

ANNUAL REPORT 2015

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

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Foreword

by Susanne Keitel, Director



Building on our 50th anniversary in the previous year, 2015 was another milestone for the EDQM: it marked the beginning of a major evolution in the scope of our activities and the way in which we pursue them.

■ At its 151st session in March, the European Pharmacopoeia (Ph. Eur.) Commission adopted the first monograph on a finished product containing a chemically-defined active substance: Sitagliptin tablets. The adoption was the culmination of a process that began in 2012, when the Ph. Eur. Commission first reconsidered its approach regarding the elaboration of finished product monographs, and then initiated a feasibility study. This new kind of quality standard at the European level will facilitate assessment of marketing authorisation applications and will provide those in charge of market surveillance studies with useful tools to test medicinal products that are on the market, thus reducing the burden on both regulators and industry across Europe and beyond.

■ The second major development relates to how the work of the Ph. Eur. is carried out. So far, this has relied on the contributions and dedication of a network of more than 700 experts in pharmaceutical sciences coming mainly from Ph. Eur. member states, but also from observer states to the Convention on the Elaboration of a European Pharmacopoeia.

Recognising the impact of the dramatic changes to the pharmaceutical world over the past 50 years, which have resulted in a truly globalised environment, the Ph. Eur. Commission decided in 2015 to revise its working procedures to allow nominations from non-Ph. Eur. member states and observers for membership of the Ph. Eur. Groups of Experts and Working Parties. This decision is part of a deliberate policy to further involve both observer states but also manufacturers from outside Europe in the work of the Ph. Eur., and will apply for the nomination of experts scheduled in 2016.

■ With these two steps, the Ph. Eur. Commission has signalled its commitment to propelling the Ph. Eur. into a new era. At the same time, the Ph. Eur. continues to demonstrate its responsiveness to specific developments in products, techniques and regulatory processes: in 2015, 53 new monographs were adopted (including seven on patent-protected active substances, elaborated in close collaboration with regulators and the respective innovators), 8 new general chapters were added and 988 texts revised to incorporate both regulatory changes and scientific progress; in all, the number of texts revised in 2015 was 1,014.

■ The impact of globalisation continues to have a determining effect also on the EDQM's other activities. For example, our Certification Division received 391 new applications for Certificates of Suitability (CEPs) in 2015, which is a significant increase compared to previous years (10 per cent higher compared to 2014), and in addition the number of requests for revision rose by some 16 per cent (almost 1,900 requests). Most of the new applications and requests for revision which originated outside Europe came from India and China, reflecting the global trend for production of generic drugs.

■ This aspect goes hand-in-hand with the EDQM's continued involvement in a number of international platforms for collaboration, such as the International Generic Drug Regulators Programme (IGDRP) and the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S).

■ The IGDRP was established in 2015, following a three-year pilot launched in 2012, reflecting the fact that the availability of safe, affordable and quality generic drugs plays an increasingly important role worldwide, and that this has led to significant pressures on medicines regulatory authorities charged with the assessment and approval of these products. The IGDRP was therefore conceived as a forum for devising concrete measures and arrangements for sharing information and regulatory work at the international level. The EDQM, which has been involved in the IGDRP from the early stages, participated in two meetings of the IGDRP in 2015: the first in Pretoria (South Africa) in June, and the second in Seoul (Republic of Korea) in November. At the Seoul meeting, the IGDRP's Active Substance Master File (ASMF)/Drug Master File (DMF) Working Group reported, among other things, on the completion of the projects to produce a common submission form, a QAR template and a Lexicon of Quality Terms.

■ The EDQM's work on certification includes an embedded inspection process, which also involves international collaboration and exchange of information and best practice. In October, the EDQM hosted the 7th meeting of the PIC/S Expert Circle on active pharmaceutical ingredients (APIs), which attracted 90 delegates from 40 different PIC/S participating authorities, applicants, partners and non-members from across Europe, the Americas, Australia, Asia and Africa. The overall objective of the meeting was to strengthen international co-operation and share experiences in the field of API inspections.

