# ANNUAL REPORT
2016

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

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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# ANNUAL REPORT 2016

European Directorate
for the Quality of Medicines
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Council of Europe, EDQM

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# Foreword

*by Susanne Keitel, Director*

Throughout 2016, the EDQM continued to deliver against its mission of promoting and protecting human and animal health. The diversity and abundance of results mentioned in this report show the relevance of our work in ensuring the basic right of access to good quality medicines and healthcare.

In the field of quality standards, the major milestone of 2016 was the publication of the 9th Edition of the European Pharmacopoeia (Ph. Eur.) which, compared to the 8th Edition published 3 years ago, contains more than 50% revised or new texts, including newly developed methods and techniques. At the EDQM we strive to ensure scientific value and excellence in all our activities, and this new edition of the Ph. Eur. was kept well abreast of the latest developments in the field of pharmaceuticals: a new monograph for *Etanercept* proved how specifications are compatible with the development of high quality biotherapeutic products, including biosimilars, while a new chapter on Chemical imaging was the first of its kind to be introduced in any pharmacopoeia worldwide. This was also the case for a new chapter in the Ph. Eur. on *in vitro* methods for the quality control of vaccines, developed in accordance with the Council of Europe's European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.

The expertise of the working groups supporting the Ph. Eur. Commission was also renewed in 2016, with more than 700 experts appointed for a new term, together with a new Chair of the Commission and two new Vice-Chairs. For the first time, experts from non-Ph. Eur. member states were also appointed - a key move reflecting the increasingly common extra-European production of pharmaceutical ingredients and finished products. Spread across 71 working groups, these experts bring added value to the scientific relevance of the Ph. Eur. and also represent its international vocation, which was further reinforced in 2016 by the addition of 2 new observer states: India and Japan.

International standards, as well as international cooperation and harmonisation in the public health sector, were also strenuously promoted across our activities. This resulted in a 5-year Memorandum of Cooperation signed with the Japanese Pharmaceutical Safety and Environmental Health Bureau. Also, our new role as observer to the International Conference on Harmonisation (ICH), the project that brings together regulatory authorities and industry in the pharmaceutical field from all around the globe, will allow us to keep abreast of scientific and technical aspects of medicines authorisation at global level. Our regular meetings with observer states to the Ph. Eur., for example, the international workshop organised between the Chinese and European Pharmacopoeias, also strengthened collaboration to this end.

We also obtained an excellent return on our investment in enhancing cooperation, recognition of procedures and dissemination of best practices. We continued to take part in a number of international platforms throughout 2016: bilateral confidentiality agreements were signed with new countries and joint inspections were carried out.

Cooperation was also a major priority for our work with the Official Medicines Control Laboratories (OMCL) Network, through which the EDQM supports member states in ensuring that no substandard product reaches European patients. New sets of guidelines further harmonised quality management systems, providing a solid basis for streamlined exchanges of results and data across Europe.

We remained committed to the fight against falsified medicines: we continued to encourage the ratification of the Council of Europe's Medicrime Convention, which entered into force at the beginning of 2016 in 5 countries and was ratified by another 4 in the course of the year. As part of our anti-counterfeiting activities, we also maintained our support for health and law enforcement authorities on cases of suspicious medical products.

Work continued on quality standards for organ transplantation, with new guidance on the quality and safety of organs for transplantation providing updated recommendations for the deceased donation process and advice on the key decisions that follow. The European Commission participated actively in the work on these subjects, to ensure consistency between European Union (EU) Directives and the Council of Europe standards. The EDQM also reached out to the general public with new plain language brochures that provide important information on organ transplants. As far as our blood transfusion activity is concerned, I would also like to highlight how our new guidelines on quality management systems for blood establishments were adopted by the European Commission as a legal standard in the EU.

Important results were obtained in relation to enhancing pharmaceutical care, as new resolutions adopted by the Council of Europe brought further harmonisation in public health systems and their performances. Cooperation was also a priority in the field of consumer protection with the European Network of Official Cosmetics Control Laboratories (OCCLs). Resource-pooling between members and coordination of Europe-wide market studies enhanced the way cosmetic products are controlled in Europe.

The support offered to the EDQM by national regulatory authorities throughout 2016 has been of particular importance. I wish to express once more my gratitude to all, in particular the Czech authorities for their support in organising the annual National Pharmacopoeia Authorities meeting in Prague, the French authorities for organising with us the annual meeting of the General European OMCL Network in Paris, the Estonian authorities for their help in preparing the conference marking the publication of the 9th Edition of the European Pharmacopoeia in Tallinn and the Norwegian authorities for the organisation of the first Medicrime workshop for GMDP and Pharmacy Inspectors.

And of course – as always – I must acknowledge the fact that the EDQM's achievements in 2016 would not have been possible without the remarkable efforts of our experts. Joining us from national and European authorities, universities, scientific institutes and industry, these experts have made an invaluable contribution to our work with their excellent scientific competence. To all of them, as well as to the dedicated staff at the EDQM, I offer my heartfelt thanks.


# Quality and use of medicines

## THE EUROPEAN PHARMACOPOEIA

### What it is and how it works

The European Pharmacopoeia (Ph. Eur.) lays down quality standards for the manufacture and control of medicines in Europe and beyond. The texts of the Ph. Eur. are elaborated and revised by a panel of 71 groups of experts and working parties which may be convened or disbanded by the Ph. Eur. Commission, which is the decision-making body of the Ph. Eur., depending on current regulatory, industrial and technical needs. Since the participation of external stakeholders and users in the Ph. Eur.'s public standards-setting process is vital for the development of authoritative and relevant monographs, these groups comprise representatives of industry, academia and the national competent authorities. Mainly covering excipients and active pharmaceutical ingredients (APIs) both in their original state and in the form of pharmaceutical preparations, Ph. Eur. monographs are legally binding across the 37 signatory member states of the Council of Europe's Convention on the Elaboration of a European Pharmacopoeia and are used in over 100 countries worldwide. 2016 was a milestone year since it saw the publication of the 9th Edition of the Ph. Eur. which contains 2343 monographs (including dosage forms), 359 general texts (including general monographs and methods of analysis) and around 2650 descriptions of reagents.

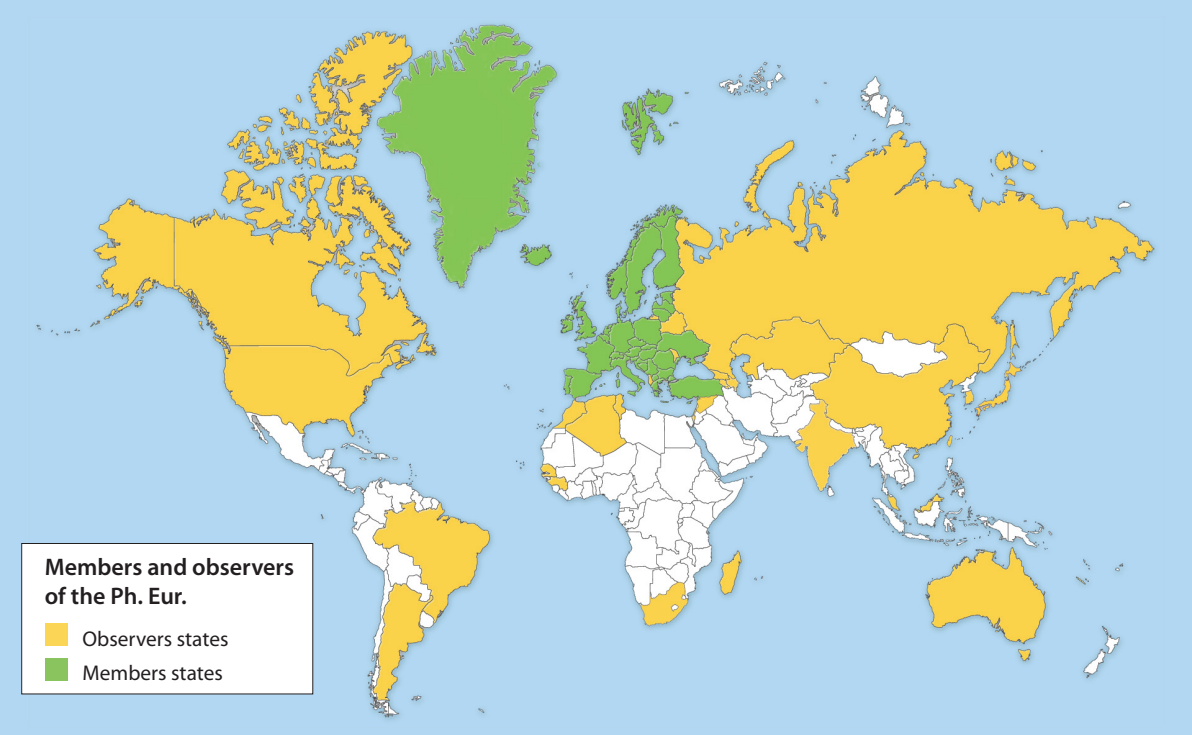
### The importance of the Ph. Eur. beyond Europe

To reflect the global status of the Ph. Eur. and keep pace with the far-reaching changes the pharmaceutical world has undergone over the past 50 years which have created a globalised operating environment for APIs and finished products, the Ph. Eur. Commission decided in 2015 to review its working procedures to allow the nomination of experts from non-Ph. Eur. member states. This decision is part of a specific policy to further involve observer states, as well as manufacturers from outside Europe, in the work of the Ph. Eur. This new policy was applied for the nomination of the Ph. Eur. experts in November 2016. This wide variety of cultural and scientific backgrounds of these experts, all volunteers, testifies to the international scope and reach of the Ph. Eur.

### Key facts and figures

#### Wide participation

37 member states and the EU are signatories of the Convention on the Elaboration of a European Pharmacopoeia. The number of observer states has grown to 30 with the addition of India and Japan in 2016.




## The Work Programme 2016

Year-on-year, the European Pharmacopoeia Commission works to provide the end-users of the Ph. Eur. with the most up-to-date and relevant information possible, revising existing monographs to incorporate newly developed methods and techniques and approving new texts for products of high market relevance. The work programme for 2016 continued to reflect these efforts: 26 new monographs were adopted (including 4 on patent-protected active substances, which were elaborated in close collaboration with regulators and the respective innovators), 4 new general chapters were added and 168 texts were revised to incorporate regulatory changes and scientific progress. In addition, during its 156th session in November 2016 the Commission appointed more than 700 experts to its groups of experts and working parties.

The work on creating relevant standards for new and emerging areas also continued throughout 2016.

The Ph. Eur. Commission adopted a new general and non-binding chapter on *Host-cell protein assays* (*2.6.34*), which provides guidance on the development and validation of host-cell protein (HCP) assays used to test products obtained through recombinant DNA technology.

The monograph on *Water for Injections (0169)* (WFI) was revised to include the use of non-distillation technologies for the production of WFI, in addition to distillation technologies. This monograph revision is the result of extensive consultations with stakeholders; it is based on the outcome of a survey conducted by the EDQM in March 2010 to gather data on the use of non-distillation technologies to produce *Water for Injections*, and it also takes into account the feedback from the EDQM's expert workshop on *Water for Injections - Potential Use of Membrane Systems for the Production* of March 2011. It was finally adopted by the Ph. Eur. Commission for publication in 2016.

The general monograph on *Substances for Pharmaceutical Use (2034)* was revised to clarify the requirements for the bacterial endotoxin test and align them with the policy on the same topic approved by the Ph. Eur. Commission at its 149th Session in June 2014. This revision goes hand-in-hand with the revision of the chapter on *Guidelines for Using the Test for Bacterial Endotoxins* (*5.1.10.*), published in Ph. Eur. supplement 8.8, which also includes recommendations for establishing limits, as well as information on how to evaluate the pyrogenicity of substances. The reference to the *Guideline on the Limits of Genotoxic Impurities* published by the European Medicines Agency (EMA) has also been replaced with a reference to the new guideline of the International Conference on Harmonisation (ICH), Guideline on Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (ICH M7).

The adoption of the *Omega-3-acid Ethyl Esters 90 (1250)* monograph represented a significant step forward in the quality control of this substance, which is used as an active ingredient in medicinal products approved in Europe for the treatment of hypertriglyceridemia, and as an adjuvant treatment in secondary prevention following myocardial infarction.

With the adoption of the monograph on *Sodium pertechnetate (99mTc) (accelerator-produced) injection (2891)*, the Ph. Eur. Commission provided a viable alternative to the production of molybdenum-99 in nuclear reactors. The technetium-99m covered by this monograph can in fact be produced directly by proton irradiation of stable molybdenum-100 in accelerators such as cyclotrons.

This may compensate for future shortages or provide an additional production route for technetium-99m, as the existing network of cyclotrons in nuclear medical departments is already capable of producing technetium-99m in an emergency.

The P4Bio pilot phase came to a successful conclusion at the 156th Session of the Ph. Eur. Commission with the adoption of the monograph for *Etanercept* (*2895*), further proof that the standardisation challenges related to the complexity and heterogeneity of biotherapeutics can be overcome and that monograph specifications are compatible with the development of biosimilars.

A new chapter on the *Substitution of in vivo methods by in vitro methods for the quality control of vaccines (5.2.14)* was adopted to facilitate the transition from *in vivo* to *in vitro* methods. It provides guidance on how to validate alternative *in vitro* methods in cases in which a direct head-to-head comparison with an existing *in vivo* method is not possible. Specific recommendations on the substitution of *in vivo* potency and safety tests are provided in the Chapter, together with practical examples. As part of the revision of the general texts on *Tests for extraneous agents in viral vaccines for human use (2.6.16)* and *Cell substrates for the production of vaccines for human use (5.2.3)* adopted by the Ph. Eur. Commission, the tests in adult mice and guinea pigs were deleted. In addition, it was decided that tests in suckling mice and control eggs should be used only when a risk assessment had indicated that they could provide risk mitigation. With the adoption of these new and revised texts, the Ph. Eur. Commission demonstrated once again its commitment to reducing animal usage wherever possible in pharmacopoeial testing. The Ph. Eur. Commission encourages all those concerned by this work to seek alternative procedures in accordance with the Council of Europe's *European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes*.

