European Directorate for the Quality of Medicines & HealthCare

Serving public health in Europe since 1964
The EDQM is a leading organisation that protects public health

edqm.eu
The European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe traces its origins and statutes to the Convention on the Elaboration of a European Pharmacopoeia (an international treaty adopted by the Council of Europe in 1964). The 37 member states and European Union (EU) that have signed the Convention are committed to achieving harmonisation of the quality of medicines throughout the European continent and beyond.

To help the EDQM carry out its missions, the member states volunteer not only the services of experts in the pharmaceutical sciences and access to equipment in national medicines control laboratories, but also the services of experts in blood transfusion, organ transplantation, pharmaceuticals and pharmaceutical care, consumer protection, as well as those involved in assessments and inspections in the context of the certification scheme.

This is one of the reasons for the success of this organisation, which is thereby able to respond to the needs and realities of public health in Europe and beyond.

Tribute should be paid to the dedication and enthusiasm of all those who have contributed to the elaboration of the European Pharmacopoeia or have participated in the achievements of the EDQM’s missions.
Vision of the EDQM

The EDQM is a leading organisation that protects public health by:

• enabling the development,
• supporting the implementation, and
• monitoring the application of quality standards for safe medicines and their safe use.

Our standards are recognised as a scientific benchmark world-wide. The European Pharmacopoeia is legally binding in member states.

Similarly, the EDQM develops guidance and standards in the areas of blood transfusion, organ transplantation, pharmaceutical care and consumer health protection.

Activities related to the elaboration of the European Pharmacopoeia

The European Pharmacopoeia has the following objectives:

• to prepare individual quality standards (monographs) for substances used in the production of medicines for human or veterinary use and other texts related to the European Pharmacopoeia;

• to respond rapidly to new risks to public health (e.g. heparin crisis, adverse thromboembolic effects of immunoglobulins, etc.) by elaborating new methods of analysis and tests and setting new specifications;

• ensuring that the analytical methods described in the monographs are experimentally verified and validated.

From a simple tablet taken with a glass of water to the most complex types of treatments, all medicines on the European market must comply with strict specifications on their composition, manufacturing processes and quality. Under the aegis of the Council of Europe, the EDQM plays a central role in the regulation of medicines. The texts adopted by the Ph. Eur. Commission apply to all signatory parties of the Convention.
The EDQM serves as the technical secretariat to the European Pharmacopoeia Commission. In addition, the EDQM is in charge of:

- establishing European Pharmacopoeia reference standards or preparations, which are needed to carry out the tests or described in the monographs;

- establishing reference standards for biological substances and validating alternatives to methods currently prescribed in the European Pharmacopoeia in order to reduce the use of animals and developing new methods for the quality control of biological medicines (under the Biological Standardisation Programme and financed in partnership with the European Commission);

- regularly organising congresses on new scientific and technical subjects, as well as seminars and training sessions on subjects related to the European Pharmacopoeia.

**The Certification Procedure**

**Evaluation of quality dossiers on the manufacture of substances for pharmaceutical use** (Certification of Suitability to monographs of the European Pharmacopoeia).

The procedure was established in 1994 and is aimed at ensuring that the quality of substances used in the production of medicines can be suitably controlled by the current specifications of the European Pharmacopoeia and that it therefore complies with the requirements of European pharmaceutical legislation.

The evaluation of quality dossiers submitted by manufacturers of substances for pharmaceutical use is complemented by an inspection programme. Inspections of manufacturing sites are aimed at checking compliance with current Good Manufacturing Practices (GMP) and verifying the accuracy of the information submitted to the EDQM in applications for a Certificate the Certificate of Suitability. The Certification procedure also provides the European Pharmacopoeia with information on the quality of substances on the European market and helps to identify the need for the revision of monographs. It provides an important contribution to the evaluation and control of medicines prior to them being marketed.

**Programmes for surveillance of marketed medicines (OMCL Network)**

As part of its surveillance activities for marketed medicines, the EDQM co-ordinates the General European Network of Official Medicines Control Laboratories (OMCL); this activity was established in 1994 at the request of the European Union. The OMCL Network is essential in facilitating mutual recognition of quality control tests carried out on medicines and ensures that patients receive the same quality of pharmaceutical products throughout Europe.

The main areas covered by the surveillance programmes are:

- general Market Surveillance Studies (MSS) on products marketed throughout Europe, for example generics and herbal preparations;

- specific testing of a number of biological products (blood derivatives and vaccines for human or veterinary use) prior to their release to the market in the context of Official Control Authority Batch Release (OCABR);

- market surveillance, according to a work programme set by the European Medicines Agency (EMA, London), of pharmaceutical products that have received a centralised (European Union) marketing authorisation;

- market surveillance for products authorised by the Mutual Recognition Procedure/Decentralised Procedure (MRP/DCP);

- quality monitoring of stockpiled medicines;

- testing of counterfeit / illegal medicines;

- testing of Active Pharmaceutical Ingredients (APIs);

- testing of unlicensed pharmacy preparations.