■ The control of the manufacture and trading of APIs and medicinal products is not limited to dossier assessment and inspections. 2015 also saw further progress in the EDQM's efforts to promote cooperation between authorities at national and international levels in the fight against counterfeit and falsified medical products (medicinal products and medical devices, including ingredients). One of the key tools for this is the MEDICRIME Convention, the first and only binding international instrument in the field of criminal law on counterfeiting and falsification of medical products. In 2015, the Convention was signed by Albania, Bosnia-Herzegovina and Croatia and was ratified by Guinea, which meant that the Convention entered into force on 1 January 2016 with the necessary five ratifications.

■ The EDQM continued to support the development of mass serialisation systems as a tool for preventing the introduction into the legal supply chain of counterfeit and falsified medicines. 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 will directly support the implementation of medicine traceability systems by performing periodic conformity assessments of the European Medicines Verification System (EMVS) developed in the European Union by the EMVO.

■ The EDQM hosts the Melclass database, which contains the recommendations which the Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO) annually issues to health authorities for the classification of medicines and their supply conditions. Melclass also contains national information about the classification status and supply conditions of medicines in the countries participating in this activity. As well as being continually updated in 2015, the Melclass database was upgraded and migrated to a full web application with a responsive design using state-of-the-art technologies and running on a Python platform. The launch of the upgraded database took place in January 2016.

■ Work on the establishment of a future harmonised "European Formulary for Paediatric Formulations" which aims to fill the lack of authorised medicines specifically designed for the paediatric population saw a major step forward with the finalisation by the Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) of guidelines and criteria for the elaboration, re-evaluation and maintenance of paediatric pharmacy preparations.

■ Finally, the EDQM's contribution to the Council of Europe's work to combat organ trafficking took a significant step forward in March 2015, with the opening for signature of the new Convention against Trafficking in Human Organs, in the context of a high-level international conference which was held in Santiago de Compostela (Spain). The Convention, which was adopted by the Committee of Ministers on 9 July 2014, aims to harmonise the penal system in Europe to prosecute more effectively individuals and criminal organisations responsible for trafficking.

■ And of course – as always – we must acknowledge the fact that the EDQM's achievements in 2015 would not have been possible without the remarkable efforts of the experts from national and European authorities, universities, scientific institutes and industry who, through their expertise in a wide variety of scientific fields, have made such valuable contributions to our work. 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. These quality standards – at the end of 2015, comprising 2,302 monographs and 354 general texts – mostly cover excipients and active pharmaceutical ingredients (APIs) in both their original state and in the form of pharmaceutical preparations, and are legally binding for the 38 signatories to the Council of Europe's *Convention on the Elaboration of a European Pharmacopoeia*. They are drafted by a large panel of currently 72 expert groups and working parties which are established by the Ph. Eur. Commission in response to current regulatory, industrial and technical needs. These experts, all volunteers, come from a wide variety of backgrounds and countries, testifying to the truly international scope and reach of the Ph. Eur.