The Ph. Eur. Commission also adopted a chapter on *Chemical Imaging (5.24)*, the first of its kind to be introduced in any pharmacopoeia worldwide. Produced by the Ph. Eur. Vibrational Spectroscopy and Analytical Data Modelling Working Party (VSADM), this non-mandatory chapter provides specific recommendations for assessing the performance of chemical imaging systems for the purpose of qualitative and quantitative investigations.

The Ph. Eur. Commission further fine-tuned its implementation strategy for the ICH Q3D Guideline on elemental impurities and adopted the revised versions of its general monographs on *Substances for pharmaceutical use (2034)* and *Pharmaceutical preparations* (*2619*), as well as revised versions of the general chapters on *Elemental Impurities (5.20)* and on *Determination of elemental impurities (2.4.20)*.

## General matters and policies

### Individual monographs on complex molecules – example of a monoclonal antibody

In 2016 the Ph. Eur. Commission reviewed the pilot phase for elaborating texts on monoclonal antibodies, using infliximab as a case study. In light of the conclusive experimental data generated by Ph. Eur. experts in support of the elaboration of a monograph on *Infliximab concentrated solution (2928)*, the Ph. Eur. Commission decided to launch this draft monograph for public comment in edition 28.4 of Pharmeuropa online. The decision on whether or not to publish this monograph in the Ph. Eur. will be taken by the Commission on the basis of the outcome of this public enquiry, which will therefore conclude the pilot phase.

### Standard Terms

Initially drawn up at the request of the EU Commission for use in marketing authorisation applications, the lists of Standard Terms provide users and prescribers with harmonised vocabularies to describe dosage forms, routes of administration, units of presentation and packaging of medicinal products. Following the substantial overhaul of the Standard Terms database in late 2014, a further major update in 2016 introduced various new elements: the "Units of presentation" terminology, a mapped terms function to allow external databases across the world to introduce and map their own terms against Standard Terms, and web services (also known as application programme interfaces) allowing registered users to extract data directly from the database. By the end of 2016, the free online Standard Terms database had almost 15 000 registered users and held 952 individual Standard Terms concepts translated into 33 languages for a total of more than 25 000 entries.

### Biological Standardisation Programme

The Biological Standardisation Programme (BSP) is a joint EU/Council of Europe initiative. Its mission is to establish reference materials for biologicals and to develop and validate new analytical methods for

the quality control of biologicals, including alternative methods for the replacement of animals in laboratory experiments based on the 3Rs principle (Refine, Reduce, Replace).

In 2016, the programme ran 29 projects in different fields, from vaccines for human and veterinary use to plasma-derived and biotechnology products. Four were concluded in the year, leading to the establishment of 4 new reference standards (*see "Pharmaceutical Reference Standards", page 11*).

The EDQM carried forward another 7 projects aimed at establishing replacement batches for existing reference standards. All were prompted by low stocks, and not by quality issues with existing standards, so it was not necessary to stop using a reference standard owing to quality issues. Eight projects for the elaboration of reference standards for new monographs or new requirements in existing monographs were also pursued.

Ten projects focused on the development of new compendial methods, and 6 of these were dedicated to applying the 3Rs principle to the field of quality control of biologicals. The continued efforts of the BSP to elaborate, validate and implement analytical methods in line with the 3Rs principle are widely acknowledged. As a result of one of these BSP projects, the Ph. Eur. will include a new standardised CHO-based clustering assay for detection of residual pertussis toxin in acellular pertussis vaccines. This test will replace the *in vivo* Histamine Sensitisation Test (HIST), and a reference standard supporting the new protocol is currently being established by the BSP.

## International harmonisation and the Pharmacopoeial Discussion Group

The Ph. Eur. continued its efforts to reduce unnecessary duplication of testing and reporting during drug development through the work of the Pharmacopoeial Discussion Group (PDG) – comprising the Ph. Eur., the Japanese Pharmacopoeia (JP) and the United States Pharmacopoeia (USP) as members, as well as the World Health Organization (WHO) as an observer. Two meetings were held in 2016, one hosted by the EDQM in Strasbourg (France) in May and the other by the JP in Tokyo (Japan) in October.

Currently, 30 of the 36 General Chapters and 49 of the 67 excipient monographs on the work programme have been harmonised. Last year's meetings saw the approval of a new monograph on *Hydroxyethylcellulose* and a new general chapter on *Colour (Instrumental method)*. Other relevant approvals included the revisions of the monographs on *Ethylcellulose* and *Cellulose acetate*, as well as the revision of the *Amino Acid Determination* chapter. In-depth discussions were carried out on a number of additional items currently on the work programme, with a view to resolving outstanding issues and bringing the items closer to approval. Highlights summarising the outcome of all PDG meetings are available on the websites of the three pharmacopoeias.

In order to make the best use of the scarce resources available to the three pharmacopoeias and respond to the need for new excipient monographs of interest across the three regions, it was agreed to add 5 new items to the work programme: *Isostearyl alcohol*, *Myristyl myristate*, *Polysorbate 65*, *Sodium cetyl sulfate* and *Calcium silicate*. With the exception of the latter (a major revision for the USP), these will be the first excipient monographs to be elaborated within the PDG and using a prospective approach to harmonisation. With these additions, the PDG work programme included 67 excipients at the end of 2016.

Following approval by the ICH of the Q3D Guideline for Elemental Impurities, PDG members confirmed their commitment to harmonising the general chapter on testing procedures for elemental impurities. Given the importance of this chapter, the PDG made significant efforts to ensure that a Stage 4 draft would be ready for public enquiry.

The PDG also focussed on another key chapter on its work programme, *Chromatography,* and expects to issue a Stage 4 draft for public enquiry in the course of 2017.

## Further harmonisation initiatives

The Ph. Eur. is actively involved in a number of other harmonisation initiatives at international level. It takes part in the International Meeting of World Pharmacopoeias, which is organised under the auspices of WHO and brings together the different pharmacopoeias to discuss possible ways of strengthening harmonisation. One example of the work accomplished is the WHO initiative to draft Good Pharmacopoeial Practices (GPhP) as a basis for cooperation and work-sharing among the pharmacopoeias of the world.

The 7th International Meeting of World Pharmacopoeias took place in September 2016 in Tokyo (Japan) and was hosted by the JP. This was an occasion for the pharmacopoeias present to discuss the outstanding annexes of the GPhP core document, i.e. the glossary, the future chapters and annexes on compounding and the monographs on herbal medicines.

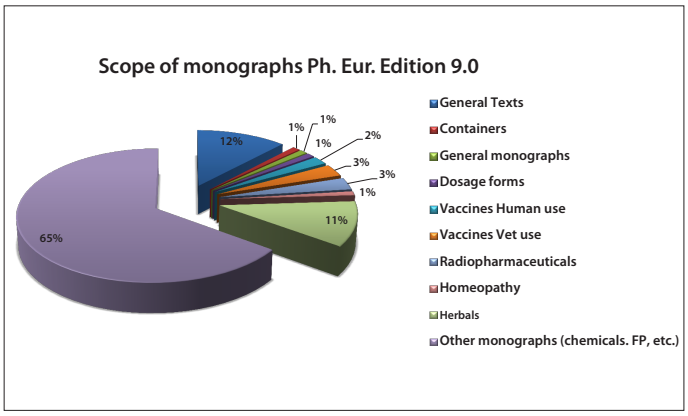
## Cooperation with National Pharmacopoeia Authorities

The EDQM organises an annual meeting of National Pharmacopoeia Authorities (NPAs) of Ph. Eur. member states to facilitate and coordinate activities of common interest, and to provide an informal forum for exchanging information. The 2016 event took place

in April in Prague (Czech Republic). It was hosted by the State Institute for Drug Control of the Czech Republic (SUKL) with 21 of the 37 member states in attendance. Among other topics, discussions focused on preparations for the re-appointment of all Ph. Eur. experts, which took place later in the year.


## Publications, databases and website

The 9th Edition of the European Pharmacopoeia (with its latest Supplement 9.2) contains 2343 monographs (including dosage forms), 359 general texts (including general monographs and methods of analysis) and around 2650 descriptions of reagents.




Pharmeuropa online is the free online publication, in which draft Ph. Eur. texts are published for public consultation. Easily and widely accessible, Pharmeuropa online aims to optimise interactions between the Ph. Eur. Commission and its stakeholders: it allows interested parties more time to leave comments on drafts and ensures greater access to all stakeholders across the globe. Texts are published on an on-going basis, but comments can be submitted on the basis of four deadlines per year. In 2016, 157 draft texts were published on Pharmeuropa online, which was accessed from 155 countries worldwide in the course of the year.

## REFERENCE STANDARDS

### What are reference standards and why are they needed?

### Ph. Eur. reference standards

Official reference standards (RSs) are essential to the quality standards in the Ph. Eur. as they are used in conjunction with the documentary texts and are produced specifically for use with the tests described. Reference standards include chemical reference substances (CRSs), herbal reference standards (HRSs), biological reference preparations (BRPs), biological reference reagents (BRRs) and reference spectra. Ph. Eur. RSs are established by the EDQM and officially adopted by the Ph. Eur. Commission. It is the official Ph. Eur. reference standards which are authoritative in case of arbitration.

The RS portfolio is subject to change, for example when new RSs are introduced to meet the needs of new or revised Ph. Eur. texts, or when replacement batches are added after corresponding stocks run out. The lifecycle management of the RS portfolio also covers all the tasks related to laboratory studies establishing RSs: from the procurement and characterisation of candidate materials, their storage, distribution, labelling and packing, to quality control, quality assurance, release and monitoring.

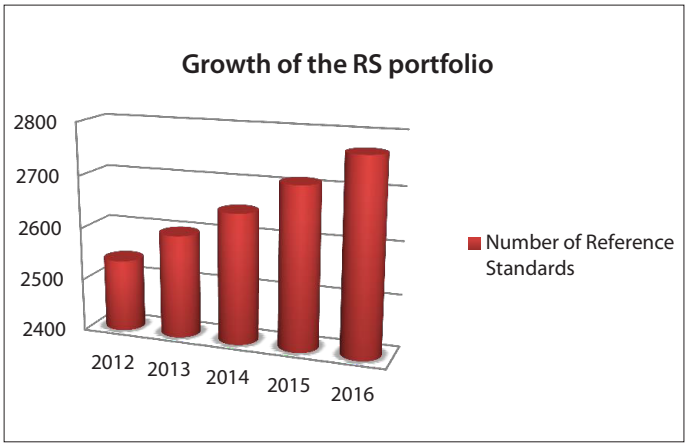
### Responsibility for WHO standards

The EDQM is responsible for the establishment, storage and distribution of WHO International Standards for Antibiotics (ISA). ISA are essential for the standardisation and quality control of antibiotic drug substances and medicinal products; they are supplied worldwide to be used in microbiological assays performed for the quality control of antibiotics.

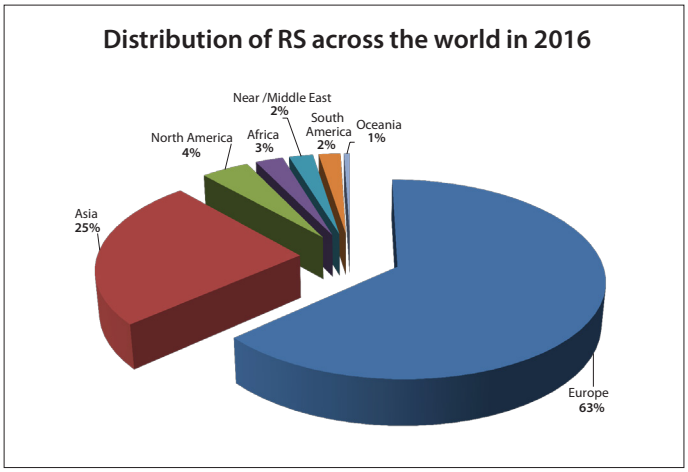
The EDQM is also responsible for the establishment, monitoring and distribution of WHO International Chemical Reference Substances (ICRS). These reference substances are used in conjunction with the monographs and texts of the International Pharmacopoeia, which is published and maintained by the WHO and used worldwide.

## Key facts and figures

At the end of 2016, there were 2768 reference standards in the Ph. Eur. catalogue.




Globalisation of the pharmaceutical industry means that Ph. Eur. RSs are widely used around the world: in 2016, the EDQM distributed Ph. Eur. RSs to 115 countries.




### RSs adopted in 2016

In 2016, the Ph. Eur. Commission adopted 84 new and 220 replacement RSs.

The RSs used for assays must be thoroughly characterised before they can be assigned a quantitative content value. In 2016, the EDQM Laboratory established 62 assay RSs, 24 of which required inter-laboratory studies involving official national control laboratories and other centres of excellence.

The international collaborative studies performed by the BSP in 2016 led to the conclusion of 4 projects and to the adoption of 2 new BRPs by the Ph. Eur. Commission (*Hepatitis E virus RNA for NAT testing BRP* and *Hepatitis A virus RNA for NAT testing BRP*) and 2 replacement batches (*Human coagulation factor IX concentrate BRP and Poliomyelitis vaccine [inactivated] BRP*) (*See "The European Pharmacopoeia", page 7*).

## EDQM activities for WHO

The EDQM is an observer to the WHO Expert Committee on Specifications for Pharmaceutical Preparations and the Expert Committee on Biological Standardisation. The tasks entrusted to these Committees include the development of standards and guidelines to promote the quality assurance and quality control of medicinal products around the world.

### International Chemical Reference Standards

In 2016, the ICRS board adopted a total of 2 establishment reports submitted by the EDQM Laboratory: *Dextromethorphan for SST ICRS 1* and *Capreomycin ICRS 1*.

### ISA

No need to establish replacement batches for any of the existing ISA emerged in the course of 2016.

## General matters and policies

## Extended competence in RS characterisation

Thorough characterisation of candidate materials is an essential part of successful reference standard establishment. In its continuous effort to improve characterisation and remain abreast of rapidly evolving technologies, the EDQM Laboratory has further developed its competence in the characterisation of reference standards through quantitative Nuclear Magnetic Resonance (NMR) and Mass Spectrometry (MS). As a result, the Laboratory successfully took part in a pilot key comparison study organised in 2016 by the intergovernmental organisation for matters related to measurement sciences and standards, the BIPM.

## Collaboration with the ISO

The EDQM participates as an observer in the activities of the International Organization for Standardization (ISO) Committee on Reference Materials.