The OMCL Network offers all the participating official laboratories a wide range of opportunities to collaborate at the European level. Special emphasis is placed on Quality Management Systems through the organisation of mutual joint audits and mutual joint visits. This system is necessary to facilitate mutual recognition of test results amongst laboratories and to make the best use of resources. In addition, training courses are provided and guidelines on quality assurance are published and updated regularly.
EDQM ORGANISATIONAL CHART

RELATIONS WITH EUROPEAN PARTNERS

NATIONAL AUTHORITIES

- Licensing
- Inspection
- OMCL
- Pharmacopoeial Secretariat

EUROPEAN AUTHORITIES

- European Medicines Agency (EMA) London
- European Directorate for the Quality of Medicines & HealthCare (EDQM) Strasbourg
- European Pharmacopoeia
- OMCL
- Certification
- Certification of Suitability to monographs of the European Pharmacopoeia

COUNCIL OF EUROPE

- European Council
- European Parliament
- European Commission

EUROPEAN UNION

- European Commission (DG SANCO) Brussels
- European Medicines Agency (EMA) London
- European Directorate for the Quality of Medicines & HealthCare (EDQM) Strasbourg
- European Pharmacopoeia
- OMCL
- Certification
- Certification of Suitability to monographs of the European Pharmacopoeia

1. OMCL: Official Medicines Control Laboratories
2. Certification: Certification of Suitability to monographs of the European Pharmacopoeia
Elaboration of guidance and standards in the fields of blood transfusion, organ transplantation, pharmaceutical care and consumer health

These activities all began within the framework of inter-governmental co-operation through the Council of Europe (the first one was initiated during the 1950s).

Blood transfusion: the guiding principles are the promotion of voluntary, non-remunerated blood donation and mutual assistance of member states (e.g. in the exchange of blood-typing reagents and access to rare blood group donations).

Transplantation of organs, tissues and cells: this work is also based on the promotion of anonymous, voluntary, non-remunerated donations. The non-commercial use of products of human origin and therefore the fight against organ trafficking is one of the priorities of the EDQM.

The guiding principles for the EDQM’s activities in this area are to guarantee human dignity and protect donors and recipients. This latter principle means improving and promoting rigorous standards for quality and safety to protect not only the donor and recipient, but also the graft itself, which is a rare and precious resource.

The EDQM works to defend these major principles by elaborating guidelines in co-operation with the EU, WHO and other international organisations.

Pharmaceutical care: there are three main areas of activity:

- the classification of medicines as regards their supply;
- setting quality and safety standards in pharmaceutical practices and pharmaceutical care;
- minimising public health risks posed by the counterfeiting of medical products and related crimes.

For this latter activity, the Council of Europe and its EDQM have adopted a multi-level, anti-counterfeiting strategy comprising various aspects such as: legislative actions against pharmaceutical crime by means of the MEDICRIME Convention; awareness campaigns against illegal internet pharmacies; multi-sectorial training for officials from member states; increased inspection and testing activities, e.g. through the network of Official Medicines Control Laboratories; and finally a project named eTACT to ensure the traceability of individual packs of medicines using mass serialisation.

The EDQM is also involved in activities aimed at improving consumer health in Europe, in particular, by harmonising testing practices and the approaches used in the various member states to ensure the quality and safety of cosmetic products and packaging materials for food and pharmaceutical products. A network of Official Cosmetics Control Laboratories (OCCL) was established in 2010, which is open to member and observer states of the European Pharmacopoeia. The work programme of the network is focussed on strengthening inter-laboratory collaboration and the sharing of resources amongst market surveillance authorities. To promote the principle of mutual recognition of analytical results, Proficiency Testing Scheme (PTS) studies are carried out.
How does the European Pharmacopoeia benefit patients?

The objective of the European Pharmacopoeia is to provide common, harmonised quality standards in Europe for the control of medicines and the substances used to manufacture them (for human and veterinary use).

The European Pharmacopoeia’s legally binding character ensures that everyone has access to high quality medicines. This means a patient can buy a medicine (such as paracetamol tablets) in a pharmacy in any European country and obtain the same quality regardless of the brand or type of medicine (original product or generic).

How is the European Pharmacopoeia used in European states?

It is an official reference to serve public health and is part of the requirements for marketing authorisation of a medicinal product. European Pharmacopoeia quality standards apply throughout the entire lifecycle of a product.

They are legally binding and become mandatory on the same date in all 37 member states. Their legally binding nature is expressly laid down in the international Convention on the elaboration of a European Pharmacopoeia of the Council of Europe and the pharmaceutical legislation of the European Union.

What is the European Pharmacopoeia?

The Convention on the elaboration of a European Pharmacopoeia (an international treaty) was adopted by the Council of Europe in 1964 and laid the groundwork for the European Pharmacopoeia to ensure the quality of medicines in Europe.

The European Pharmacopoeia consists of monographs describing individual quality standards (sets of controlled tests applicable to a substance or ingredient) and general quality standards applicable to families of ingredients (such as fermentation products) or to dosage forms, as well as general methods of analysis e.g. dissolution test for solid dosage forms, uniformity of mass of single-dose preparations, etc. The European Pharmacopoeia covers all therapeutic areas.

SCOPE OF EUROPEAN PHARMACOPOEIA MONOGRAPHS*

- **Biologics products**: 3.3%
- **Chemicals**: 56.5%
- **Dosage forms**: 1.3%
- **Herbals**: 11.8%
- **Fats**: 6.3%
- **Radiopharm. products**: 3.1%
- **Human vaccines**: 3.4%
- **Vet. Vaccines**: 3.9%
- **Plastics**: 0.2%
- **Blood derivatives**: 1.4%
- **Antibiotics**: 6.7%
- **Gases**: 0.6%
- **Homeopathy**: 1.1%
- **Med. Devices**: 0.6%

*2011 data
What is the governing body of the European Pharmacopoeia? How does it work?

While the EDQM provides the technical secretariat services for the European Pharmacopoeia, the governing body is the European Pharmacopoeia Commission. All 37 member states and the European Union are represented and have the right to vote. The 25 observers including the World Health Organization (WHO) are welcome to attend its sessions.