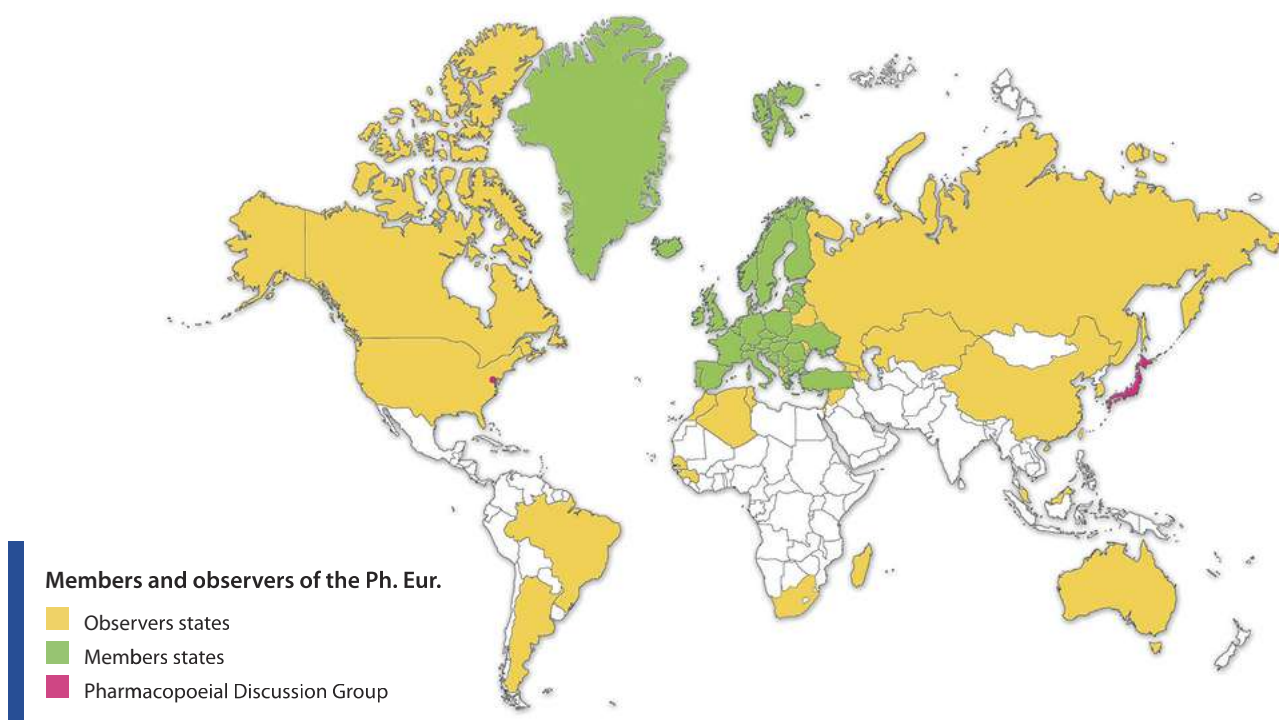
Key facts and figures

Wide participation

■ 37 Member States and the European Union are signatories to the Convention on the Elaboration of a European Pharmacopoeia. With the addition of the Republic of Korea in 2015, there are now also 28 observers

The Work Programme 2015

■ Year-on-year, the European Pharmacopoeia works to provide its users with the most up-to-date and relevant information possible, revising existing monographs to incorporate newly developed methods and techniques and drafting new texts for products of high market relevance. This year's achievements clearly reflect these efforts, with **53 new monographs adopted** (including seven on patent-protected active substances, elaborated in close collaboration with regulators and the respective innovators), **8 new general chapters added** and **988 texts revised** to incorporate both regulatory changes and scientific progress; these include 760 revised individual monographs from which the reference to



the chapter *Heavy metals* (2.4.8) has been deleted in the context of the implementation of the newly-adopted ICH Q3D Guideline for Elemental Impurities. The 9th Edition of the Ph. Eur. will also include 26 revised monographs whose titles have been modified by deleting the word “anhydrous”, a change made necessary by the new policy for hydrates adopted by the Ph. Eur. Commission in 2014. This brings the total number of texts revised in 2015 to 1,014.

At its 151st session, the Ph. Eur. Commission adopted the first monograph on a finished product containing a chemically-defined active substance, Sitagliptin tablets (a widely-used type 2 diabetes medication). With the adoption of this monograph, the Ph. Eur. Commission has signalled its commitment to propelling the Ph. Eur. into a new era.

Work on creating relevant standards for new and evolving areas continued in 2015:

- ▶ The field of radiopharmaceuticals is fast-moving, and the elaboration of specific monographs for non-radioactive precursors for radiopharmaceutical preparations presents many challenges. The product lifecycles of the precursors can be relatively short, since the substances employed can change rapidly and materials can become redundant due to technological and scientific advances. As a result, information on the quality control of the substances is often not readily available and thus the need for a general monograph had been identified. By elaborating and adopting a new general monograph on *Chemical precursors*

for radiopharmaceutical preparations (2902), the Ph. Eur. Commission filled a gap in a rapidly evolving field. This new general monograph provides a self-contained set of quality criteria for chemical precursors and gives guidance on further aspects to be considered. This text is an important complementary monograph to the existing general monograph for *Radiopharmaceutical Preparations* (0125), which has been updated accordingly and keeps the Ph. Eur. at the forefront in terms of quality standards in this area. The Ph. Eur. Commission also adopted a chapter on *Extemporaneous preparation of radiopharmaceuticals* (5.19), which describes non-binding standardised procedures for preparing radiopharmaceuticals of appropriate quality. This chapter does not replace existing national legislation.