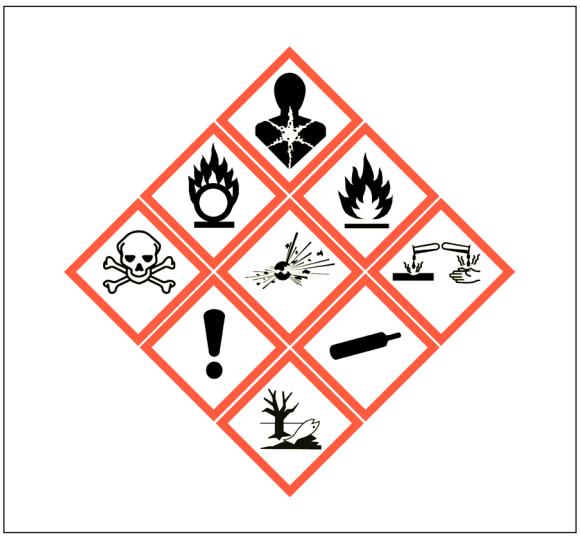
In 2016, the EDQM also played an active role in the ISO Drafting Group for ISO 17034 General requirements for the competence of reference material producers. This is the ISO standard that specifies the requirements for the production of all reference materials, including certified reference materials.

## Collaboration with national laboratories

Some RSs (generally for assay/potency tests) are established through collaborative studies involving several laboratories. Continuous collaboration with national laboratories and centres of excellence is fundamental for these studies, and in 2016 37 Official Medicine Control Laboratories from 26 different countries provided their contribution .

## Publications, databases and website

Throughout 2016, the EDQM continued to run and maintain its Online Database which gives access to all reference standards officially valid for the uses prescribed in the European Pharmacopoeia monographs. The database is designed to help users locate the standards they need as quickly as possible. RSs can be searched by code, name, monograph number or CAS number and RS Batch Validity Statements (BVSs) can be printed out by users in order to document the validity of the particular RS batch supplied at the time of use. Downloadable Safety Data Sheets, Safety Data Statements and leaflets are also available from the EDQM's Online Database[1].



In 2016, the EDQM issued 363 leaflets giving RS users additional information such as a typical chromatogram, assigned value, etc. for a given substance. By the end of 2016, a leaflet was available for each RS.

In addition, 2467 Safety Data Sheets (for hazardous chemicals only) and Safety Data Statements have been either created or updated (for materials outside the scope of the Registration, Evaluation, Authorisation and Restriction of Chemicals Regulation [REACH], such as biohazards and harmless chemicals). Safety Data Sheets are translated into 24 languages. This brings to a total of 58 382 Safety Data Sheets and Safety Data Statements, all directly downloadable from the EDQM website.

# CERTIFICATION OF SUITABILITY TO THE PH. EUR. MONOGRAPHS

## Why Certification is more important than ever

As the world's economy continues to evolve, extra-European production of pharmaceutical ingredients has become increasingly common. This creates new challenges for authorities as regards the monitoring and quality control of substances used in the manufacture of medicines.

The Certificate of Suitability (CEP) procedure has been set up to evaluate and validate the capacity of Ph. Eur. standards to control the quality of substances used in the manufacture of medicinal products. To apply for a Certificate, manufacturers must submit a dossier describing how their product is manufactured and how its quality is controlled. The EDQM evaluates the data in this dossier and may then grant a CEP. The procedure centralises the evaluation of data for the benefit of regulatory authorities and industry, and contributes to keeping the relevant Ph. Eur. monographs up to date.

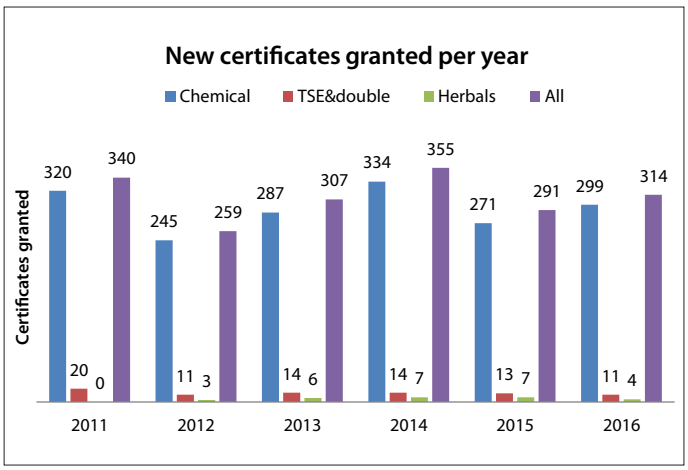
The EDQM also carries out inspections of manufacturing and/or distribution sites of drug substances covered by CEPs, to ensure that Good Manufacturing Practices (GMPs) are enforced and that the information supplied under the Certification Procedure is accurate.

An increasing number of licensing authorities worldwide accept CEPs to support (fully or partially) the quality section of the registration file submitted for substances used in medicinal products.

1. The Online Database can be accessed: https://crs.edqm.eu/

## Key facts and figures

The EDQM received 305 new applications and 1684 requests for revision of CEPs in 2016, and 314 new certificates and 1263 revised certificates were issued. Overall, about 90% of applications received were dealt with within official timelines.




In order to assess the applications, the Certification Department relied on a network of about 100 assessors from 25 different competent authorities, which were joined by the licensing authority of Croatia in 2016.

There are currently more than 4400 valid CEPs covering chemical purity, the risk of transmissible spongiform encephalopathy (TSE) and herbal drug preparations.

As part of the EDQM inspection programme, 40 manufacturing sites across the world were inspected in 2016. These inspections were conducted jointly with inspectors from national supervisory authorities. In addition, by exchanging data with inspectorates from member states and international partners, the EDQM obtained information on compliance with Good Manufacturing Practices (GMP) for 39 other sites. In some cases, actions were taken on CEPs after EU/EEA supervisory authorities issued statements of non-compliance.

The non-compliance rate for sites inspected by the EDQM was 18%, which is the same as in 2015. It was estimated that, by the end of 2016, about 60% of the sites located in Asia and covered by CEPs had already been inspected under this programme.

## General matters and policies

In the course of 2016, the Certification Department published a number of guidelines and policies[2] to support applicants in their communication with the EDQM and in the preparation of their CEP dossiers.

The ICH Q3D "Guideline on elemental impurities" triggered a major change in the assessment of CEP dossiers for chemical purity. In August 2016, the EDQM published a policy for the assessment of new and revised CEP applications.

In 2016, the EDQM also reviewed its roadmap for the submission of CEP applications in electronic format, with the result that paper dossiers were no longer accepted from June 2016. The EDQM expects to move towards the exclusive use of the Electronic Common Technical Document (eCTD) format within the next 4 years (with the exception of TSE/BSE dossiers and of substances for veterinary use only).

## Communication with partners and stakeholders


*EDQM stand at the CPhI trade exhibition, Mumbai (India)*

In 2016, the Certification Department continued to take part in a number of international platforms for collaboration, such as the International Generic Drugs Regulatory Pilot (IGDRP), the European Union's Working Group on Active Substance Master File Procedures (ASMF WG), the international API inspection programme, the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and the ICH Q11 Implementation Working Group.

Also in 2016, bilateral confidentiality agreements were signed between the EDQM and the health authorities of Armenia, Israel and Japan to allow the exchange of confidential information on the quality of active substances.

2. https://go.edqm.eu/CEPgl

As part of its collaboration with international partners worldwide, the EDQM performed 4 joint inspections in 2016, with the US Food and Drug Administration (FDA) and with WHO.

The Certification Procedure also featured in the EDQM's annual meetings with industry associations throughout 2016. These meetings provide a forum for exchanges on the EDQM's work and are an ideal occasion to gather feedback from stakeholders on their use of CEPs.

# THE EUROPEAN NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES

## The importance of a network for pan-European cooperation

Throughout 2016, the EDQM continued to coordinate the activities and programmes of the Official Medicines Control Laboratories (OMCL) Network, which supports the national authorities responsible for controlling the quality of medicinal products for human and veterinary use marketed in Europe. The OMCL Network is partly funded by the EU Commission.

Created to prevent substandard medicinal products from reaching patients and compromising the efficacy of their treatment and potentially their health, the OMCL Network brings together OMCLs located in 41 member states. Operating independently of manufacturers and thus without any conflict of interest, this Network allows resources and the latest technologies to be pooled with a view to saving public money and sharing expertise and best practices across European laboratories.

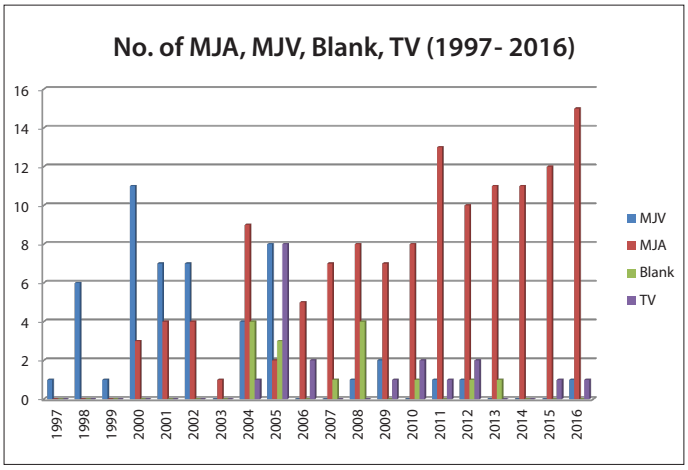
This pan-European collaboration network operates on the basis of common standards, procedures and guidelines, and its work also offers the advantage of recognition of test results. Its work gives member states the support they need to monitor the quality of medicines and to ensure that no substandard product reaches European patients.

## Quality Management programme

In 2016, the Network continued to implement, maintain, assess and improve the Quality Management (QM) programme for the activities of its members. This particularly important programme supports the harmonisation of quality management systems (QMS) among OMCLs, and ensures appropriate quality levels in the increasing exchanges of results and data among members (e.g. batch release of biologicals, market surveillance of CAPs).

## Mutual Joint Audits/Visits and Training Visits

Mutual Joint Audits/Visits (MJAs/MJVs) are designed to assess the compliance of OMCL quality management systems with the requirements of ISO/IEC 17025, of the Network QM guidelines and of the European Pharmacopoeia. In the course of 2016, 14 MJAs and 1 MJV were carried out at OMCL sites and 1 MJA was organised at the EDQM laboratory. Since the Quality Management Programme was launched in 1997, a total of 145 MJAs (including blank audits), 51 MJVs and 22 Training Visits (TVs)/Tutorials have been carried out in the OMCL Network.




## OMCL Network Quality Management Guidelines

New QM Guidelines are drafted by experts from the OMCL Network and updated on a regular basis, to provide support to laboratories in the implementation of the ISO/IEC 17025 requirements.

In 2016, the Network adopted new guidelines for the "Qualification of atomic absorption and atomic emission spectrometers". The former guideline on archiving was replaced by two new documents, "Management of documents and records" and "Management of samples". The guidelines for the "Qualification of gas-chromatography", and "Qualification of automatic titrators" were revised and published. The Network also adopted the new recommendation documents "Management of environmental conditions", "Management of volumetric glassware" and "Interpretation of screening results for unknown peptides and proteins by mass spectrometry-based methods". Following adoption, all documents were made available to stakeholders on the EDQM website.

## Collaboration with the EA

The EDQM reached out to the European Co-operation for Accreditation (EA), with the aim of evaluating the possibility of future cooperation between the two institutions, focusing on exchanges

*Participants at the 21st Annual Meeting of the GEON in Paris*

of know-how, participation in mutual meetings as observers and running joint audits with National Accreditation Bodies (NAB) and EDQM/MJA auditors. One joint audit was carried out in 2016.

## Training Courses/workshops

As part of the EDQM's commitment to sharing experience among OMCLs and harmonising approaches, a workshop on validation of computerised systems for OMCLs was organised in 2016.

## Proficiency Testing Scheme studies

The Proficiency Testing Scheme (PTS) organised by the EDQM provides laboratories with an objective means to assess and demonstrate the reliability of their data.

In 2016, five such studies were organised in the physico-chemical field. 58 OMCLs and 57 other pharmaceutical control laboratories, industry, hospital pharmacies, universities and pharmacy associations took part in "PTS165 Volumetric titration", "PTS166 Loss on drying", "PTS167 Semi-micro determination of water", "PTS168 Liquid chromatography assay" and "PTS169 UV-Vis spectrophotometry".

Five biological studies with an average of 21 participating laboratories were also organised in 2016. These were "PTS163 Low-molecular-mass heparins, chromogenic assay (anti-Xa and anti-IIa activity)", "PTS170 Parvovirus B19-Nucleic Acid Amplification Test (NAT)", "PTS171 Hepatitis C virus NAT", "PTS172 Anti-D antibodies in human immunoglobulin" and "PTS173 Prekallikrein activator in human albumin".

# General OMCL Network activities

## General OMCL (GEON) Annual General Meeting

The 21st Annual Meeting of the GEON was held in Paris (France) from 23 to 27 May 2016. The meeting was co-organised by the French National Agency for the Safety of Medicines and Health Products (ANSM), the French Food Safety Agency (ANSES) and the French Agency for Veterinary Medicines (ANMV). More than 230 experts from 61 OMCLs and national medicine agencies based in 38 different countries, including Canada, Israel, Singapore and - for the first time - Kazakhstan, attended the meeting. The programme was divided into 9 individual sessions.

## General market surveillance studies

Market Surveillance Studies (MSSs) provide an overview of the quality of medicinal products in a given therapeutic class available on the European market.

In 2016, three MSSs were finalised: "MSS046 on telmisartan APIs and tablets", "MSS047 on pramipexole APIs and tablets" and "MSS049 on irbesartan APIs and tablets".

In addition, the testing phase of "MSS048 Subdivision of tablets" launched in 2015 was completed. Four new studies were initiated: "MSS051 Foreign matter in herbal drugs", "MSS052 Repaglinide tablets", "MSS053 Leflunomide tablets" and "MSS050 Hyaluronic acid-based dermal fillers". The latter was the second MSS organised within the Network to focus on medical devices.

## Active Pharmaceutical Ingredients Working Group

Over recent years, the increasingly global dimension of the manufacture and trade of APIs has generated the need to step up testing of active pharmaceutical ingredients (APIs). The adoption of the Medicrime Convention in 2010 and the implementation of the Falsified Medicines Directive (2011/62/EU) across the EU in 2013 were important measures which confirmed the role played by OMCLs in the monitoring of APIs across the European market.