Role of the Commission

The Commission determines the general principles applicable to the elaboration of the European Pharmacopoeia; it decides the programme of work of the European Pharmacopoeia, establishes specialised groups responsible for preparing monographs and appoints experts to these groups. It adopts these monographs and recommends the time limits within which its decisions shall be implemented within the territories of the contracting parties.
Sessions of the Commission

The Commission holds private sessions in Strasbourg three times a year, to adopt texts proposed by its groups of experts and to decide on its programme of work and general policies.

Items are added to the work programme in response to requests received by the Secretariat from the member states and Community authorities, based on current scientific and health issues in Europe.

Each delegation has one vote. In all technical questions, decisions of the Commission are taken by a unanimous vote among the national delegations that can cast votes. The Commission works in English and French - the official languages of the Council of Europe. From 1964 to 2013, there were 145 sessions of the Commission in Strasbourg and 16 terms of office of the Chair of the Commission. Chairs are elected for 3 years and they cannot be re-elected immediately.

Groups of experts respond to current scientific and public health issues

At the beginning, in 1964, there were 13 groups of experts. Currently, in 2013, there are 19 permanent groups supplemented by 50 “ad hoc” specialised working parties, which meet as required by the work programme. These working parties are created to enable the European Pharmacopoeia to deal with new scientific and technical developments.

For example, the European Pharmacopoeia Commission has recently approved the creation of several new working parties:

- Non-Biological Complexes Working Party to cover new topics such as nanoparticle solutions,
- Raw Materials for the Production of Cellular and Gene Transfer Products Working Party, which will elaborate text(s) on such raw materials including antibodies, basal media (for cell culture), serum/serum replacements, growth factors and cytokines,
- Host-Cell Proteins Working Party, which shall draft recommendations with regard to the development, validation and use of in-house or commercial kits or test methods for the detection and quantification of host-cell derived proteins.

The European Pharmacopoeia is elaborated collectively by experts from all the member states, from universities, national medicines control laboratories, national competent authorities responsible for medicines, inspectorates, as well as the pharmaceutical and chemical industries.

The experts are nominated by the national delegations and are appointed by the Commission on the basis of their expertise. All the meetings of groups of experts take place in Strasbourg, the headquarters of the Council of Europe.
How is the European Pharmacopoeia work programme implemented?

Within the EDQM, the European Pharmacopoeia Department co-ordinates the work programme of the Commission and its groups of experts. More than 800 European experts, from all the member states, participate in the work of the European Pharmacopoeia.

However to remain “state-of-the-art”, the European Pharmacopoeia has a continuous process for adding and revising quality specifications (in 2013, the 8th Edition of the European Pharmacopoeia was comprised of over 2500 monographs and general chapters).

As shown in the figure to the right, there is a continuous need to update monographs, taking account of new developments and requirements arising, for example, for scientific and regulatory reasons.

How quality standards are regularly reviewed and revised to remain “state-of-the-art”

The draft texts prepared by the groups of experts are published in a periodical called ‘Pharmeuropa’ for public consultation. The respective group of experts then analyses the comments, revises the text if necessary and submits it to the Commission for adoption.

The EDQM Laboratory Department makes an important contribution to the work of the European Pharmacopoeia.
ACTIVITIES RELATED TO MEDICINES

The need for reference standards

Most European Pharmacopoeia monographs refer to the use of reference standards (samples of thoroughly characterised substances, intended for use in the tests and assays described in the European Pharmacopoeia). The availability of these standards is essential for the application of the European Pharmacopoeia.

The collection of reference standards used for the implementation of the European Pharmacopoeia now consists of more than 2,500 substances or mixtures derived from chemical, biological or herbal origin. Their use extends far beyond the European continent.

The EDQM’s expertise in the establishment, production and distribution of pharmaceutical reference standards has been acknowledged by the WHO. For example, the EDQM is the WHO custodian centre for antibiotics. The EDQM prepares, stores and distributes the WHO International Standards for Antibiotics (ISA) and, since 2010, the EDQM is responsible for the establishment, storage and distribution of the WHO’s International Chemical Reference Substances (ICRS).

Specific activities in the field of biologicals

The Biological Standardisation Programme (BSP), a joint effort with the European Commission, pursues the following goals in the area of standardisation of biologicals: establishment of Biological Reference Preparations (BRP) and Biological Reference Reagents (BRR), development and validation of new analytical methods and validation of alternative methods based on the 3Rs concept i.e. the Refinement, Reduction and Replacement of animal experiments. To this end, collaborative studies are performed involving all interested partners, e.g. Official Medicines Control Laboratories (OMCLs) and manufacturers, both European and non-European. Whenever possible, such studies are run jointly with the WHO in order to economise the resources of participating laboratories and to add a worldwide dimension to biological standardisation. Since the start of the programme in 1992, over 115 projects have been initiated.

The efforts of the EDQM and, in particular, the BSP in the elaboration, validation and implementation of 3Rs methods are widely acknowledged, for instance by the European Partnership for Alternative Approaches to Animal Testing (EPAA), which is a high level initiative of the EU Commission and industry sectors. The EDQM is represented on the Steering Committee of the EPAA Vaccine project, as well as on the Technical Committee, and future studies will be run by the BSP.
The European Pharmacopoeia and International Harmonisation (Pharmacopoeial Discussion Group)

The European Pharmacopoeia is one of the co-founders of the Pharmacopoeial Discussion Group (PDG) set up in 1990 with the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP), this group meets twice a year. European, American and Japanese manufacturers’ associations in the pharmaceutical industry play an active role in identifying the priorities of the PDG work programme. The WHO participates as an observer at PDG meetings.