- ▶ The Ph. Eur. Commission adopted a new chapter on *Raw materials of biological origin for the production of cell-based and gene therapy medicinal products* (5.2.12). This general chapter aims to assist stakeholders in ensuring that raw materials are of suitable quality and to foster harmonisation in the qualification practices and standards to apply. It is published for information in the Ph. Eur. and includes sections on the risk, origin, production and quality requirements of raw materials of biological origin used for the production of cell-based and gene therapy medicinal products for human use.

- ▶ The Ph. Eur. Commission also continued to revise monographs on vaccines for veterinary use to align them with the Veterinary International Conference on Harmonization (VICH) guidelines 41 and 44 and to delete the target animal batch safety test (TABST). Further emphasis was placed on the use of *in vitro* test methods to control inactivated veterinary vaccines – in line with the 3Rs principles, i.e. Replacement, Refinement & Reduction of the use of animals in research – with the revision of around 40 inactivated vaccine-specific monographs and of the general monograph *Vaccines for veterinary use* (0062).
- ▶ Regarding herbal drugs, the Ph. Eur. Commission elaborated and adopted a general method on *High performance thin-layer chromatography of herbal drugs and herbal drug preparations* (2.8.25), in order to improve the reproducibility of identification methods and tests for adulteration by better standardising the high performance thin-layer chromatography. Together with the general chapter, several monographs on herbal drugs and herbal drug preparations – such as *Birch leaf* (1174), *Roman Chamomile flower* (0380), *St. John's wort* (1438) and *St. John's wort dry extract, quantified* (1874) – were adopted, showing the practical application of the new chapter. To support the user, sample chromatograms were published in the Knowledge database showing the natural variability of the herbal drugs and herbal drug extracts.
- ▶ The Ph. Eur. Commission adopted the general chapter on *Chemometric methods applied to analytical data* (5.21), which provides an introduction to the use of chemometric techniques for processing analytical data sets. The aim of this non-binding chapter is to provide recommendations and requirements for good chemometric practice.

General matters and policies

Developments in 2015

■ By nature, a pharmacopoeia is a work in progress, and by necessity it is influenced by developments in its environment, both internal and external. In 2015, the Ph. Eur. Commission therefore continued its reflection on the implementation strategy for the ICH Q3D Guideline for Elemental Impurities: several general chapters and monographs will need to be revised.

■ The work of the Ph. Eur. would not have been possible without the contributions and dedication of a network of more than 700 experts in pharmaceutical sciences; most of these experts come from Ph. Eur. member states but some are from observer states to the Convention on the Elaboration of a European

Pharmacopoeia. The participation of outside stakeholders in the Ph. Eur.'s public standards-setting process is vital for the development of authoritative and relevant monographs. To further reflect the Ph. Eur.'s global status and the pharmaceutical world which has undergone dramatic change over the past 50 years, becoming a globalised operating environment for drug substances and medicinal products, the Ph. Eur. Commission reviewed its working procedures to allow the nomination of experts from non-Ph. Eur. member states. This decision is part of a deliberate policy to further involve not just observer states but also manufacturers from outside Europe in the work of the Ph. Eur. This new policy will apply for the nomination of experts scheduled in 2016.

Development of international harmonised vocabularies

■ For a number of years, the EDQM has been actively participating in the development of the set of five ISO Standards to harmonise the identification of medicinal products (IDMP) from a regulatory perspective. As part of Working Group (WG) 6 of Technical Committee ISO/TC 215-Health Informatics, the EDQM provided the project lead for ISO 11239, related to the preparation of controlled vocabularies for pharmaceutical dose forms, routes of administration, units of presentation and packaging. ISO 11239 was published as an International Standard in 2012 and, since then, the EDQM has continued to participate in WG 6 by providing the project lead for TS 20440, the Implementation Guide for ISO 11239. In 2015, TS 20440 was accepted for publication as an ISO Technical Specification, and is due to be published in early 2016.