The 9th meeting of the API Working Group took place in June 2016. Discussions focused on Fingerprint MSSs, on omeprazole and morphine and on other classical API MSSs. Other core topics including the API testing database, the application of chemometric analysis as a tool for OMCLs, and ways of improving collaboration with Good Manufacturing Practices (GMP) inspectors in order to get access to samples from third country API manufacturers were also addressed at the meeting.

The sampling phase of the morphine project started in September 2016, and a new sampling procedure has been elaborated for the omeprazole study. The testing phase will start in 2017.

## Counterfeit/Illegal Medicines Working Group

The Counterfeit/Illegal Medicines Working Group met twice in 2016. Much of the meeting was devoted to discussing possible future Market Surveillance Studies on Suspected Illegal Products (MSSIPs) and on ways of exploiting existing test data for retrospective analysis of the usage and distribution of illegal medicines/products across Europe.

The Group was also involved in developing the programme for the 3rd Counterfeit Symposium for OMCLs, to be held in Nicosia (Cyprus) in March 2017. Closer collaboration with stakeholders is one of the top priorities of the Counterfeit/Illegal Medicines Working Group and so far, several measures have been identified as a means of enhancing exchanges with external partners.

Three technical training sessions for OMCL members were organised by the EDQM jointly with the Swiss, Dutch and Swedish OMCLs: they took place respectively in Berne (Switzerland) in February, in Bilthoven (Netherlands) in May/June and in Uppsala (Sweden) in October.

The Know-X database (launched in March 2014) was further amended throughout 2016 and, by the end of the year, numbered more than 3500 individual cases uploaded by OMCLs.

## Gene Therapy Products Working Group

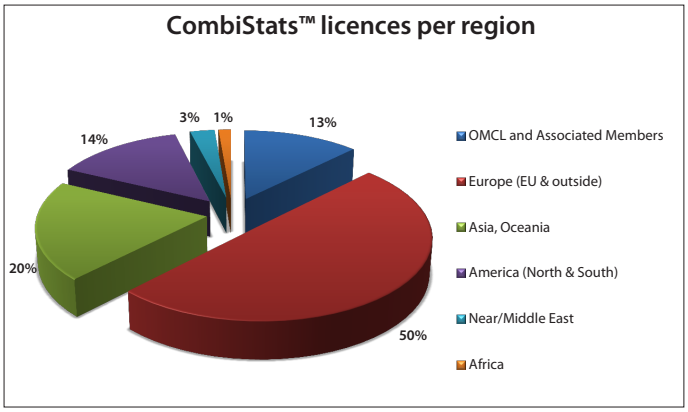
The OMCL Working Group for Gene Therapy Products (GTP) was created in 2008 to foster collaboration between OMCLs working in the GTP field, and to save time and resources through the sharing of knowledge and the latest technologies. Currently, 11 OMCLs are active members of this Working Group.

The validation of standard methods for the determination of viral and infectious genomes in adeno-associated virus (AAV) vector products was pursued throughout 2016. The ongoing projects were joined in 2016 by a new project launched to validate a standard method for determination of residual mammalian host cell DNA in gene therapy products. This method may be applicable to other types of products, such as vaccines or recombinant DNA technology products. An ad-hoc meeting with stakeholders in the field, including academics and manufacturers, was organised in Strasbourg in December 2016 to gather more information on existing methods and technical needs. Furthermore, a study designed to validate an ELISA method for AAV8 Physical Particles Titre (PPT) was also initiated in 2016.

A manuscript on the validation of UV-spectrometry methods for the determination of plasmid DNA concentration and purity was submitted for publication in PharmeuropaBio and Scientific Notes, and is set to be published in the course of 2017. Other related publications are also foreseen for 2017, including a text on the validation of an ELISA method for the determination of AAV2 PPT.

## CombiStats™

CombiStats™ is a computer programme for the statistical analysis of data generated through biological dilution assays in accordance with Chapter *5.3* of the European Pharmacopoeia. Initially designed for laboratories of the OMCL network, this programme is also available to non-OMCL laboratories. The current version (5.0) includes new features such as equivalence testing, robust regression, password-protection of datasheets and 5-parameter asymmetric sigmoid curves.



The number of users has steadily increased since the public release of the software. By December 2016, 13% of licences were issued to OMCL laboratories in 26 countries and 87% to non-OMCL users in 49 countries. The pie-chart above shows that, on average, half of the non-OMCL licences were issued within the EU, and the other half in the rest of the world. CombiStats™ has thus evolved into a common internationally-agreed reference in its domain, and it contributes to the mutual recognition of data and results by all concerned parties.

## EU/EEA-specific activities

### Market Surveillance for Products with a Centralised Marketing Authorisation

Every year since 1999, the EMA and the EDQM have joined forces on an annual programme for Centrally Authorised Products (CAPs) Sampling & Testing. The EMA sponsors the programme and has overall responsibility for it, while the EDQM coordinates the sampling and testing operations. The list of products to be included in the annual programme is prepared by the EMA Secretariat together with the EMA Scientific Committees and is defined taking a risk-based approach. This programme was successfully pursued in 2016 with 30 products for human use (10 biologicals and 20 chemical products) and 7 products for veterinary use (3 immunobiological products and 4 chemical products) on the work programme. API testing was performed in 3 cases. In addition to the regular CAP programme, two generics programmes were run in 2016, during which 11 branded repaglinide and leflunomide products (generic medicinal products and their respective reference medicinal products) were tested.

125 sampling operations were performed as part of the 2016 CAP Programme, and 36 OMCLs were involved in the testing operations. The results showed that the vast majority of the products tested were of the expected quality and complied with the authorised specifications. Two "confirmed out-of-specification" results and several regulatory or technical findings were reported and followed up by the EMA.

Lastly, a first feasibility study on CAP biosimilars involving 5 filgrastim products, including the originator's product, was finalised in 2016, thereby paving the way for future CAP biosimilar testing programmes.

### Mutual Recognition Procedure/ Decentralised Procedure post-marketing surveillance scheme

The OMCLs involved in the programme met twice in 2016 (28th and 29th meetings) to evaluate the programme and discuss ways to optimise collaboration. Progress was made with discussions on common risk-assessment procedures, including CAPs, Mutual Recognition Procedures (MRPs)/Decentralised Procedures (DCPs) and nationally authorised products during the meetings.

The 12th regular programme for the market surveillance of medicinal products authorised in the EU/EEA via the MRP or DCP was carried out. About 1100 product-testing projects were added to the 2016 programme, representing an increase of about 10% over the previous year. The testing reports for 2016 were submitted by 25 different OMCLs and 8% of the tested products were for veterinary use. The most frequently tested generic products in 2016 included olanzapine (antipsychotic), amlodipine, carvedilol and bisoprolol (treatment of high blood pressure), escitalopram (antidepressant), donepezil (treatment of Alzheimer's disease) and methylphenidate (treatment of hyperactivity disorder).

Regulatory issues were identified in about 1% of the materials tested. These mostly consisted of mistakes in leaflets, insufficient details of testing methods and primary packaging issues; in addition, one or more out-of-specification results were reported in a further 3% of the cases.

As of December 2016, the database held some 8400 MRP- and DCP-product testing records, with contributions from 34 different OMCLs.

### Official Control Authority Batch Release of Biologicals for Human Use

The harmonised application of Article 114 of EU Directive 2001/83/EC across Europe is carried out through the activities of the network for Official Control Authority Batch Release (OCABR) of Biologicals for Human Use. This network fosters the mandatory mutual recognition of batch release for human vaccines and medicinal products derived from human blood and plasma. Testing and protocol review of the more than 12 000 final lots proposed for OCABR and close to 13 000 plasma pools were carried out by the network, so that their quality could be independently confirmed before the products reach patients.

The OCABR sessions of the Annual Meeting in Paris were attended by more than 80 participants, who used this opportunity to exchange expertise with the goal of optimising resources for solving common problems. The OMCLs discussed technical issues and strategies that would lead to better control of products such as vaccines for haemophilus influenza and childhood combination vaccines. The EDQM hosted a successful training session on OCABR of human vaccines in November, which was attended by more than 50 participants from OMCLs and manufacturers from Europe and beyond.

In the course of 2016, 1 new and 16 revised guidelines for vaccines, as well as 2 revised guidelines for blood-derived products came into force, together with a revised version of the EU Administrative Procedure and a number of internal network guidelines.

### Official Control Authority Batch Release of Immunological Veterinary Medicinal Products

Together with competent authorities at national level, this subset of specialised OMCLs is responsible for the independent control of immunological veterinary medicinal products (IVMPs) according to Articles 81 and 82 of EU Directive 2001/82/EC as amended.

Thirty participants from 17 member states took part in the Veterinary Batch Release Network (VBRN) session of the OMCL annual meeting. The focus was on improving sharing of work, maintaining competences, sustaining the development of a strong and reactive network and fostering active participation within it. Follow-up activities included the participation of a representative of the VBRN Advisory Group in the September and November meetings of the Heads of Medicines Agencies. The VBRN's testing priorities were re-evaluated using a risk based approach, and the outcome was further refined on the basis of scientific evidence, as well as consensus among the members of the Network.

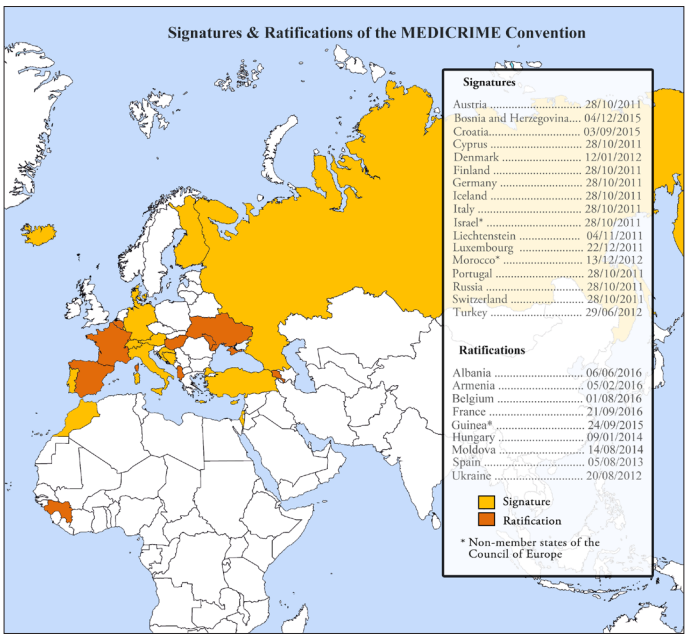
## ANTI-COUNTERFEITING ACTIVITIES

### Combating crime to protect public health

The EDQM continued to promote cooperation between authorities at national and international level in the fight against counterfeit and falsified medical products (medicinal products and medical devices). One of the most powerful weapons at its disposal in this campaign is the Council of Europe's Medicrime Convention, the first and only binding international instrument in the field of criminal law to address counterfeiting and falsification of medical products. The experts working on the steering body of the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and its subordinate Committee of Experts on Minimising the Public Health Risks Posed by Counterfeiting of Medical Products and Similar Crimes (CD-P-PH/CMED) continued to develop and promote programmes and projects aimed at disseminating best practices.

### Key facts

Efforts focused on encouraging authorities and governments to sign and ratify the Convention. Together with the Council of Europe's Criminal Law




Division of the Directorate General Human Rights and Rule of Law, the EDQM contributed to various regional conferences and workshops promoting the Medicrime Convention. The Convention entered into force on 1 January 2016, following the 5th ratification, and has since been ratified by 4 more countries (Albania, Armenia, Belgium and France). As the 10 ratification threshold draws closer, the EDQM, together with the Criminal Law Division, has started laying down the foundations for the future Medicrime Committee of the Parties, which will play an active role in supervising implementation of the Convention by the signatory states.

The promotion of the Medicrime Convention goes hand-in-hand with the action taken by the EDQM and its experts to implement the Convention and its tools. One example is the creation of a network of Single Points of Contact (SPOCs) involving the health authorities, customs and law enforcement agencies and other competent authorities at local, national and international level, through which information and data on counterfeit and falsified products is collected and shared. The EDQM continued to deliver training to these authorities for this particular purpose and in 2016 a SPOC training event was organised in Senegal in collaboration with the EU-funded project "Responding Effectively to the Production and the Trafficking in Falsified Medicines (REPT)".

The active role of the SPOC Network in updating the Know-X database was promoted by a webinar run in March 2016 which was attended by 38 officers from health, police and customs authorities from 20 countries.

Since 2007, the EDQM has organised 18 training sessions and courses for 423 officials from health, police and customs authorities, mostly in Europe but

also further afield (a complete list of these training courses is available on the EDQM website[3]).

In November 2016, the first Medicrime workshop for GMDP (GMP - Good Manufacturing Practice and GDP - Good Distribution Practice) and Pharmacy Inspectors took place in Oslo (Norway). Jointly organised with the Norwegian Medicines Agency, this technical workshop was attended by 22 inspectors based in 5 Northern-European countries liable to encounter counterfeit/falsified medicines in the course of their inspections of the legal supply chain.

## Mass serialisation systems for medicines

The EDQM continued to support the development of mass serialisation systems as tools to prevent the contamination of the legal supply chain with with counterfeit/falsified medicines. To this end, the EDQM promotes a harmonised approach for managing mass serialisation systems in Europe by working closely with supervisory authorities and those operators in the supply chain in charge of developing and managing systems for secure data handling.

As a result of the agreement signed in 2015 between the EDQM and the European Medicines Verification Organisation (EMVO), which is comprised of various European supply-chain operators, the EDQM is currently preparing the first conformity assessment of the EMVO's traceability system, European hub. The EDQM will verify that the system is designed, managed and operated in accordance with the standards in the delegated regulation on the Unique Identifier (EU 2016/161)[4], which implements the EU Falsified Medicine Directive (Directive 2011/62/EU). This initiative will help establish member states in their role as supervisors of traceability systems.

## Publications, databases and website

The EDQM's secure and restricted database Know-X stores comprehensive information on individual cases of counterfeit and falsified medical products, after criminal investigations. The database enables health and law enforcement authorities to act on cases of suspect medical products more rapidly, and provides support to the signatory states of the Medicrime Convention in monitoring and following-up trends.