In line with the goals of The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the main objective of this programme of work is to provide common standards, harmonised between the three regions and beyond, so that for a product manufactured at the same site but marketed in different countries so that the manufacturer does not have to repeat testing according to different specifications for the various pharmacopoeias (Europe, Japan and United States).

The Ph. Eur. is also very supportive of the World Health Organization’s (WHO) initiative to achieve global pharmacopoeial harmonisation.

The European Pharmacopoeia: an unprecedented experience in the world

The European Pharmacopoeia is open to the world. Since 1964, it has successfully been carrying out harmonisation work between European countries (as of today, numbering 37). In addition, observer status can be granted to countries from all over the world.

The official edition of the European Pharmacopoeia is regularly updated in English and French, the two official languages of the Council of Europe. Both print and electronic versions (online and USB Key) are available.

Translations into other languages e.g. German, Hungarian and Polish are the responsibility of the member states.

Since December 2012, pharmacopoeial activities from monograph development until distribution of the Pharmacopoeia are ISO 9001:2008 certified by the official French standardisation body, Association française de normalisation (Afnor), via Afnor Certification (AFAQ).
The Certification procedure, established as a routine procedure in 1994, provides a centralised evaluation of the quality of substances for pharmaceutical use. The certificates granted by the EDQM are recognised by the states that have signed the Convention on the elaboration of a European Pharmacopoeia and by a number of other countries, e.g. Australia, Canada, Singapore, Saudi Arabia and South Africa. These certificates are referred to in the EU pharmaceutical legislation and can be used by marketing authorisation applicants to demonstrate the quality and compliance with the European Pharmacopoeia of the substances they use in the production of medicines.

The Certification procedure of the EDQM is based on a Resolution of the Public Health Committee (Partial Agreement) of the Council of Europe, which is regularly revised to deal with new risks to public health (the version currently in force is AP-CSP (07) 1).

The procedure concerns the evaluation of the quality of substances for pharmaceutical use with respect to the specifications prescribed in the relevant European Pharmacopoeia monograph(s).

It assesses whether the monograph(s) adequately controls the quality of a substance from a specific source. The certificate of suitability ensures that all the impurities related to the manufacturing process are satisfactorily controlled by applying the tests of the monograph, and if the monograph is not sufficient, it is supplemented with additional appropriate tests annexed to the certificate, for example to control residues for the solvents used.

There are currently more than 3500 valid certificates, which have been granted to manufacturers in 50 countries from every continent, for about 850 substances or preparations used in the manufacture of medicines.

In order for a manufacturer to be awarded a certificate, a detailed dossier is submitted to the EDQM. This dossier describes the manufacturing process and the tests performed on the raw materials and the substance produced. It demonstrates that the product complies with the quality required by the European Pharmacopoeia and European regulations and, in particular, that the monograph can be used to control the impurities. The applicant must also agree to comply with Good Manufacturing Practice (GMP).

The dossier is processed according to a procedure that guarantees the confidentiality of intellectual property and is evaluated by experts nominated by the national competent authorities of participating countries and appointed by the Steering Committee of the Certification procedure. To guarantee their impartial status, these experts sign a confidentiality agreement and declare the absence of conflicts of interest.
In 1999, the procedure was extended to include products with a risk of transmissible spongiform encephalopathy (TSE), thus enabling their certification on the basis of European Pharmacopoeia general chapter Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (5.2.8) and of the monograph on Products with risk of transmitting agents of animal spongiform encephalopathies (1483). General chapter 5.2.8 is a verbatim reproduction of the guidance issued by the European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) and by their Committee for Medicinal Products for Veterinary Use (CVMP).

The procedure was further revised to allow for the control of herbal drugs and herbal drug preparations. So far, six such CEPs have been granted, all of them for herbal drug preparations.

The EDQM inspection programme is an integral part of the Certification procedure and is elaborated in the context of the mandate given to the EDQM by the European Commission in application of Directives 2001/83/EC and 2001/82/EC as amended. It has been set up to verify compliance with Good Manufacturing Practices (GMP) and to ensure substances are indeed produced as described in the application for the Certificate of Suitability (CEP).

The EDQM is responsible for organising the inspections and their follow-up, including taking any subsequent action regarding related CEPs and communication with the authorities concerned.

The inspection programme is elaborated based on priorities recommended by the competent authorities of member states and is adopted by the Certification Steering Committee. The inspections are jointly carried out by:

- GMP inspectors from the competent authorities in the European Economic Area (EEA) or in countries which have a Mutual Recognition Agreement (MRA) with the EU in the GMP sector,
- EDQM inspectors having the same qualification.

About 30 on-site inspections are carried out each year, mainly in Asia. Overall, the EDQM has performed 283 inspections since the inspection programme started in 1999. Of these, 229 were carried out outside the EEA. Since 2003, the vast majority of the inspected sites have been outside the EEA as the production of substances for pharmaceutical use has largely shifted to non-European countries.

The EDQM’s Certification Division is also involved in a number of international projects on sharing information related to inspections of active pharmaceutical ingredients. This international co-operation has made it possible to cover a higher number of manufacturing sites worldwide and make best use of scarce resources.

The certification activities (both assessment and inspection) have been ISO 9001:2008 certified since 2009.

