Testing Scheme (PTS) Studies

These studies have become a regular programme within the network. In 2005, six studies were organised in the physico-chemical field, with an average participation of 34 national control laboratories, while in the biological area 4 studies were organised, involving on average 11 national laboratories. A third PTS programme, agreed with the WHO in 2004, and scheduled for July 2004 to June 2006, was further developed. In 2005, 3 out of the 5 studies included in the programme were conducted, 1 was finalised and 1 was prepared. On average, 34 governmental control laboratories from Africa, Asia (South East and Western Pacific), Europe and Central and South America participated in each study. The EDQM also participated in a special ASEAN training programme for the PTS involving official control laboratories (central and regional) from 9 countries of South East Asia sponsored by the EU.

General studies on market surveillance (MSSs)

These studies, aimed at screening the quality of products commercialised in countries of the OMCL Network, were carried out for the following preparations, with the participation of 15 national laboratories on average: equisetum stem, cadmium in herbal drugs and trimethoprim (raw material and tablets).

2 additional MSSs on sub-division of tablets and on uniformity of dosage units (Ph. Eur. general method 2.9.40), each involving 20 or more OMCLs of the network, were finalised during 2005.

Where necessary, the results of these studies support the revision of the relevant Ph. Eur. monographs and/or general chapters and methods. This was the case for the MSS on sub-division of tablets. As an outcome of the study, the Ph. Eur. Commission agreed to revise the monograph on tablets in June 2005.

Extranet site - OMCLnet

The extranet site OMCLnet, which was established in 2003 and fundamentally restructured in 2004, has meanwhile become a standard information platform for OMCLs within the network. It hosts information about adopted general OMCL guidelines, as well as minutes and presentations of meetings covering the general activities of the network as well as the MSS, PTS and QA topics. At the beginning of 2005, the OMCLs were asked to re-register to obtain new access to the extranet site. The password will be changed regularly to guarantee data security. Due to the general acceptance of this IT tool by the OMCLs, it was decided to make meeting documents only available on OMCLnet prior to the corresponding meeting, and not to re-distribute them during the session. This new policy has proven to work satisfactorily and contributes to reducing the paper document and postal distribution costs.

OMCL inventory database project

At the end of 2004/beginning of 2005, a campaign of questionnaires was initiated by Division IV of the EDQM, addressed to the OMCLs of the general network (launched in 4 steps). The purpose of these activities was to gain information about the competences and know-how in the field of quality control of medicinal products throughout the network. The data collected by the questionnaires will be the basis for an OMCL inventory database, scheduled for development in 2006. A list of specifications for this database has been established with the help of an external IT expert and under the participation of a representative of the OMCLs in the 4th quarter of 2005. The future database should provide:

- basic information on OMCLs of the network (name, address, contact points, etc.);
- basic information on competences available within the network;
- an IT platform to improve communication between the members of the network.

Data will be stored in a secure, access-controlled environment. In a future step it might be envisaged to grant access to other stakeholders (e.g. licensing authorities, inspectorates etc.).

CombiStats

In 1999, the EDQM initiated the development of a computer programme for the statistical evaluation of biological dilution assays in accordance with Chapter 5.3 of the Ph. Eur. At that time, most laboratories of the OMCL network used software developed in-house, so there was a strong demand for a common programme to harmonise the presentation of assay data and the analysis thereof. The lack of availability of suitable commercial software resulted in the development of 'CombiStats', which has been used to the general satisfaction of the network since 2000. Initially the software was only available to OMCLs but as of 1 November 2005 nonOMCL laboratories can also

obtain a user licence. Together with the public release of the software an official website has been launched at www.pheur.org/combistats on which an online manual, tutorial, examples and background information can be found. A free demonstration version can also be downloaded.

EU/EEA SPECIFIC ACTIVITIES

Official Control Authority Batch Release (OCABR) of biologicals

For the second consecutive year all 25 EU member states, including those integrated as of 1 May 2004, took part in the traditional confidential exchange of information on issues related specifically to OCABR during the annual meeting in specific dedicated sessions. EEA member states and Switzerland, an MRA partner, also participated as usual.