■ As a result of its management of the Standard Terms database and its involvement in the development of ISO 11239 and TS 20440, the EDQM has been widely acknowledged as the maintenance organisation of choice for the ISO 11239 controlled vocabularies, which form an essential part of the global IDMP project.

Standard Terms

■ Initially drawn up at the request of the Commission of the European Union (EU Commission) for use in marketing authorisation (MA) applications, the lists of Standard Terms provide users and prescribers with harmonised vocabularies to describe dosage forms, routes of administration and packaging for medicinal products. Following the substantial overhaul and relaunch of the Standard Terms database in late 2014 in line with the IDMP Standard ISO 11239, the new-look database – now accessible free of charge – attracted almost 10,000 registered users within twelve months. As of the end of 2015, the Standard Terms database held 870 individual terms and definitions with over 23,000 translations in 33 languages.

Achievements of the Biological Standardisation Programme (BSP)

■ The BSP is a joint EDQM-EU Commission initiative whose mandate is to establish reference materials, develop and validate new analytical methods, and validate alternative methods based on the 3Rs concept for the quality control of biologicals.

■ In 2015, 26 projects were pursued in different fields, ranging from vaccines for human and for veterinary use to plasma-derived and biotechnology products. This led to the establishment of five new reference standards (see section “Pharmaceutical Reference Standards”, page 12).

■ Eight projects were underway to establish replacement batches for existing reference standards, all prompted by low stocks; it was not necessary to stop using a reference standard owing to quality issues. Five projects were underway for the elaboration of reference standards for new monographs or new requirements in existing monographs.

■ Eight projects aimed at the development of new compendial methods. Six of these concerned the application of the 3Rs concept to the field of quality control of biologicals. The continued efforts of the BSP to elaborate, validate and implement analytical methods following the 3Rs principles are widely acknowledged. The results of the BSP130 project on the replacement of animal tests for the determination of the Minimum Lethal Dose (MLD) and the Total Combining Power (TCP) antigenicity test in mice required by the Ph. Eur. for *Clostridium septicum* vaccines for veterinary use were presented in a workshop co-sponsored by the European Partnership for Alternative Approaches to Animal Testing (EPAA) and the EDQM. On the basis of this positive study outcome, an optimised protocol for the cell-based assay methodology was designed for a follow-up study with broad participation; a new collaborative study will start in 2016.

International harmonisation and the Pharmacopoeial Discussion Group

■ The Ph. Eur. continued its efforts to reduce duplication of testing and reporting during drug development and quality control through the work of the Pharmacopoeial Discussion Group (PDG) – comprising the Ph. Eur., the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP) as members and the World Health Organization (WHO) as an observer. Two meetings were held in 2015; one was hosted by the JP in Tokyo (Japan) in July and the other by the USP in Rockville (USA) in November.

■ **29 of the 36 General Chapters and 48 of the 62 excipient monographs** currently on the work programme have been harmonised. This year's

meetings saw the signing-off of three new excipient monographs as well as the revision of *Povidone*, and a new general chapter as well as a revised general chapter (*Uniformity of Content/Mass*). In-depth discussions on a number of additional items currently on the work programme took place with a view to resolving outstanding issues and progressing towards sign-off. Highlights summarising the outcome of each PDG meeting are available on the websites of the three pharmacopoeias.

■ Following the sign-off of the ICH Q3D Guideline for Elemental Impurities, PDG members confirmed their commitment to harmonising the general chapter on testing procedures for elemental impurities. A Stage 3 draft was sent by the coordinating Pharmacopoeia and commented by the two other Pharmacopoeias.¹

■ The *Chromatography* chapter is another key item in the PDG's work programme. The coordinating pharmacopoeia had submitted a revised Stage 3 draft of the chapter based on decisions made during a teleconference with experts from the three regions. Comments will be further discussed with the Experts of the coordinating Pharmacopoeia with a view to presenting a Stage 4 draft for public inquiry.