The Know-X database provides information related to the analytical identification of medicinal products (*see The European Network of Official Medicines Control Laboratories, page 19*) and data on the *modus operandi* of criminals, as well as specific risk management and prevention measures taken by the competent health or enforcement authorities. The CD-P-PH/CMED assists the OMCL Counterfeit/Illegal Medicines Working Group with database maintenance and is also involved in promoting the base and providing user training.

In 2016, a version of the EDQM concept guide with a cartoon booklet for teachers and pupils was published by the Serbian authorities and actively used in workshops in schools in the country as a means of raising awareness among children and adolescents of the risks related to the use of counterfeit and falsified medical products.

## Communication with partners and stakeholders

Throughout 2016, representatives of the EDQM have been regular participants in the meetings of the European Union Heads of Medicines Agencies' Working Group of Enforcement Officers (HMA-WGEO), and have also attended a number of conferences in Europe and Africa with the purpose of raising awareness of the Medicrime Convention.

# PHARMACEUTICALS AND PHARMACEUTICAL CARE

## Optimal use of medicines for improving patients' quality of life

Activities in this area are led by the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and its subordinate bodies.

## Key Facts

In 2016, the Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC) finalised and published the report of the workshop "Quality Indicators for Pharmaceutical Care: Outcomes of the EDQM Project and Next Steps", (held in November 2015) which discussed strategies to improve public health and health system performances in Europe.

2016 also saw the completion of the report on "Quality indicators for pharmaceutical care", which included validated indicators and their respective data collection tools. The report is expected to be made available to the public in 2017.

Following-up on its work on quality indicators, the CD-P-PH/PC also established a subordinate working party entrusted with developing a guidance document for the implementation of the pharmaceutical care philosophy and the applicability of related working methods in daily practices across Member States.

3. https://go.edqm.eu/MDCRacts16
4. https://go.edqm.eu/2016161regu

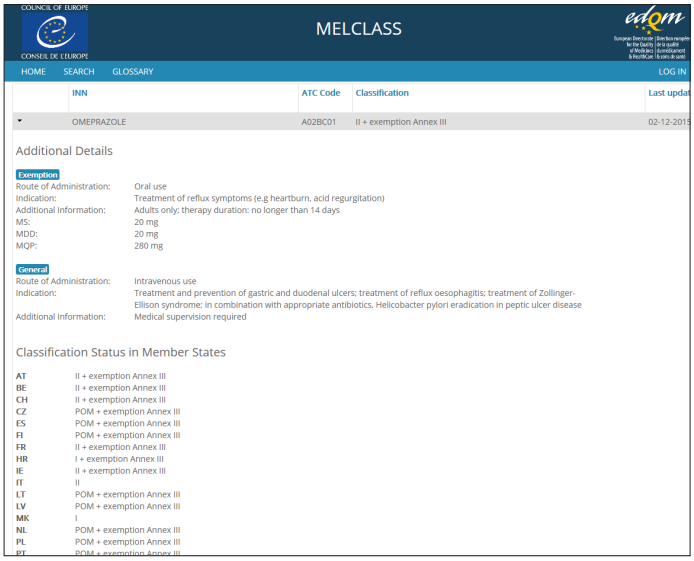
In 2016, the CD-P-PH/PC approved and released for comment draft guidelines on best practices for Automated Dose Dispensing (ADD) systems and their implementation in Europe, to a targeted audience of healthcare professionals, stakeholders and experts, through their corresponding associations at European level. The guidelines provide member states with a set of recommendations for the emerging practice of automated preparation of individual and customised containers or pouches, which contain different medicinal products prescribed for individual patients (for instance, in care homes for the elderly). They cover a broad range of issues related to ADD, from technical requirements and risk assessments, to the handling of medicinal products once they have been removed from their outer packaging and how to determine whether a patient is a suitable candidate for ADD.

The new Resolution CM/Res(2016)2 on "Good Reconstitution Practices in Health Care Establishments for Medicinal Products for Parenteral Use" was adopted on 1 June 2016. The Committee of Experts, the Steering Committee, the Ph. Eur. Commission and various European professional associations, in particular hospital pharmacies, have already started monitoring the implementation of this new resolution at member state level. At the same time, the revised former "Resolution on Quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients" was adopted as Resolution CM/Res(2016)1.

The Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO) issued its annual recommendations to health authorities for the classification of medicines and their supply conditions (prescription and non-prescription), and established good practices to this end. This work, which is of relevance to all stakeholders across the European medication chain, supports consumer health protection by harmonising the practices that ensure the quality, efficacy and safety of medicinal products in Europe. The annual update by the CD-P-PC/PHO Committee, including the 2016 classification recommendations[5], is available on the EDQM website and has also been added to the Melclass database[6] (*see following paragraph).*

## Publications, databases and website

The reviews of the classification of medicines containing H2-receptor antagonists, proton pump inhibitors, corticosteroids for topical use and triamcinolone were published on the EDQM website. The review of medicines containing imidazole derivatives (for gynaecological use) was completed and will be available on the EDQM website in 2017. The Melclass database which presents information on the classification and conditions for supply of medicines in member states and the CD-P-PC/PHO classification recommendations, was continually updated throughout 2016. In addition, in January 2016 the database was upgraded and migrated to a new web application which has a responsive design and uses state-of-the-art technology.




## Communication with partners and stakeholders

The work on Pharmaceutical Care was presented to stakeholders and authorities on various occasions, including at the Pharmaceutical Care Network Europe (PCNE) Working Symposium in Hillerød (Denmark) in February, at the 21st Congress of the European Association of Hospital Pharmacists (EAHP) in Vienna (Austria) in March and at the Congress of the Polish Pharmaceutical Society Pharmacy 21 in Wroclaw (Poland) in September.

5. See Revisions of the appendices of Resolution ResAP(2007)1 on the classification of medicines as regards their supply (2015 Edition) at https://go.edqm.eu/PHO
6. https://melclass.edqm.eu/

# HealthCare

The EDQM has continued to work diligently to protect public health in Europe by proposing trusted and ethical safety and quality standards for the collection, preparation, storage, distribution and appropriate use of blood components for blood transfusions, as well as for the transplantation of organs, tissues and cells. The work related to enhancing and developing standards in the field of food contact materials was also continued, along with the coordination of market studies and proficiency schemes in the area of quality control for cosmetics.

## BLOOD TRANSFUSION

### Promoting blood safety and quality in Europe and beyond

The EDQM is responsible for the Council of Europe's activities in the area of blood transfusion, which are built around three major principles: promoting voluntary and non-remunerated donations, optimal use of blood and protecting both donors and recipients of labile blood components. The EDQM actively addresses the ethical, legal and organisational aspects of blood transfusion with a view to ensuring the safety, quality and optimal use of blood supplies, increasing their availability and avoiding wastage.


The European Committee on Blood Transfusion (CD-P-TS) is the steering committee in charge of blood transfusion activities at the EDQM. It elaborates guidelines and recommendations, and is composed of internationally recognised experts from Council of Europe member states, observer countries, the EU Commission, WHO, the US FDA and the Council of Europe's Committee on Bioethics (DH-BIO). The CD-P-TS oversees the work of subordinate groups working on specific issues relevant to this field.

### Key facts and figures

In 2016, the achievements of the CD-P-TS and its subordinate groups included:

- the adoption of the text of the 19th edition of the "Guide for the Preparation, Use and Quality Assurance of Blood Components" (commonly referred to as the "Blood Guide"),
- six Blood Proficiency Testing Scheme (B-PTS) studies,
- one Blood Training Visit (B-TV) and 3 Blood Mutual Joint Visits (B-MJVs),
- the organisation of the second training course on "Quality Management for Blood Establishments" (BEs), and
- the organisation of a symposium on the "Optimal use of clotting factors and platelets" in Freising (Germany).

### General matters and policies

#### Risk behaviours with an impact on blood donor management and transfusion safety

Working group TS100 (taking over from former TS057 which elaborated Resolution CM/Res(2013)3)[7] is responsible for the continuous collection of data on the incidence and prevalence of sexually transmitted infections that jeopardise the safety of transfusions. Different decisions were taken on the deferral policies for men having sex with men by several member states: the Group will be mapping these policies in order to illustrate the lack of harmonisation in this field. The Group is also expected to provide advice on the need for future revisions of the Resolution.

7. For the full text of the Resolution, see https://go.edqm.eu/BTrec

## QM Programmes

The EDQM continued to run the two programmes it established to help BEs implement a QMS: the B-PTS Programme and the Blood Quality Management (B-QM) Programme. Both programmes support BEs in the implementation of EU blood legislation, the Blood Guide and the Good Practice Guidelines (GPG, see below), and both receive financial support from the EU Commission and the EDQM.

**Nucleic Amplification Techniques**

- ☐ **B-PTS024 - HBV/HCV/HIV**

**Serology**

- ☐ **B-PTS025 – Anti-HCV**
- ☐ **B-PTS026 – Anti-HIV/p24**
- ☐ **B-PTS027 – Anti-Treponema**
- ☐ **B-PTS028 – HBsAg/anti-HBc**

**Immuno-Haematoligy**

- ☐ **B-PTS029 ABO, Rhesus, extended phenotyping and irregular antibodies**

*B-PTS studies conducted in 2016*

## B-PTS Programme

The external assessment of the testing capability of European BEs continued through PTS studies in 2016[8]. A total of 6 studies were organised in this field with an average of 58 participants taking part in each.


*Participants in the second European Training Course on Quality Management for Blood Establishments*

## B-QM Programme

This programme[9] provides the tools that enable European BEs to develop, implement and improve their QMSs. Strongly supported by the CD-P-TS, the EU Commission and BEs, the programme offers 3 types of schemes, all run by experts from European BEs:

- *Blood Training Visits (B-TVs)*: on-site visits and tailor-made training on technical and QMS topics;
- *Blood Mutual Joint Visits (B-MJV)*: scrutiny of QMSs under development; observation of the level of implementation of the following minimum standards: the Blood Guide, the GPG, EU blood legislation and standards used in BEs (e.g. ISO Standards, GMP); recommendations on the implementation of QMSs and their improvement;
- *Blood Mutual Joint Audit (B-MJA)*: checking compliance of the QMSs with the Blood Guide, the GPG, EU blood legislation and standards used in the BEs.

In 2016, 1 B-TV and 3 B-MJVs were conducted. In addition, the second European Training Course on QM for BEs was organised in September in Skopje ("The former Yugoslav Republic of Macedonia"), involving 27 participants. This training session was intended to raise QM standards across countries in the South Eastern European (SEE) region.

## Publications, databases and website

### Guide to the Preparation, Use and Quality Assurance of Blood Components – 19th Edition

A dedicated working group is entrusted with the task of updating the Blood Guide and keeping it abreast of the scientific developments and regulatory changes that have occurred in the two-year period between editions of the guide. The 19th edition of the Blood Guide is expected to be published in 2017.

8. https://go.edqm.eu/BPTS

9. https://go.edqm.eu/BQM

## Good Practices Guidelines

The EU published Commission Directive 2016/1214 in July 2016, which made the Good Practice Guidelines (as published in the 19th edition of the Blood Guide) a new legal instrument that member states will bring into force by 15 February 2018.

## Proceedings on optimal use of clotting factors and platelets

In May 2016, a symposium on the "Optimal use of clotting factors and platelets" was held in Freising (Germany) in partnership with the Paul-Ehrlich-Institut (PEI) and Ludwig-Maximilian-University (LMU). More than 100 experts took part in this symposium, and the proceedings are available for download from the EDQM website[10]. A proposal for amending the Council of Europe's Resolution CM/Res(2015)3[11] will be elaborated by the CD-P-TS, as one of the recommendations resulting from this symposium.

## European Database of Frozen Units of Rare Blood Groups

The database has been fully operational since January 2016. Five BEs have already provided on a voluntary basis a list of frozen units of rare blood groups which were made available to patients through the system.

### Communication with partners and stakeholders

## EU Commission

2016 was a year of intense and fruitful collaboration with the EU Commission in 2016 which led to incorporation of the Good Practice Guidelines into EU legislation. This collaboration will continue in the coming years, to ensure that the EU Commission is updated regularly on regulatory changes and the latest scientific developments in the field.

In May and December, the EDQM was invited, as an observer, to attend the meetings of the competent authorities for blood which were organised by the EU Commission's Directorate General for Health and Food Safety.

## Pharmaceutical Inspection Co-operation Scheme

In the context of the revision of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP Guide for Blood Establishments, the EDQM took part in the "22nd PIC/S Expert Circle on Human Blood, Tissues and Cells". As an outcome, relevant texts of the Good Practice Guidelines published by the EDQM will be included in the PIC/S Guide.

## International Society of Blood Transfusion

The EDQM has observer status on the International Society of Blood Transfusion (ISBT) Board of Directors and is also a member of two dedicated ISBT working groups, i.e. the Quality Management and the Code of Ethics Working Parties. The EDQM took part in last year's ISBT annual congress held in Dubai (UAE).

# ORGAN TRANSPLANTATION AND TISSUES AND CELLS FOR HUMAN APPLICATION

### Promoting strict quality and safety standards

The European Committee on Organ Transplantation (CD-P-TO) is the steering committee in charge of transplantation activities at the EDQM. Its mandate includes elaborating guidelines and recommendations aimed at improving access to transplantation and high ethical, safety and quality standards in the field. The CD-P-TO is composed of internationally recognised experts from the Council of Europe member states, observer countries, the EU Commission and WHO, together with members of the Council of Europe's Committee on Bioethics (DH-BIO) and representatives of several professional non-profit organisations.

### Key facts and figures

Key achievements of the CD-P-TO in 2016 include:

- the publication of the 6th edition of the "Guide to the Quality and Safety for Organs for Transplantation"[12],
- the publication of Newsletter Transplant 2016,
- the publication of the 2nd edition of the brochure "Umbilical Cord Blood Banking. A Guide for the Parents",
- the publication of the brochure "Exercise your way to better post-transplant health", and
- the organisation of the 1st "Workshop for National Focal Points on Transplant Related Crimes", in November in Madrid (Spain).

10. https://go.edqm.eu/proceedings
11. https://go.edqm.eu/BTrec
12. The EDQM publications are available here: https://register.edqm.eu/freepub

## General Matters and Policies

### Legislative and policy efforts

Transplantation is now a well-established, life-saving therapy that transforms the lives of more than 110 000 patients with chronic organ failure worldwide every year. However, the supply is unable to keep pace with the demand for organs and this has led to the rise of trafficking in human organs (THO) and trafficking in human beings for the purpose of organ removal (HTOR).