In addition, continuing the effort to facilitate the integration of the new member states into the harmonised system and following the successful workshop held for the blood network at the Austrian Federal Institute for Medicines (BiFA) in Vienna on 1-3 December 2004, a similar training workshop was held for the vaccine network at the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) in Lyon on 4-6 April 2005. 13 representatives from 8 of the 10 new member states and 3 participants from the candidate states of Bulgaria, Croatia and Romania participated in discussions, and saw presentations from representatives of several of the long-standing member states with a focus on the practical application of batch-release techniques, including laboratory sessions. The meeting was concluded with a visit to the Sanofi-Pasteur manufacturing and control laboratories sites in Marcy l'Etoile. All participants expressed enthusiasm for this successful exchange of experiences.

Another important workshop was held on 16-17 November 2005 at the National Institute for Biological Standards and Control (UK) on the batch release of oral poliomyelitis vaccines. 10 participants from 5 member states and observers from the EDQM and the WHO participated in this hands-on workshop to gain experience in the new transgenic mouse neurovirulence assay, which will replace the neurovirulence assay in monkeys, and to develop guidelines for the implementation of training and testing procedures at OMCLs.

Human biologicals

At the annual meeting, a review of OMCL batch release activities since 2004 for both blood and vaccines and special scientific presentations were highlighted. Of key importance was the revision of the terms of reference for the network to better integrate the new members states and to increase the size of the advisory group to accommodate the new depth of activity. The use of the established communication network was also emphasised. An increased interest in work-sharing and possible subcontract testing between OMCLs for OCABR was highlighted and will be pursued in 2006.

A revision of the administrative procedure for batch release of biologicals to fully commit OMCLs to external assessment of QA standards based on ISO 17025 was adopted. A revision to the terms of reference for the network was adopted and a position paper on a common policy for access to information in the OCABR network was

approved and will be followed up. In a related issue, an administrative procedure for application of batch release in the context of Article 58 of EU Council Regulation 726/2004 was presented.

Blood products and plasma derivatives

The following guideline was newly adopted:

- Official control authority protocol for approval of plasma pools.

The following guideline revisions were adopted:

- revisions to all blood and plasma-derived product-related guidelines and the annex II d of the administrative procedure for batch release of biologicals to accommodate the change to plasma pool approval in the newly adopted guideline (see above);
- revisions to all blood and plasma-derived product-related guidelines to delete the need for hepatitis C serology test for plasma pools to be in line with the relevant Ph. Eur. Monograph, which had been revised;
- revisions to the guideline for clotting factor concentrates, plasma inhibitor concentrates and fibrin sealants to adapt to new products available on the market;
- revisions to the guideline for normal immunoglobulin to be in line with monograph revisions.

Human Vaccines

The following new internal procedures/position papers were adopted in 2005:

- OCABR procedure for pandemic situations;
- Position paper on Japanese encephalitis vaccines marketed in the EU;
- Position paper on the need for interaction between OMCLs and licensing bodies.

Adopted internal procedures/position papers are available to OCABR network members on OCABRnet, a restricted-access extranet site maintained by the EDQM.

5 new guidelines were adopted in 2005 as follows:

- Approval of poliomyelitis vaccine (oral) (OPV) – monovalent bulk;
- Poliomyelitis vaccine (oral) (OPV) – trivalent vaccine;
- Hepatitis A (inactivated) and typhoid polysaccharide combined vaccine (adsorbed) for mix at use format products;
- Pandemic influenza vaccine;
- Varicella vaccine.

The following guideline was approved for external consultation:

— Influenza vaccine (surface antigen, inactivated, virosome).

All adopted guidelines and administrative procedures are available in a booklet published by the EDQM at the end of December 2005. They are also available for download on the EDQM website (http://www.pheur.org/site/page_611.php).