1. The European Economic Area (EEA) is an economic union consisting of 30 European states; the 27 member states of the EU and 3 of the 4 member states of the European Free Trade Association (EFTA).
4

Market surveillance programmes for medicines (OMCL Network)

ACTIVITIES RELATED TO MEDICINES

Since 1995, market authorisation procedures are in place in the European Economic Area (EEA) that result in identical products being on the market in EEA Member States. The establishment of a co-ordinated European approach for market surveillance of medicinal products was a necessary step to avoid duplication of work between member states.

Therefore, on 26 May 1994, the European Commission and the Council of Europe decided to set up a network of Official Medicines Control Laboratories (OMCLs). This was a new co-operative venture in the area of the quality control of medicines for human and veterinary use on the market.

While the creation of the European Network of OMCLs was favoured by the needs and impetus of the European Union, it was nevertheless established within the remit of the European Pharmacopoeia, which has a long tradition of European and international collaboration. Hence the Network is open to all countries that have signed the European Pharmacopoeia Convention and to its observers.

This international collaboration reduces public health expenses by pooling resources. The sharing of workload, resources and expertise among the competent national authorities makes it possible to avoid duplication of work and gives them access to the latest technologies and selective methods of analyses.

Levels of collaboration and work programmes

The role of the Network is to enable co-ordination of control activities throughout Europe and to influence future development through harmonised common standards.

Today, the Network consists of independent public laboratories that are appointed by the national authorities and are responsible for the quality control of medicinal products for human and veterinary use. There are two levels of collaboration:

- **general network**: member states of the Convention on the Elaboration of a European Pharmacopoeia and observer countries that are involved in the general activities of the Network; all official control laboratories are invited to participate in meetings and in collaborative studies in all the areas of general interest;

- **restricted network**: includes member states of the European Union and the EEA; a number of activities take place within the more restrictive regulatory framework for medicines in the European Union, notably those connected to the centralised (Community) authorisation, mutual recognition and decentralised procedures and to Official Control Authority Batch Release (OCABR) of biologicals. With respect to the latter, the restricted network also includes non-EU countries that have entered into specific agreements with the EU in relation to batch release, e.g. Switzerland.

This approach means that know-how can be shared and all parties can progressively attain the same level of quality assurance while respecting each party’s constraints.

Since 2010, the EDQM’s ISO 9001:2008 certification covers the co-ordination of the OMCL Network including organisation of market surveillance programmes, audits, training sessions, meetings and the management of related databases, as well as the co-ordination of the preparation of guidelines for OCABR of immunologicals and blood derivatives for human use.
Activity areas of general interest

- **Quality Management Programme (QM)**

The OMCL Network has developed and implemented a common approach for their quality management systems. This is a prerequisite for the increasing exchange of results and data and mutual recognition of results for OCABR of biologicals and results for market surveillance of products authorised via the centralised or decentralised mutual recognition procedure.

Work in the area of quality management systems has intensified since 1999.

This has resulted in the adoption of:

- a harmonisation programme for the quality management policies of all the members of the Network;

- a specific assistance and maintenance programme for quality management systems in the Network;

- guidelines on validation of analytical procedures used in testing programmes, evaluation and reporting of results, qualification of equipment and management and handling of reagents and reference standards.

Within the Network, it has been agreed to apply the quality standards of ISO/IEC 17025, and audits are also based on the European Pharmacopoeia and OMCL Guidelines. An annual programme of audits and visits of the different OMCLs of the Network is routinely performed.

In total, since the beginning of the QM programme in December 1997, 95 mutual joint audits, including 14 blank audits, 50 mutual joint visits, 2 tutorials and 18 training visits have been carried out in the OMCL Network, (as of December 2012). These figures demonstrate the strong commitment of the Network towards a common approach for upgrading their quality systems to a harmonised high standard and to benefit from each other’s experience.
ACTIVITIES RELATED TO MEDICINES

- New working groups to respond to current scientific and public health issues

In 2011, the Network decided to set up additional working groups on Active Pharmaceutical Ingredients (API) testing, counterfeit/illegal medicines testing and testing of unlicensed pharmaceutical preparations.

- Proficiency Testing Scheme (PTS) studies

To ensure that the results obtained by the various laboratories in the Network are comparable, proficiency testing scheme (PTS) studies are regularly carried out on basic methods of analysis. These studies help build mutual trust between OMCLs. They constitute an important component of an effective common system for quality management and the measurement of performance.

Every year studies are organised in the physico-chemical and biological areas. These studies are open to members of the Network, to manufacturers and universities. The programme is available online at the EDQM website.

Study programmes on specific topics are also set up jointly with the WHO and these are open to governmental control laboratories from Africa, Asia (South East Asia and Western Pacific), Europe and Central and South America.

The EDQM has also participated in a special ASEAN (Association of Southeast Asian Nations) training programme for PTS studies involving official control laboratories (central and regional) from countries of Southeast Asia and sponsored by the EU.

- Collaborative Market Surveillance Studies (MSS)

These studies are designed to compare the quality of medicinal products in the different member states and includes herbal drugs. They are developed in close collaboration with inspectors, national authorities and quality control personnel in the various countries.

Usually, several studies are organised each year, with the participation of national control laboratories of various countries of the Network. The results of these studies provide valuable information on the potential need to revise the relevant European Pharmacopoeia monographs and/or general chapters and methods.


Specific Community activities based on mutual recognition of testing

**The batch release procedure for human vaccines and blood-derived medicinal products**

The procedure is based on Article 114 of EU Directive 2001/83/EC as amended and is applicable to human vaccines and blood-derived medicinal products. The goal, through a review of manufacturers’ protocols and targeted OMCL testing, is to confirm that batches comply with the specifications defined in the relevant approved marketing authorisation dossier. It allows Official Control Authorities to test each batch of human vaccines and blood-derived medicinal products before they are placed on the market. Compliant batches receive a certificate that is accepted within the EU/EEA and Switzerland and is recognised as a sign of quality in other countries.