Over the years, the Committee of Ministers of the Council of Europe has adopted a set of resolutions and recommendations in the field of organs, tissues and cells. Although not legally binding, these have had a profound impact on national legislation, on strategic plans for donation and transplantation, and on professional practices. For example, Council of Europe Resolution CM/Res(2013)55 calls on member states to adopt procedures and methods for the regular collection of data on illicit transplantation procedures performed outside the domestic transplantation system and to communicate results to the CD-P-TO.[13]

With the aim of ensuring that National Focal Points (NFPs) in charge of data collection at member state level have the necessary knowledge and tools to carry out their tasks, the EDQM organised a Workshop for National Focal Points on transplant-related crimes in collaboration with the Spanish national transplant organisation (ONT) in Madrid. A multidisciplinary expert panel shared knowledge and expertise on a number of topics. Through this workshop, the EDQM/Council of Europe aims to establish a network of HTOR/THO NFPs and provide them with the resources they need to elaborate national protocols for the prevention, detection and reporting of transplant-related crimes.

### Technical guidance to improve the quality and safety of organs, tissues and cells

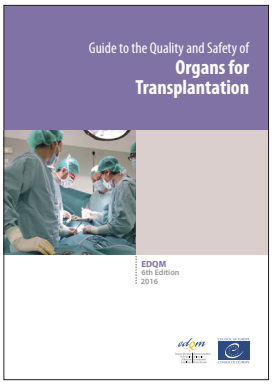
The EU Commission has been actively involved in the elaboration of the EDQM guides in the field, thus ensuring that the standards set out under the EU Directives are compatible with and complemented by the Council of Europe's guidance and that the same quality and safety provisions are applied throughout the Union.

The 3rd edition of the "Tissues and Cells Guide" was finalised in 2016 and it is expected to be submitted for open consultation before it is finally published in the course of 2017. This Guide was partially funded by the EU Commission.

Several other professional associations have actively participated in the elaboration of both Guides. Most notably, the European Donation and Transplant Coordination Organization (EDTCO) contributed to the Organ Guide, whereas the American Association of Tissue Banks (AATB), the European Eye Bank Association (EEBA), the European Society for Human Reproduction and Embryology (ESHRE), the European Society for Blood and Marrow Transplantation (EBMT), the Joint Accreditation Committee-ISCT & EBMT (JACIE) and the International Council for Commonality in Blood Banking Automation (ICCBBA) contributed to the Tissues and Cells Guide.

## Publications, databases and website

The "Guide to the Quality and Safety of Organs for Transplantation" (usually referred to as the "Organ Guide") and the "Guide to the Quality and Safety of Tissues and Cells for Human Application" (referred to as the "Tissues and Cells Guide") have become gold standard references in Europe and beyond, providing quality, safety and ethical guidance for professionals in the field[14].



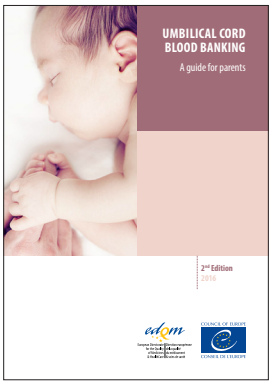

The 6th edition of the Organ Guide was published in September 2016. Experts from all over the world contributed to this new edition which provides useful information for both Health Authorities and clinicians at the point of care. In order to ensure maximum dissemination, the electronic version of this guide was made available free of charge on the EDQM Freepub website.

The Newsletter Transplant is the only official source of international figures on organ, tissue and haematopoietic stem-cell donation and transplantation. Using the information it provides, it is possible to analyse trends in donation and transplantation activities and then amend policies accordingly. This work is coordinated by the Spanish national transplant organisation (ONT) which, every year, analyses international figures collected through a network of health authorities and officially designated focal points worldwide. The latest issue of the Newsletter Transplant provides figures on organ, tissue and cell donation and transplantation from 67

13. Resolution CM/Res(2013)55 on establishing procedures for the collection and dissemination of data on transplantation activities outside a domestic transplantation system. See: https://go.edqm.eu/OTrec

14. The EDQM publications are available here: https://register.edqm.eu/freepub

countries for the year 2015. The information on organ donation and transplantation also included data for waiting lists and family refusals.





The EDQM also strives to provide clear and balanced information on transplants to both patients and the general public, to help them improve many aspects of their quality of life. Two layman brochures were published in 2016: the 2nd edition of "Umbilical Cord Blood Banking. A Guide for the Parents"[15] which provides clear and factual information about the use of cord blood in medical treatment and guides parents through their blood storage options, and a new brochure, "Exercise your way to better post-transplant health", which stresses the importance of regular exercise as a means of addressing some of the common side-effects of post-transplant treatments.

# COSMETICS AND FOOD CONTACT MATERIALS

## Protecting consumer health

The Consumer Health Protection Committee (CD-P-SC, Steering Committee), composed of representatives from national ministries with public health responsibilities, elaborates the work programme for cosmetics and for materials that come into contact with food. In 2016, more than 250 experts in 34 member states and 5 observers to the Ph. Eur. Convention monitored or contributed actively to this work. Representatives of the EU Commission, its Joint Research Centre (JRC) and the European Food Safety Authority (EFSA) can attend the meetings of this Committee and of its subordinate expert groups.

The work programme in the field of food contact materials is defined by the Committee and executed by its subordinate Committee of Experts on Food Contact Materials (P-SC-EMB). 2016 saw the start of harmonisation work on quality and safety requirements, together with further efforts to develop and update testing methods.

In the field of cosmetics, the focus is on product safety and surveillance. Collaboration between member states is facilitated by the European Network of Official Cosmetics Control Laboratories (OCCLs).

## Key facts

### OCCL Network

The European OCCL Network was set up in 2010, and now has around 40 OCCLs participating in regular network activities, including laboratories from 19 member states of the European Union. The main task of an OCCL is to check the quality of products on the market. Under the aegis of the EDQM, testing competences are compiled in an inventory that is accessible to all Network members; this brings considerable added value in terms of better use of resources and enhanced management of quality in accordance with international standards. The long-standing experience with the OMCL Network is also an asset for the coordination of the OCCL Network, which has established close contacts with the European Commission and its JRC and the European Committee for Standardization (CEN).

The EDQM organised the "Working together for the Quality of Cosmetics" symposium in June 2016, which was attended by 38 experts from 20 countries, including observers from Singapore and the Taiwan FDA, who represented competent authorities, control laboratories and inspectorates. The programme covered collaborative studies in the Network, experience in sharing expertise - national viewpoints, and analytical challenges in the field of cosmetics.

The Network's activities and achievements in the first five years were presented. These included market surveillance findings, the proficiency testing scheme and the results from collaborative studies for method validation. It was demonstrated that analytical methods can be reproduced within the OCCL Network. With a view to the optimisation of resources and enhanced identification of emerging issues, the OCCL Network members agreed to share analytical results and step-up cooperation.

In 2016, two successfully harmonised methods were published that will serve as a reference for the quality control of some cosmetic products (see *Publications and Website page 28*):

- measuring the amount of tooth-whitening agent hydrogen peroxide in dental products using liquid chromatography,
- and determining the amount of formaldehyde present in cosmetic products such as face creams, shampoos or toothpastes.

15. The EDQM publications are available here: https://register.edqm.eu/freepub

## Quality check for cosmetics: Market Surveillance Studies

Following some alarming findings in a study on cosmetic products that appeal to children, the EDQM continued throughout 2016 to collect data on the quality of shampoos, skin creams and make-up, lotions and several other types of products for children. Data collection is expected to continue in 2017.

A new MSS was initiated on tooth whitening products and their compliance with EU Regulation No 1223/2009.

## Proficiency testing scheme

Proficiency testing is an essential part of quality control management in testing laboratories. Analytical studies are carried out on identical samples in different laboratories to verify each laboratory's ability to quantify, for example, the amount of prohibited substance, and to ensure that test results are comparable across Europe. In 2016, the programme included a High Performance Liquid Chromatography (HPLC) assay for hydrogen peroxide and an HPLC assay for parabens in lipstick.

The EDQM proficiency testing scheme is designed as a benchmarking tool for study participants which allows them to share expertise and improve their technical skills in the field of analytics.

## Food contact materials and articles

Throughout 2016, the Committee of Experts on Food Contact Materials (P-SC-EMB) continued to review the resolutions and technical documents which had been elaborated under the former Council of Europe Partial Agreement in the Social and Public Health Field (dissolved on 31 December 2008). The P-SC-EMB updated the provisions for materials such as cork, ion-exchange resins or paper and board. In addition, two working group meetings in 2016 were dedicated to paper and board; the first meeting was hosted by the Federal Institute for Risk Assessment (BfR) of Germany and the second meeting by the Agency for Health and Food Safety (AGES) of Austria.

Food contact materials made from metals and alloys have been addressed in a practical guide for manufacturers and regulators, which was first published in 2013. Amendments are being prepared for the second edition of this guide. To this end, an adhoc working group with experts from competent authorities, official and private control laboratories and industry, held two meetings in 2016 hosted by the Scientific Institute of Public Health (SIPH) of Belgium.

## Tattoos and permanent make-up

In order to implement the recommendations of Council of Europe Resolution AP(2008)1, the EDQM started compiling the safety and documentation requirements for tattoos and permanent make-up. This document is expected to be finalised and published in 2017.

On 19-20 January 2016, the EDQM was invited to present the work on the safety of tattoos and permanent make-up at a workshop organised by the European Commission on the Implementation of the recommendations of the Restriction Task Force and discussion on new restriction proposals.

## Communication with partners and stakeholders

Joint meetings of the Platform of European Market Surveillance Authorities for Cosmetics Analytical Methods group (PEMSAC-AM), the JRC and the European network of OCCLs have proved to be a fruitful and effective way of dealing with matters of common concern. In December, the EDQM was also invited to present the activities of the OCCL Network to the PEMSAC working group on market surveillance.

## Publications and website

"Determination of free formaldehyde in cosmetics"[16]: this procedure has been harmonised as a follow-up of a PTS and describes a high-performance liquid chromatography method for the determination of free formaldehyde in cosmetic products.

"Determination of hydrogen peroxide in cosmetics": this procedure has been harmonised through a peer review process throughout the network and describes a high-performance liquid chromatography method for the quantification of hydrogen peroxide present in or released from tooth whitening or bleaching products.



16. The EDQM publications are available here: https://register.edqm.eu/freepub

# Quality management system

## Committed to continuous improvement

Investment in the EDQM's quality management system continued to be a priority in 2016, with the migration of the ISO 9001 certification to the 2015 version of the standard, and the renewal of ISO 17025:2005 accreditation for 20 analytical techniques. The EDQM's customers and stakeholders can therefore rest assured that the goods and services provided are of consistent quality and that the Organisation is committed not only to maintaining, but also to continuously improving its standards for quality throughout all its activities.

493-TEST

# Cooperation with international partners

In all its endeavours, the EDQM especially values its cooperation with a range of international partners, which would not be possible without the support of NPAs, national competent authorities, official control laboratories, inspectorates and more than 1200 experts in pharmaceutical sciences and specialists in healthcare issues, such as blood transfusion and organ transplantation. Similarly, as an integral part of the European regulatory network, the EDQM meets and collaborates regularly with national regulatory authorities, the EU Commission and its technical agencies, such as the EMA.

## COOPERATION WITH NATIONAL AUTHORITIES

The Ph. Eur. Commission also works closely with competent authorities at national level. This crucial cooperation ensures continued consistency between the approaches of licensing authorities across Europe and the Ph. Eur. Representatives of national authorities are members of the Ph. Eur. Commission and its 71 groups of experts and working parties. The authorities also take part in the work of the Ph. Eur. by submitting requests for elaboration or revision and by reviewing the draft texts published in Pharmeuropa online. In 2016, the EDQM was also granted observer status to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

The 2016 annual meeting of the NPAs of Ph. Eur. member states took place in April in Prague (Czech Republic). Hosted by the State Institute for Drug Control of the Czech Republic (SUKL), the event was attended by 21 of the 37 member states. The EDQM is grateful to the Czech authorities for their support and assistance in preparing this event (*see "The European Pharmacopoeia", page 7*).

The Ph. Eur. continued its efforts to avoid duplication of testing and reporting during drug development through the work of the PDG – comprising the Ph. Eur., the JP and the USP as members and WHO as an observer *(see "The European Pharmacopoeia", page 7)*.

In 2016, a special meeting was organised for Ph. Eur. observer delegations to discuss the work of the Ph. Eur. Commission and the EDQM, and identify ways for observers to become more involved. Observer status to the Ph. Eur. Commission allows national authorities to take part in a large range of activities. The meeting brought together 31 delegates from 19 countries around the world. The main objectives of the meeting were to strengthen links and communications and to achieve closer collaboration between all relevant stakeholders to improve the quality of medicines and public health.

The EDQM also brought forward its international collaboration for certificates of suitability and inspections of drug substances manufacturers, and new confidentiality agreements were signed with the health authorities of Armenia, Israel and Japan.

The Annual Meeting of the GEON network, which was held in Paris and coorganised with French Authorities, was attended by more than 230 experts from OMCLs and from national medicines agencies based in 38 different countries across the globe (see "The European Network of Medicines Control Laboratories (OMCLs)", page 15). The EDQM is grateful to the French authorities for their support and assistance in preparing this event.

## COOPERATION WITH ICH

In line with its new role as observer to the ICH Assembly, the EDQM has participated in the activities of the Implementation Working Party (IWG) of the ICH Q3D Guideline (Elemental Impurities). The IWG key deliverable in 2016 has been the Q3D training package, which is expected to pave the way for a smooth and successful implementation of the guideline across the regions concerned.

The EDQM has also been involved in the ICH Q11 IWG, which is in charge of preparing a set of Questions and Answers for the selection of starting materials for active substances.

## COOPERATION WITH THE EUROPEAN UNION AND EMA

The EDQM works closely with the EU Commission, communicating regularly to share information on current developments in work programmes and potential developments in EU legislation.