Immunological Veterinary Medicinal Products (IVMPs)

Competent Authorities (CA) and OMCLs involved in the control of veterinary immunological products took part in the annual meeting again in 2005 with the other branches of the OMCL network. The veterinary participants focused on annual reports of activities and scientific issues with a brief update on the progress made on formalising procedures for harmonisation and transparency of an OCABR system in the EU/EEA as implemented under the current legislation.

In addition to the annual meeting, over the course of 2005, 2 meetings open to all EU/EEA interested parties and a conference call were organised by the EDQM. These and a number of other meetings hosted by the EU Commission and the Veterinary Pharmaceutical Committee were held to further advance the finalisation of procedures and guidelines required for application of the new Directive for Veterinary Medicine, which came into force on 31 October 2005.

As a result, the following procedures and guidelines have been developed and approved by the CA/OMCL network and Veterinary Pharmaceutical Committee for use during a pilot phase of 1 year. At the end of the pilot phase an evaluation including an impact assessment will be completed in cooperation with industry representatives, and the future needs of the program determined.

- Administrative procedure for harmonised application of Article 81 of Directive 2001/82/EC as amended by 2004/28/EC (Official batch protocol review – OBPR)
- Administrative procedure for application of Article 82 of Directive 2001/82/EC as amended by 2004/28/EC (Official control authority batch release – OCABR)
- Models for submission of batch protocols by a Marketing Authorisation Holder for OCABR/ OBPR
 - Inactivated bacterial vaccines
 - Live bacterial vaccines
 - Inactivated viral vaccines
 - Live viral vaccines
 - Tuberculin PPD/ brucellin preparations
- Product-specific technical guidelines for OCABR
 - Aujeszky's disease vaccine (inactivated)

- Aujeszky's disease vaccine (live)
- Brucellosis vaccine (live)
- Brucellin preparations
- Equine influenza vaccine (inactivated)
- Infectious bovine rhinotracheitis vaccine (inactivated)
- Infectious bovine rhinotracheitis vaccine (live)
- Newcastle disease vaccine (inactivated)
- Newcastle disease vaccine (live)
- Rabies vaccine (inactivated) for veterinary use
- Rabies vaccine for foxes (live)
- Swine erysipelas vaccine (inactivated)
- Swine erysipelas vaccine (live)
- Tuberculin PPD, avian
- Tuberculin PPD, bovine

All of the above noted procedures and guidelines are available on the EDQM website for download (http://www.pheur.org/site/page_634.php).

Meeting with manufacturers' associations

Each of the sub-networks for OCABR of biologicals held separate meetings in Strasbourg with the relevant manufacturers' association in the course of 2005 to allow for exchange and feedback and to ensure transparency and good will.

Representatives from the vaccine network met with members of vaccine manufacturers (the European Vaccine Manufacturers (EVM) Association and other independent manufacturers) on 6 October 2005 and representatives from the blood network met with representatives from the International Plasma Fractionators Association (IPFA) and the Plasma Protein Therapeutics Association (PPTA) on 25 November 2005. Representatives from the veterinary network for IVMPs met with representatives from the International Federation for Animal Health (IFAH) Europe on 12 December 2005.

Market surveillance for products with a centralised marketing authorisation

The programme for sampling and testing of centrally authorised products (CAP) was successfully continued in 2005. Since its implementation in 1999, the programme has been continuously improved thanks to the collaboration between all stakeholders:

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

The CAP programme covers medicinal products for both human and veterinary use. In 2005 it included 39 products (13 biotech products and 26 chemical/pharmaceutical products). In addition, testing was also carried out on the active substances of 4 of these products. These figures correspond to a decrease of 5% compared to the 2004 CAP programme and an increase of 5% compared to the 2003 CAP programme, and follow the trend seen with the number of MAs granted. Products to be included in the 2005 programme were selected by EMA expert committees from those authorised in 2002 (year $n-3$), thus guaranteeing that selected products have been launched and manufactured on a large scale. Some products tested in previous years were included as well for re-testing.