The activity of the Network in this area, which is co-ordinated by the EDQM, consists of elaborating guidelines that define the testing requirements for each product and establishing administrative procedures and guidance for OCABR-related activity in order to facilitate mutual recognition. Guidelines are published by the EDQM exclusively on its website.

The EDQM, on behalf of the EU Official Control Authority Batch Release (OCABR) Network, has signed a Memorandum of Understanding (MoU) with the Biologics and Genetic Therapies Directorate (BGTD) of Health Canada. The MoU, in force as of 27 July 2012, will see the participation of Health Canada in numerous OCABR network activities in the field of vaccines for human use and medicines derived from human blood and plasma.

**The batch release procedure and the batch protocol review for immunological Veterinary Medicinal Products (IVMPs)**

A series of product-specific guidelines and administrative procedures have been developed by the Network, which are co-ordinated by the EDQM in close collaboration with the EU Commission, the Veterinary Pharmaceutical Committee and industry.

Article 82 of EU Directive 2001/82/EC as amended, allows, for human or animal health reasons, a member state to request samples of each batch of a given IVMP to be submitted to a Competent Authority for testing by an OMCL before it is placed on the market and establishes conditions under which a restricted test scheme can be applied. This is referred to as the batch release procedure.

It involves testing of samples and a review of the manufacturer’s protocol to confirm compliance with the approved marketing authorisation. The results of the procedure must be mutually recognised. The Network regularly reviews the list of products eligible for batch release procedure testing using a restricted test scheme.

Compliant batches receive an EU certificate (as appropriate) which is accepted within the EU/EEA and Switzerland and is also recognised as a sign of quality in other countries.

The Network provides an effective platform for information exchange and work sharing through mechanisms that include regular meetings and electronic data exchange.
Surveillance of products that have received a Community Marketing Authorisation (CAP or Centrally Authorised Products)

Since 1995, Community Marketing Authorisations have been granted for innovative medicines that can then be marketed throughout the EU and the EEA. A co-ordinated approach to control their quality in the various markets is necessary and involves the OMCL Network of the European Union.

The selection of medicinal products to be included is based on an evaluation of the risk to public health and includes products for which testing has been requested by the EMA or its committees (CHMP and CVMP).

The procedure describes a common protocol for sampling and testing of products based on the collaboration between the EMA, the EDQM and the national authorities.

Products to be tested are sampled in three EU/EEA Member States. The samples are sent to the EDQM, which allocates them to national control laboratories for testing in accordance with well-established protocols derived from Marketing Authorisation (MA) dossiers. The EDQM collects the analyses and results and establishes a report that includes the quality control results and proposals for follow-up action if necessary. This report is then sent to the EMA.

In 2011, a pilot programme was initiated to test generic medicines that had received a Community Marketing Authorisation.

In all, OMCLs from 27 EU/EEA countries regularly participate in the testing phase of the programme. A total of 3771 quality parameters were tested between 1999 and 2012.
Studies on counterfeit and illegal medicines

Over the last decade, the laboratories in the Network have been increasingly involved in testing activities related to counterfeit / illegal medicines. OMCLs have initiated close collaboration with forensic laboratories in order to share their expertise in the quality control of medicines.

Since the end of 2006, study reports on counterfeit and illegal medicines have been standardised and are shared throughout the Network using a common data platform to which access is restricted to members of the Network.

In 2012, the first Market Surveillance Study on Suspected Illegal Products (MSSIP) was performed involving dietary supplements with a supportive slimming effect. After initial testing, it was proposed that this programme would develop and continue to expand in the coming years.

The performance of OMCLs in identifying (and, where possible, quantifying) unknown active pharmaceutical ingredients is checked on a regular basis in a specifically-developed programme called the Suspicious Unknown Products (SUP) programme.

Finally, since 2012, technical training programmes for Network members on testing of counterfeit and illegal medicines have been offered by the EDQM in collaboration with volunteering OMCLs that have technical expertise in this field.
Activities in the areas of blood transfusion; transplantation of organs, tissues and cells; pharmaceutical care; prevention of counterfeit medicines and consumer health protection

**Blood transfusion**

The work of the Council of Europe in the blood transfusion area started in the 1950s. The Committee in charge of enquiries relating to blood transfusion is the European Committee on Blood Transfusion (CD-P-TS).

This Committee bases its work programme on three major principles: the non-commercialisation of substances of human origin (voluntary and non-remunerated donation), the achievement of self-sufficiency, and the protection of the health of blood donors and recipients.

The primary responsibilities of the CD-P-TS, according to the terms of reference, are to:

- examine questions related to human blood transfusion, with regard to quality and safety standards and their implementation, including collection, preparation, storage, distribution and appropriate use;
- assist member states in improving and, if necessary, restructuring their blood transfusion services by promoting principles of voluntary non-remunerated donations;
- define and promote the implementation of quality and safety standards in the collection, storage, distribution and use of blood and blood components;
- propose ethical safety and quality standards on professional practices and on product specifications;
- ensure the transfer of knowledge and expertise through training and networking;
- monitor practices in Europe and assess epidemiological risks, in particular those related to the emergence of new transmissible diseases;
- ensure the availability of rare blood products by means of the European Database and Bank of Frozen Blood of Rare Groups.