The EDQM is a member of the European Union Network Data Board (EUNDB), an organisation co-chaired by the EMA and a National Competent Authority, and is also a member of the task force working on the implementation of ISO IDMP and its Referentials subgroup.

The EDQM works closely with the EMA. The EMA scientific guidelines and Ph. Eur. monographs and chapters are complementary instruments for ensuring the quality of medicinal products in Europe:

- the Ph. Eur. sets legally binding standardised specifications for pharmaceutical preparations, their constituents and containers; and
- the EMA guidelines provide advice on the best or most appropriate way to fulfil obligations under the EU legal framework.

Members of the EMA working groups (those for which the EMA provides the Secretariat) and members of the EMA Secretariat itself are observers to some of the Ph. Eur. Commission's groups of experts, steering committees and working parties. Likewise, the EDQM has observer status within a number of EMA bodies, e.g. the Committee for Advanced Therapies (CAT), the Herbal Medicinal Products Committee (HMPC), the joint CHMP/CVMP Quality Working Party (QWP), the Biologics Working Party (BWP), the GMDP Inspectors Working Group (GMDP IWG) and the Immunologicals Working Party (IWP).

The EDQM and the EMA communicate regularly with regard to the Certification Procedure: the EMA is a member of the EDQM's Certification Steering Committee, and regular communication channels are in place for exchange of assessment reports for active substances, as well as for the inspection programmes and their outcomes.

The EDQM and the EMA continue jointly run a long-established CAP Sampling & Testing Programme for products for human and veterinary use. The EMA sponsors the programme and has overall responsibility for it, while the EDQM coordinates sampling and testing operations. The EMA and its Scientific Committees define the list of products to be included in the annual programme through a risk-based approach (*see The European Network of Medicines Control Laboratories (OMCLs), page 18*).

## COOPERATION ON INSPECTIONS

In 2016, the EDQM's Certification Department continued to be involved in the International API Inspection Programme (coordinated by the EMA) and the Pharmaceutical Inspection Co-operation Scheme (PIC/S). These initiatives are important tools that help improve the supervision of API manufacturing sites while saving resources. In 2016, 4 joint inspections were performed with international partners (*see Certification of Suitability to the Ph. Eur. monographs, page 15*).

## COOPERATION WITH WHO

Throughout 2016, the EDQM continued to collaborate with WHO, which has the status of observer to the Ph. Eur. Commission, and took part in a number of joint meetings, consultations and activities including:

- participation as an observer to the WHO's Programme on International Non-proprietary Names (INN), since INN are used in Ph. Eur. monographs,
- participation in the WHO Expert Committee on Biological Standardization (ECBS), with WHO participating as an observer in the meetings of the EDQM's BSP Steering Committee, thus guaranteeing a seamless exchange of information;
- participation in the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) (*see Pharmaceutical reference Standards, page 12*);
- sharing of evaluation reports and inspection information related to the quality of active substances for the Certification Procedure and the WHO API Prequalification Programme.

The EDQM is responsible for establishing, monitoring and distributing WHO ISA and ICRS (*see Pharmaceutical Reference Standards, page 12*).

The Ph. Eur. also takes part in the International Meeting of World Pharmacopoeias organised under the auspices of WHO, the 7th Meeting took place in September 2016 in Tokyo (Japan).

The EDQM also collaborates with WHO in the fields of blood transfusion and organ transplantation.

## COOPERATION WITH IGDRP

The EDQM is involved in the activities of the IGDRP, which promotes global collaboration and convergence in generic drug regulatory programmes. The EDQM has taken part in this programme since it was launched: it is an observer to the Steering Committee and Quality Working Group focusing on sharing work practices and quality information on Active Substance Master Files (ASMF)/Drug Master Files (DMF). In 2016, the EDQM hosted the 3rd meeting of the programme (*see section "2016 a year rich in events and meetings", page 33*).

## COOPERATION WITH MANUFACTURERS AND INDUSTRY ASSOCIATIONS

It is crucial for the quality of Ph. Eur. texts that manufacturers are involved in their elaboration and revision, and the EDQM strives to ensure regular exchanges with all those concerned by its work. Its *Pharmeuropa online* is a free online publication containing the draft pharmacopoeial texts on which the Ph. Eur. Commission is seeking feedback from the public and the industry.

Throughout 2016, bilateral meetings were held with industry associations to promote exchanges on all aspects related to the work of the EDQM, and also to ensure that the feedback from users could be taken into account.

# 2016: A year rich in events and meetings

## SYMPOSIA AND WORKSHOPS – FOCUSED TOPIC MEETINGS

### Symposium: The Challenges of Quality Requirements for Fish Vaccines

The EDQM organised a symposium with the support of the Norwegian University of Life Sciences (Oslo, Norway) on the challenges related to the quality requirements for fish vaccines. The symposium focused on current and alternative methods (presently being used or under development) for developing batch potency tests. Other topics of discussion included the opportunity to introduce humane endpoints in Ph. Eur. monographs for fish vaccines, and the revision of four monographs already published. The potential need for a general fish vaccine monograph together with new individual fish vaccine monographs for specific diseases (e.g. those observed in the Mediterranean basin) was also considered.

The symposium was attended by over 80 participants including officials and experts from 14 countries, as well as representatives from European licensing authorities, academia and manufacturers of fish vaccines. The discussions were very constructive and many good proposals were put forward for possible future developments.

### International Conference: Ph. Eur. Tackling Future Challenges of the Quality of Medicines Together

Nearly 220 delegates and experts from 41 countries gathered in Tallinn (Estonia) in September for a conference organised to mark the publication of the 9th Edition of the European Pharmacopoeia. The two-day conference brought together representatives from European and international regulatory authorities, WHO, pharmacopoeias from different continents as well as industry and associations from Europe and beyond.

This conference was held under the Estonian Chairmanship of the Committee of Ministers of the Council of Europe. The EDQM is grateful to the Estonian authorities, in particular the Ministry of Social Affairs and the Estonian State Agency of Medicines (Ravimiamet) for their support and assistance in preparing this event. Presentations covered the EDQM's role in the context of the European regulatory environment, the current challenges faced by the European regulatory network and the important contribution of the EDQM in ensuring access to good quality medicines for patients.

In addition to presentations, the conference also featured panel discussions, round tables on various issues and four workshops dedicated to key topics including new technologies, the control of elemental impurities (e.g. the impact of the ICH Q3D Guideline),

setting pharmacopoeial standards for biotherapeutic products, excipients and other components, and international harmonization.

The outcome of the workshops and recommendations were submitted to the Ph. Eur. Commission in November and all the presentations were published on the EDQM website for easy access and wider dissemination[17].

## TRAINING SESSIONS

The EDQM organised three specific European Pharmacopoeia training sessions last year in Strasbourg (France).

The first was in April and focused entirely on Ph. Eur. Reference Standards. The aim was to provide participants with an in-depth understanding of the different types of standards available together with an insight into their use in the Ph. Eur. In addition, two parallel workshops were organised and covered topics such as the quality of reference standards and standards for synthetic peptides, for recombinant proteins, in herbals and for biologicals established via the BSP. The training session was recorded and the videos were later published on the website to reach a wider audience.

The second session was held in July. It was dedicated to the Ph. Eur. and it also covered elements of the Certification Procedure, sharing advice on preparing an application, revisions and the inspection programme.

A one-day training session on homoeopathic products took place in December. The first Homoeopathy Working Party was created in 1997 and the chapter on *Homoeopathy* has existed in the European Pharmacopoeia since its 4th Edition. Homoeopathic medicinal products are part of a long-standing European therapeutic tradition and their inclusion in the Ph. Eur. contributes to improving healthcare in Europe. Over 50 participants from 17 countries attended this training session.

17. https://go.edqm.eu/proceedings

And finally, the EDQM was invited in December to give technical training on OMCL guidelines to OMCL staff members from Israel.

## WEBINARS

With internet technology, it is now possible to connect people everywhere across the globe at any time we want. In 2016, the EDQM continued to make the most of this technology both for training purposes and to share information on concrete topics of common concern and interest.

In January, the EDQM organised a special webinar for Ph. Eur. experts on the "7th edition of the Technical Guide for the elaboration of monographs". This guide was approved at the 152nd Session of the Ph. Eur. Commission (June 2015) and represents the technical/scientific basis for the elaboration of new monographs and the revision of existing texts. The webinar highlighted the changes in the new guide and explained the technical background to it.

In February, the EDQM organised a webinar on "Finished products monographs containing chemically defined active substances". In 2012, the Ph. Eur. Commission had agreed, in response to feedback from its users, to reconsider its general policy on finished products. Two years later, the Ph. Eur. Commission decided to expand its work programme to become more active in the area of quality standards for finished products containing chemically defined active substances. With over 800 people taking part worldwide, the webinar focused on the general principles related to finished product monographs and their content in the Ph. Eur., the example of sitagliptin tablets and how users can participate in the work.

In March, the EDQM organised a webinar entitled "How to use the Know-X Database for Health, Police and Customs Authorities" with the aim of explaining to users within enforcement authorities how the database works, how they can gain access to it and enter closed cases. The presentation focused on the type of information, both administrative and technical, that needs to be entered and gave a "how-to" overview of a number of its key features, such as conducting searches, exporting reports and creating and editing

cases. During the live demonstration, the participants were also given a number of practical exercises and case studies on which to practice their skills.

The next webinar took place in May and was organised by the Certification Department. The subject was "Electronic Submissions for CEP applications", the aim being to explain the current EDQM expectations concerning electronic formats for CEP submissions. Over 400 people took part worldwide.

Finally, another webinar was held in July on the "Call for Experts" campaigns of the EDQM during which the new working policy allowing nominations from non-member states and observers for membership of the European Pharmacopoeia Groups of Experts and Working Parties was explained and promoted. The webinar was very successful, with more than 230 participants joining in from across the globe.

Live Q&A sessions followed each of the webinars, allowing delegates to raise specific issues covered in the presentations. Some of the webinars recordings were posted on the EDQM website and made available for later access.

## PARTICIPATION IN KEY INTERNATIONAL MEETINGS

In 2016, the EDQM took part in several major international meetings and events worldwide.

"7th International Meeting of World Pharmacopoeias", September in Tokyo (Japan): the group continued discussions on the pending chapters of the GPhP core document, i.e. on compounding, herbals and the glossary. In the context of this meeting, the Japanese Pharmacopoeia organised a conference to celebrate their 130th anniversary and offered the possibility to a number of pharmacopoeias to present their current topics and recent developments."

ICH meetings in June in Lisbon (Portugal) and November in Osaka (Japan): these meetings followed the entry into force of the ICH reform. The Assembly approved new members and observers, including the EDQM, and discussions focused on a number of strategic issues, such as the optimisation of data collection. The EDQM has participated in the activities of the ICH Q3D and Q11 working groups.

USP Workshop on "Therapeutic Proteins & Peptides", February in Hyderabad (India): discussions focused on the current challenges regarding recombinant proteins and synthetic peptides, which will be the subject of future monograph development by the USP.

"European Symposium on Radiopharmacy & Radiopharmaceuticals", April in Salzburg (Austria): the EDQM gave a presentation on how smaller settings, such as hospital radiopharmacies, can use the Ph. Eur. as a tool to control the quality of radiopharmaceutical preparations.

"International Reference Standards Symposium", hosted by the USP in November in Rockville (USA). Last year, this major discussion forum involving stakeholders from all over the globe focused on the role of compendial reference standards for the USP and the Ph. Eur.

Other international meetings and events included:

- Annual conference of International Pharmaceutical Excipients Council (IPEC), Europe Excipients Forum, February, Nice, France
- Meeting of the Board of Pharmaceutical Sciences of the International Pharmaceutical Federation (FIP), February, The Hague (Netherlands)
- Int. Conference on the 2nd edition of the State Pharmacopoeia of Ukraine, April, Kiev (Ukraine)
- Forum for harmonization of herbal medicines (FHH), July, Rockville (USA)
- 18th Annual Conference *PharmMed Obrashenie*, November, Moscow (Russian Federation)
- PQRI/USP Workshop on Implementation Status of ICH Q3D Elemental Impurities Requirements, November, Rockville (USA)
- Workshop on New Technologies in Haemophilia Care, November, European Haemophilia Consortium (EHC), November, Berlin (Germany)
- 19th APIC/CEFIC European Conference on Active Pharmaceutical Ingredients, November, Barcelona (Spain)
- Conference on "Non-animal approaches – the way forward", RSPCA (Society for the Prevention of Cruelty to Animals), December, Brussels (Belgium)

## MEETINGS HELD IN PARTNERSHIP WITH THE EDQM

In May, the EDQM hosted the 3rd meeting of the International Generic Drug Regulators Programme (IGDRP) This programme was created to promote collaboration and convergence in the assessment of generic medicines and with a view to addressing the challenges associated with increasing workloads, globalisation and complex scientific issues.

Under the aegis of the IGDRP, a one-day stakeholder workshop was organised by the EDQM to present the mission, scope and organisation of the IGDRP to pharmaceutical industry representatives and to obtain their feedback on how to address some of the challenges faced in this field. Discussions focused in particular on biowaivers, sharing information on Active Substance Master File/Drug Master File (ASMF/DMF) assessments and on work-sharing models. This workshop was attended by 80 participants from 29 countries.


*International Generic Drug Regulators Programme (IGDRP) Stakeholder Workshop, Strasbourg*

In October, the EDQM organised a joint international workshop in cooperation with the Chinese Pharmacopoeia (ChP) Commission and the China Pharmaceutical Association of Plant Engineering (CPAPE), to mark the launch of the 9th Edition of the European Pharmacopoeia, as well as the 2015 Edition of the Chinese Pharmacopoeia. The workshop was a unique opportunity for participants to better understand the mission and role of both pharmacopoeias and also provided an insider view of the challenges that both pharmacopoeias face. Other topics discussed included the importance of pharmaceutical standards and their added value to stakeholders, the Certification Procedure and its inspections programme. The roundtable debate that followed brought together representatives from Chinese and European industry associations and provided a valuable occasion to look into strengthening international cooperation and cross-collaboration. More than 80 participants attended.


*Joint international workshop of the European and Chinese Pharmacopoeias, Strasbourg*

The EDQM was also invited to take part in the 11th meeting of the Heads of National Control Laboratories (LNCQs) of the Franco-African Network. The meeting was organised by the ANSM, the French Medicines Agency and took place in January 2016 in Paris (France).