Market samples were collected for each product in 3 EU/EEA countries in order to have an overview of the actual product quality of distributed batches. Sampling took place mainly at wholesalers (75%), with less than 10% in retail or hospital pharmacies, mainly because of the distribution scheme of centrally authorised products, which are generally difficult to obtain in sufficient quantities at the very end (pharmacies/hospital) of the distribution chain without depleting the essential stock needed for patient care. Overall, 93 sampling operations were carried out by national inspection services in 24 EU/EEA countries. The market samples and non-commercially available standards and specific reagents provided by the manufacturers represented 309 stock items. Initial storage, coding and dispatching to OMCLs for testing was dealt with by the EDQM.

Testing was usually performed by 2 OMCLs, independently from the product manufacturers. A new testing scheme was successfully introduced for chemical products. 8 products (about one third) were tested by a single OMCL. A second OMCL could be involved at a second stage only in case of analytical or compliance issues. This was the case for only one product during 2005. It is intended to gradually phase in such a testing format so that by 2007 all chemical products will be tested according to the new scheme. Given this background, it is planned that the OMCLs that have successfully undergone external assessment of their QA system, fulfilling the requirements for market surveillance of medicinal products, will progressively be given preference for participation in such CAP projects.

Overall, 31 OMCLs (human and veterinary sides) from 24 EU/EEA countries took part in the testing phase of the 2005 programme, and a total of 77 testing operations were carried out.

In 2005, all tested products were of appropriate quality. Nevertheless, some minor issues related to the quality of the analytical documentation (MA dossier and/or Standard Operating Procedures for quality control) were reported. Difficulties were also encountered during the setting-up of methods, e.g. for automated methods or unusual techniques. All issues were thus reported to the EMEA and their scientific experts, when necessary proposing follow-up actions on the registration dossier and/or on analytical testing methods. The MA holder obtains access to the reports via the EMEA.

The collaboration between all parties was facilitated by the extensive use of IT tools (EMEA Eudralink, EDQM CAPnet server) and 3 productive meetings at the EDQM; 3 QA documents were finalised by the Advisory Group of the CAP programme and adopted during the annual meeting, which took place in December 2005 in Strasbourg. Participants emphasised that the implementation of a risk-based approach in the selection of products to be tested to optimise the use of OMCL resources should be carefully evaluated.

Post-marketing surveillance of products with an MA according to the Mutual Recognition Procedure (MRP)

2005 has been an eventful year for the MRP-product testing programme mainly due to 2 important steps taken to enhance the programme.

In May 2005, at the annual OMCL meeting, the plenum decided to continue with a regular programme after having run a successful trial phase over approximately 4 years. At the same time, several OMCLs, mainly from the new EU member states, announced their interest in contributing to the programme in the future. Meanwhile, Division IV of the EDQM has granted 36 OMCL contacts access to its extranet site MRPnet, which is the shared IT communication platform of the MRP-product testing group and the EDQM. At the beginning of 2005, it was agreed henceforth to make all individual Summary Reporting Sheets available to the MRPnet users. These reports include concise information about the outcome of testing of MRP-products performed in the course of the annual programmes, and provide complementary information to the results sheets, which have been established previously on MRPnet.

The year 2005 was also the starting point for the development of an MRP-product testing database, which will be a common database hosting MRP-product information and data on tests performed in the course of this programme.

4. NEW EDQM BUILDING

The foundation-stone-laying ceremony took place in Strasbourg (allée Kastner) on 28 April 2005. The ceremony was opened by Mr. Terry Davis, Secretary-General of the Council of Europe. Speeches were made by Mr. Robert Grossmann, Deputy Mayor and President of the Communauté Urbaine de Strasbourg, Ms Fabienne Keller, Mayor of Strasbourg, Mr René van der Linden, President of the Parliamentary Assembly, and Mr Adam Daniel Rotfeld, Chairman-in-Office of the Committee of Ministers of the Council of Europe and Minister for Foreign Affairs of Poland. Work progressed as planned in 2005 and the building should be ready, barring unforeseen circumstances, by the end of December 2006. This new building is critical to the future development of the EDQM/European Pharmacopoeia and will help it to respond to new public health needs in Europe.