The CD-P-TS (which is comprised of 35 members and 9 observer states, the EU Commission and the WHO) meets for two days in a plenary session, once or twice a year.

The following priorities have been set for the work programme:

- updating the "Guide to the Preparation, Use and Quality Assurance of Blood Components"; this is done by an expert working group consisting of members from Europe, Australia, New Zealand and the USA;
- establishing a database listing information on frozen blood units available for international exchanges;
- annual online reporting from the Council of Europe’s member states on the collection, testing and use of blood and blood components;
- addressing the issues of donor selection, e.g. through the elaboration of resolutions (e.g. Resolution CM/Res(2008)5 on “donor responsibility and on limitation to donation of blood and blood components”, adopted by the Committee of Ministers on 12 March 2008);
- addressing the issues in the field of blood supply management - a critical process for granting access of patients to blood components of suitable quality in the necessary amounts and guaranteeing optimisation of blood donation management.

Since 2010, inter-institutional cooperation with the EU Commission has been established to facilitate the implementation of Quality Management Systems in the field of blood transfusion.
Blood Proficiency Testing Scheme (B-PTS) Studies

These studies aim at assessing the performance of laboratories with regard to screening tests used for the qualification of individual blood donations. They constitute an important component of an effective common system for quality management and the measurement of performances of blood establishments.

Since 2010, nine studies have been organised for testing of nucleic acid amplification techniques (2 studies for Hepatitis C (HCV) and 2 studies for Human Immunodeficiency (HIV) viruses), serology (2 studies for Hepatitis B surface antigen (HBsAg) and 1 study for HIV antibodies) and immuno-haematology methods (2 studies for ABO grouping and Rhesus phenotyping).

Blood Quality Management Programme

This programme aims at helping blood establishments in implementing and improving their Quality Management System (QMS).

Mutual Joint Visits and Audits by peers are organised for blood establishments. This programme started in 2012 as a pilot phase programme. It should ultimately lead to the harmonisation of Quality Management policies in Europe and improve mutual confidence between European countries in the context of exchange of blood components, especially for the sourcing of plasma used for the production of blood-derived products.

Organ transplantation

The work of the Council of Europe in the area of organ, tissue and cell transplantation started in 1987 and actively contributes to the implementation of high standards for the protection of public health and for the promotion of human rights and dignity.

The committee responsible for this activity is the European Committee on Organ Transplantation (CD-P-TO). Forty-one countries from Europe and beyond are represented on this committee. It actively promotes the non-commercialisation of organ donation, the fight against organ trafficking and the development of ethical, quality and safety standards in the field of organ, tissue and cell transplantation. Its activities include the collection of international data and monitoring of practices in Europe, the transfer of knowledge and expertise between organisations and experts through training and networking and the elaboration of reports, surveys and recommendations.

The mission of the CD-P-TO is to:

• examine questions related to the transplantation of organs, tissues and cells, with regards to quality and safety standards and their implementation;
• monitor practices in Europe and assess risks linked to procurement, storage and transplantation of organs, tissues and cells;
• assist member states in improving their organ transplantation services whilst promoting the principle of voluntary non-remunerated donations;
• provide guidelines on ethical, quality and safety standards and their implementation;
• examine the organisational structures concerning organ transplantation with a view to addressing the causes of organ shortages;
• develop links between organ exchange organisations and experts throughout Europe and ensure the transfer of knowledge and expertise;
• contribute to raising the awareness of the general public on organ, tissue and cell donation for transplantation.
Additionally, the CD-P-TO regularly works on the elaboration of the following publications:

- **Guide to the quality and safety of organs for transplantation**: This Guide deals with different aspects of the organ transplantation process, from risk assessment to disease transmission, collating information to provide transplant professionals with a useful overview of the most recent advancements in the field. The 5th Edition of the guide is expected to be published in 2013.

- **Guide to the quality and safety of tissues and cells for human application**: The CD-P-TO is currently working on the elaboration of specific guidance for tissues and cells, which will be published in 2013. This new guide will provide sound information and guidance for all professionals involved in donation, banking, release, distribution and transplantation of tissues and cells for human application, and inspection of the associated establishments. The combination of all these standards will help optimise the quality and minimise the risks of these complex procedures, which will ultimately help improve the rate of successful tissue and cell clinical applications.

- **Newsletter Transplant**: The CD-P-TO elaborates Newsletter Transplant, which annually collates international figures on organ donation and transplantation.

As part of its effort to promote the non-commercialisation of organ donation and the fight against organ trafficking, the CD-P-TO, together, together with the European Committee on Crime Problems and the Committee on Bioethics from the Council of Europe, has been involved in the elaboration of a criminal law Convention to fight organ trafficking.

**Pharmaceuticals and pharmaceutical care**

Worldwide, it is estimated that half of all medicines are inappropriately prescribed or dispensed, and that half of all patients fail to take their medicines properly. Errors relating to medication use, lack of documentation on how medicines are prescribed, used and dispensed, as well as insufficient communication have a considerable impact on mortality and morbidity. The large amount of resources spent on the development and regulatory control of medicines are only reasonably invested if the medicine is used appropriately and the necessary information to ensure this is accessible to all.

The European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) oversees the work of three committees of experts related to the appropriate use of medicines and the prevention of counterfeit medicines and similar crimes.

**Classifying medicines into prescription and non-prescription medicines - balancing patient safety and accessibility of medicines**

The classification status of medicines authorised in Europe remains a competency of the individual countries. Based on Council of Europe Resolution Res AP(2007)1, the Committee of Experts on the classification of medicines as regards their supply issues recommendations to authorities for the classification of medicines, whether or not they are licensed for use in the EU.