About 25 participants attended the meeting, including heads of LNCQs of Benin, Cameroon, Mauritania, Niger, Senegal and Tunisia, ANSM staff including the heads of the Agency and its OMCL, and representatives from different institutions at French and international level: the French ministry for foreign affairs (MAE), the French development agency (AFD), the French international technical expertise agency (Expertise France), the West African Economic and Monetary Union (UEMOA),the French pharmacists' aid organisation (CHMP), WHO and the Council of Europe.

The main aim of the Franco-African Network is to strength the cooperation between its members through common collaborative studies and training programmes, and to achieve and maintain the prequalification of all laboratories.

## INTERNATIONAL FAIRS & EXHIBITIONS – EXPANDING GLOBAL PRESENCE

As global trade in substances for pharmaceutical use, generics and finished pharmaceutical products continues to grow, international trade fairs are an excellent means for the EDQM to keep in touch with local manufacturers, associations and stakeholders and provide an ideal opportunity to showcase its latest products and services.

The EDQM took part in three pharmaceutical fairs in 2016, namely CPhI China (Shanghai), CPhI Europe (Barcelona) and CPhI India (Mumbai). Every year, these specialised tradeshows attract a large number of visitors from the chemical and pharmaceutical


*EDQM stand at the CPhI trade exhibition, Barcelona (Spain)*

industries and are a great platform for the EDQM not only to present its products and services but also to meet potential new customers and increase its international presence. It is also a good opportunity for staff from the Certification Department to meet with visitors and reply to questions related to the Certification Procedure and its inspection programme. Specific one-to-one meetings are generally organised for those who need further assistance understanding the process and to overcome difficulties they may be experiencing.

In 2016, the 9th Edition of the Ph. Eur. took centre stage at all three fairs. Visitors were able to get a glimpse of the latest edition which is available in three initial volumes and applicable in 37 European countries from 1 January 2017.

In June, the EDQM was invited to take part in a symposium organised by the China Chamber of Commerce for Import and Export of Medicines and Health Products (CCCPMHPIE). Over 150 participants, mainly from China, attended the event, and the EDQM presentations focused on the Ph. Eur. and the Certification Procedure.

## PUBLIC AWARENESS CAMPAIGNS

As part of its work to heighten its profile and increase public awareness of its activities at all levels, the EDQM ran an information stand during the Strasbourg Races in May, a major sporting event which attracts athletes and visitors from the city and neighbouring regions. A number of visuals and materials including posters and information brochures were handed out to inform the public about the many facets of the EDQM's activities, its achievements and its role in protecting public health.

Two blood donor sessions were also organised by the EDQM for Council of Europe staff and their families, in order to raise awareness on blood donation among staff based in Strasbourg.

# List of committees coordinated by the EDQM

## THE EUROPEAN PHARMACOPOEIA COMMISSION

The Ph. Eur. Commission was set up in 1964 in accordance with the Convention on the Elaboration of a European Pharmacopoeia. The Commission has 38 members, all signatory parties to the Convention (37 states and the European Union). Also, 30 observers from all over the world confirm the importance of the work of the Ph. Eur. Commission at international level. The Commission sets out the work programme and adopts the quality standards for medicines and their components to be applied in the territories of its member states. A total of 71 expert groups and working parties established by the Commission carry out the Ph. Eur. work programme. As of the end of 2016, 2343 quality standards and 359 general texts including methods of analysis had been elaborated, adopted and implemented. These texts are constantly being revised in order to keep pace with the latest technical and scientific advances in the development, production and quality control of medicines. The Ph. Eur. is essential for the protection of public health. It is intended for use by healthcare professionals working with medicines, and has become the gold standard reference in the sector.

## THE BIOLOGICAL STANDARDISATION PROGRAMME STEERING COMMITTEE

The BSP focuses on the standardisation of the methods and tools for the quality control of biologicals by establishing reference standards and validating new methods with particular focus on reducing, refining and replacing the use of animals (3Rs initiative). These activities are supervised by the BSP Steering Committee which is composed of the chairs of Ph. Eur. Groups of Experts 6, 6B, 15, 15V as well as co-opted experts and delegates from the EU Commission, EMA, BWP, IWP and WHO and the EDQM Director.

## NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES ADVISORY GROUPS

The role of this Network is to ensure that the quality of medicines marketed in the member states is consistent; this also happens through the mutual recognition of results of the processes for the control of medicines quality. Major decisions are taken during the annual plenary meetings of the OMCL Network. Advisory groups prepare and ensure the implementation of the annual work programme. There are two levels of collaboration within the network:

- general activities involving all of the member states of the Ph. Eur. Convention and the observer states. These activities cover work in the area of quality management systems, such as audits and proficiency testing studies, as well as market surveillance studies and contribute towards combating counterfeit and illegal medicines. General activities are prepared and followed by the General OMCL Advisory Group; and,
- activities restricted to the EU and the European Economic Area (EEA), and concerning products approved via the centralised procedure and the mutual recognition or decentralised procedure (MRP/DCP) and the OCABR system for biological products (human and veterinary). The latter activity also involves Switzerland and Israel (for human vaccines only). For the CAP and the OCABR activities, advisory groups ensure continuity of operations in the interval between the annual meetings of each specific network.

## CERTIFICATION OF SUITABILITY TO PH. EUR. MONOGRAPHS STEERING COMMITTEE

A network of about 100 assessors and 30 national inspectors participates in the work required for the evaluation of API quality dossiers and the inspection of manufacturing sites. The activities associated with the procedure for certification of suitability to Ph. Eur. monographs are guided by a Steering Committee and three Technical Advisory Boards (TAB). This Steering Committee is composed of representatives of European licensing authorities and inspectorates. It takes decisions on general policy, examines and comments on matters brought to its attention by the Technical Advisory Boards, adopts guidelines and the inspection programme and co-ordinates questions amongst the represented parties. It is also responsible for appointing assessors, as well as the members of the Technical Advisory Boards and their Chairs.

## EUROPEAN COMMITTEE ON BLOOD TRANSFUSION

This Steering Committee addresses ethical, legal and organisational issues related to blood transfusion, in order to ensure the safety and quality of transfusions and the protection of donors and recipients, and to promote the optimal use of blood and minimal wastage. It supervises the work of a number of individual projects and working groups, e.g. the European Database of Frozen Blood of Rare Groups, Plasma Supply Management and the ad hoc Working Group on the Guide to the Preparation, Use and Quality Assurance of Blood Components.

## EUROPEAN COMMITTEE ON ORGAN TRANSPLANTATION

This Steering Committee focuses on elaborating and promoting the principle of non-commercialisation of organ, tissue and cell donation, strengthening measures to avoid trafficking and elaborating high ethical, quality and safety standards in the field of transplantation. It supervises the activities of a number of individual projects and the ad hoc Working Groups on the "Guide to the Quality and Safety of Organs for Transplantation" and the "Guide to the Quality and Safety of Tissues and Cells for Human Application".

## EUROPEAN COMMITTEE ON PHARMACEUTICALS AND PHARMACEUTICAL CARE

This Steering Committee on pharmaceuticals and pharmaceutical care (CD-P-PH) is in charge of activities in the field of the classification of medicines as regards their supply, pharmaceutical practices and pharmaceutical care, and combatting falsified medical products and similar crimes. It is supported by its subordinate committees: the Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO); the Committee of Experts on Quality and Safety Standards for Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC); and the Committee of Experts on Minimising Public Health Risks Posed by Counterfeiting of Medical Products and Similar Crimes (CD-P-PH/CMED).

## CONSUMER HEALTH PROTECTION COMMITTEE

The Consumer Health Protection Committee (CD-P-SC) is responsible for managing work programmes and decision-making processes in the areas of cosmetics and food contact materials. The Committee examines health-related issues, evaluates their risks and draft reports and recommendations for regulatory approaches. In addition, it coordinates the European network of Official Cosmetics Control Laboratories (OCCLs). Its work is supported by two sub-committees: the Committee of Experts on Packaging Materials for Food (P-SC-EMB) and the Committee of Experts on Cosmetic Products (P-SC-COS).

# Glossary

| | |
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| 3Rs | Reduction, Refinement and Replacement of animal testing |
| AAV | Adeno-Associated Virus |
| ADD | Automated Dose Dispensing |
| AGES | Austrian Agency for Health and Food Safety |
| ANMV | French Agency for Veterinary Medicines |
| ANSES | French Food Safety Agency |
| ANSM | French Agency for the Safety of Medicines and Health Products |
| API/s | Active Pharmaceutical Ingredient/s |
| ASMF | Active Substance Master File |
| B-MJA | Blood Mutual Joint Audits |
| B-MJV | Blood Mutual Joint Visits |
| B-PTS | Blood Proficiency Testing Scheme |
| B-QM | Blood Quality Management |
| B-TV | Blood Training Visits |
| BE | Blood Establishment |
| BIPM | Bureau International des Poids et Mesures |
| BRP | Biological Reference Preparation |
| BRR | Biological Reference Reagents |
| BSP | Biological Standardisation Programme |
| BVS | Batch Validity Statement |
| BWP | Biologics Working Party |
| CAP | Centrally Authorised Product |
| CD-P-PH | European Committee on Pharmaceuticals and Pharmaceutical Care |
| CD-P-SC | European Consumer Health Protection Committee |
| CD-P-TS | European Committee on Blood Transfusion |
| CD-P-TO | European Committee on Organ Transplantation |
| CEN | European Committee for Standardization |
| CEP | Certificate of Suitability to the Monographs of the European Pharmacopoeia |
| CHMP | EMA's Committee for Medicinal Products for Human Use (see EMA) |
| CHO | Chinese Hamster Ovary (CHO) |
| ChP | Chinese Pharmacopoeia |
| CM | Committee of Ministers |
| CRS | Chemical Reference Substances |
| CVMP | EMA's Committee for Medicinal Products for Veterinary Use (see EMA) |
| DCP | Decentralised Procedure |
| DG SANTE | EU Directorate General for Health and Food Safety Health |
| DH-BIO | Council of Europe's Committee on Bioethics |
| DMF | Drug Master Files |
| EA | European Cooperation for Accreditation |
| EAHP | European Association of Hospital Pharmacists |
| ECBS | WHO Expert Committee on Biological Standardization |
| ECSPP | WHO Expert Committee on Specifications for Pharmaceutical Preparations |

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| eCTD | electronic Common Technical Document |
| EDQM | European Directorate for the Quality of Medicines & HealthCare |
| EDTCO | European Donation & Transplant Coordination Organisation |
| EEA | European Economic Area |
| EFSA | European Food Safety Authority |
| EMA | European Medicines Agency |
| EMVO | European Medicines Verification Organisation |
| EU | European Union |
| FDA | Food and Drug Administration |
| GPG | Good Practice Guidelines |
| GDP | Good Distribution Practice |
| GEON | General European Network of Official Medicines Control Laboratories (OMCLs) |
| GMDP | Good Manufacturing and Distribution Practice |
| GMP | Good Manufacturing Practice |
| GPhP | Good Pharmacopoeial Practices |
| GTP | Gene Therapy Products |
| HCV | Hepatitis C Virus |
| HIST | Histamine Sensitisation Test |
| HIV | Human Immunodeficiency Virus |
| HPLC | High Performance Liquid Chromatography |
| HRS | Herbal Reference Standards |
| HTOR | Human Trafficking for the purpose of Organ Removal |
| ICH | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| ICRS | International Chemical Reference Substance |
| IDMP | Identification of Medicinal Products |
| IGDRP | International Generic Drugs Regulatory Programme |
| ISA | International Standard for Antibiotics |
| ISBT | International Society of Blood Transfusion |
| ISO/IEC | International Organization for Standardization/International Electrotechnical Commission |
| IVMP | Immunological Veterinary Medicinal Products |
| IWP | Immunologicals Working Party |
| JP | Japanese Pharmacopoeia |
| JRC | Joint Research Centre of the European Commission |
| LBP | Live Biotherapeutic Products |
| LNCQ | National Quality Control Laboratory of the Franco-African Network |
| MA | Marketing Authorisation |
| MJA | Mutual Joint Audit |
| MHLW | Japanese Pharmaceutical Safety and Environmental Health Bureau of the Ministry of Health, Labour and Welfare |
| MJV | Mutual Joint Visit |
| MRP | Mutual Recognition Procedure |
| MSSIP | Market Surveillance Studies on Suspicious Illegal Products |
| MS | Mass Spectrometry |
| MSS | Market Surveillance Studies |

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|---|---|
| MSSIP | Market Surveillance Studies on Suspected Illegal Products |
| NAB | National Accreditation Body |
| NAT | Nucleic Acid Test |
| NMR | Nuclear Magnetic Resonance |
| NPA | National Pharmacopoeia Authorities |
| OCABR | Official Control Authority Batch Release |
| OCCL | European network of national Official Cosmetics Control Laboratory |
| OMCL | Official Medicines Control Laboratory |
| P4 | Procedure 4 |
| P-SC-COS | EDQM Committee of Experts on Cosmetic Products |
| P-SC-EMB | EDQM Committee of Experts on Food Contact Materials |
| PCNE | Pharmaceutical Care Network Europe |
| PDG | Pharmacopoeial Discussion Group |
| PEMSAC | Platform of European Market Surveillance Authorities for Cosmetics |
| Ph. Eur. | European Pharmacopoeia |
| PIC/S | Pharmaceutical Inspection Co-operation Scheme |
| PPT | Physical Particles Titre |
| PTS | Proficiency Testing Scheme |
| Q3D | Code for ICH Guideline on Elemental Impurities |
| QM | Quality Management |
| QMS | Quality Management System |
| QWP | Quality Working Party (EMA) |
| REACH | Regulation (EC) No 1907/2006 |
| RS | Reference Standard |
| SDS | Safety Data Statement |
| SPOC | Single Point of Contact |
| SUKL | State Institute for Drug Control of the Czech Republic |
| THO | Trafficking in Human Organs |
| TSE/BSE | Transmissible Spongiform Encephalopathy/Bovine Spongiform Encephalopathy |
| TV | Training Visits |
| USFDA | United States Food and Drug Administration |
| USP | United States Pharmacopoeia |
| VBRN | Veterinary Batch Release Network |
| WFI | Water For Injections |
| WGEO HMA | Working Group of Enforcement Officers of the Health and Medicines Agencies of the European Union |
| WHO | World Health Organization |

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