Currently, recommendations for about 2400 substances are published in the database on the classification of medicines hosted by the EDQM, (www.edqm.eu/melclass). In 2012, a review of the recommendations was performed.
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 an individual patient. Pharmaceutical care is understood as a quality concept and working method for the responsible provision of medicine therapy for definite outcomes in the interest of patients’ quality of life.

The Committee of Experts on quality and safety standards in pharmaceutical practices and pharmaceutical care develops scientific indicators for measuring the quality of pharmaceutical care in Europe. The information provided through indicators is of practical utility for policy-makers and professional associations.

The preparation of medicinal products in pharmacies is not harmonised throughout Europe. To respond to this need, the Committee of Experts supports the development of legal texts and best practices in this field.

There is a demand for foreign traditional therapies, such as traditional Chinese medicines, in Europe. With a view to supporting safe practices, in 2012, the Committee of Experts developed models for curricula for therapists and health professionals in Europe and for balanced information for the European public.
The Council of Europe Convention on counterfeiting of medical products and similar crimes involving threats to public health (MEDICRIME Convention)

This Convention is the first international treaty that criminalises counterfeiting of medical products and similar crimes with a view to public health protection (http://www.conventions.coe.int). At the time of preparation of this brochure, twenty-two states had signed the convention, of which one had ratified it.

Part of the holistic anti-counterfeiting strategy of the Council of Europe/EDQM is to provide international support for the implementation of the MEDICRIME Convention, focussing on prevention and inter-disciplinary co-operation and drug enforcement. The EDQM also seeks to improve “know-how” among officials in terms of applying the provisions and best practice models described in the MEDICRIME Convention. This adds value to active co-operation under the Convention through synergies in protecting the legal supply chain and combating crime and the establishment of a strong evidence base for best practices, experiences, new criminal trends and harm and impact evaluations.

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

The Council of Europe/EDQM has made significant progress in its project for an anti-counterfeiting traceability service for medicines. The eTACT service aims to provide a traceability and mass-serialisation system that can be used by authorities and stakeholders (i.e. manufacturers, suppliers, distributors, healthcare professionals and patients) across the entire pharmaceutical supply chain, from the 37 member states of the European Pharmacopoeia and beyond.

Preventing and managing risks posed by counterfeit medical products and similar crimes to patients

Having been involved in the development and adoption process of the Council of Europe MEDICRIME Convention from the very outset, the relevant Committees continue to support the implementation of the MEDICRIME Convention, e.g. by supporting the implementation of relevant legislation, transfer of know-how and training, specific policy proposals and practical tools.

In the framework of the EDQM-supported training platform to combat medicrime, the Committee of Experts co-organised several regional training sessions with national authorities. At the time of preparation of this brochure, more than 180 officials from 40 countries in Europe and other regions of the world had participated.
Consumer health protection

Public health tasks and food were included in the Council of Europe’s agenda in 1959. Since 1 January 2009, the EDQM has been engaged in efforts to strengthen consumer health protection in Europe and to define common policies related to the quality and safety of cosmetics and packaging for food and medicines.

The Consumer Health Protection Committee (CD-P-SC) manages the related work programme. Two subordinate expert groups examine health-related matters and prepare reports and recommendations for improvements of policies and practices: the Committee of experts on packaging materials for food and pharmaceutical products (P-SC-EMB) and the Committee of Experts on cosmetic products (P-SC-COS).

These committees enjoy close co-operation with equivalent bodies in other international institutions; in particular, the Commission of the European Union, the European Food Safety Authority (EFSA) and the Joint Research Centre (JRC). Contact is also maintained with manufacturers and European manufacturer associations in each sector, which may participate in ad hoc working groups or may be consulted during the drafting process concerning new requirements.

In accordance with the terms of reference of the P-SC-COS, the Committee examines questions related to the use of natural or synthetic ingredients in cosmetics and responds to health risks posed by substances with pharmacological or toxic effects. This work aims at assisting national authorities in their work and also other professionals in the area of health and safety.

A new Resolution on safety criteria for cosmetic products intended for infants was adopted in March 2012 by the Council of Europe’s Committee of Ministers. Cosmetic products must be safe for the health of young children and should only contain ingredients that are non-toxic; potent allergens or substances with endocrine-disrupting activity should not be present and preservatives should be used at their lowest effective concentrations. “Safe Cosmetics for Young Children – A published Guide for Manufacturers and Safety Assessors” (2012, 1st Edition), provides detailed recommendations for the risk assessment of baby creams and lotions that were agreed by experts in the field.

Official Cosmetics Control Laboratories of many European countries have established a competence network to share the work linked to cosmetics surveillance. This network is open to Council of Europe member states and observers of the European Pharmacopoeia. The relevant competent national authorities were surveyed in 2010 to collect information about the national programmes and structures linked to cosmetics surveillance and on the benefits of pan-European collaboration and complementarity with the activities of the European Union. The long-standing experience with the network of OMCLs was an asset in the pilot phase.

Network activities include inter-laboratory studies, Proficiency Testing Scheme (PTS) studies, Market Surveillance Studies (MSS) and the implementation of harmonised quality management systems. Priority is given in the network to testing products that may present a health risk for consumers, either linked to the presence of prohibited or restricted substances (according to EU legislation) or to trace metals.
HOW TO CONTACT THE EDQM?

Information and orders via the Internet:
www.edqm.eu

Questions must be submitted through the HELPDESK, which is accessible on the EDQM Internet site:
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