Further harmonisation initiatives

■ The Ph. Eur. is also actively involved in a number of other international harmonisation initiatives, such as the WHO initiative to draft “Good Pharmacopoeial Practices” (GPhP), which may serve as a basis for future work-sharing and collaboration amongst pharmacopoeias worldwide.

■ The International Meeting of World Pharmacopoeias is organised under the auspices of WHO, with the aim of bringing together the different pharmacopoeias and discussing potential ways to strengthen collaboration and harmonisation, for example, via the elaboration of the GPhP. Two meetings took place in 2015, one in April in Washington DC (USA) and the other in September in Suzhou City (People's Republic of China). The main text of the GPhP was finalised, approved by the WHO's Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) at its 50th meeting and was finally approved by all participating Pharmacopoeias.

1. At Stage 4 of the PDG process, a harmonised document is prepared, accompanied by a commentary discussing comments received from the relevant expert committees regarding the previous text; these are then published in the forum of each pharmacopoeia for public enquiry.

Cooperation with National Pharmacopoeia Authorities (NPAs)

■ The EDQM organises an annual meeting of NPA Secretaries to facilitate and coordinate activities of common interest and to provide an informal forum for exchanging information. The 2015 annual meeting of the NPAs of Ph. Eur. member states took place in Utrecht, The Netherlands, in June, hosted by the RIVM (National Institute for Public Health and the Environment). Twenty-five of the 37 member states took part; they discussed the publication schedule for the 9th Edition and started to prepare for the re-appointment of all Ph. Eur. experts scheduled to take place in 2016.

Publications, databases and website



■ The 8th Edition of the European Pharmacopoeia – incorporating its 2015 updates (8.6, 8.7 and 8.8) – contains 2,302 monographs, including general standards that apply to groups of ingredients or dosage forms, and 354 general texts including methods of analysis.

■ *Pharmeuropa online* is a free online publication, in which draft Ph. Eur. texts are published for consultation. Easily and widely accessible, the objective is to optimise interaction between the European Pharmacopoeia Commission and its stakeholders. Texts are published on an ongoing basis, but the principle of four deadlines per year has remained unchanged, as have channels and procedures for sending comments on published draft texts. In 2015, 157 draft texts were published on *Pharmeuropa online*, which was accessed from over 150 countries worldwide by almost 22,000 registered users as of 1 January 2016.

PHARMACEUTICAL REFERENCE STANDARDS

What are reference standards and why are they needed?

Ph. Eur. reference standards

Official reference standards (RSs) are an essential component of most texts of the Ph. Eur. They 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. They alone are authoritative in case of arbitration.

Responsibility for WHO reference standards

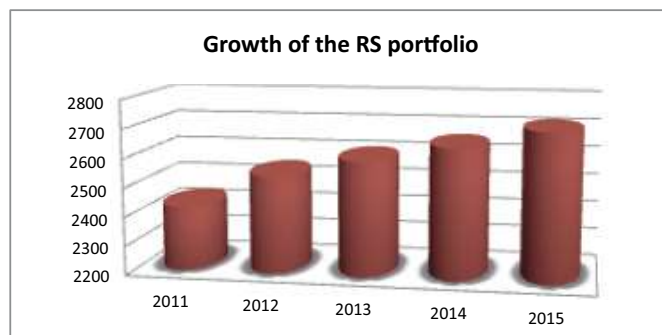
■ The EDQM is responsible for the establishment, monitoring and distribution of WHO International Standards for Antibiotics (ISA) and for WHO International Chemical Reference Substances (ICRS). ISA are supplied worldwide for use in microbiological assays performed for quality control of antibiotics, and are essential for the standardisation and quality control of antibiotic drug substances and medicinal products. ICRS are prescribed by the International Pharmacopoeia, which is published and maintained by WHO and used worldwide.

■ The EDQM also participates in the WHO's ECSPP, contributing to the development of norms, standards and guidelines to promote quality assurance and quality control.

Key facts and figures

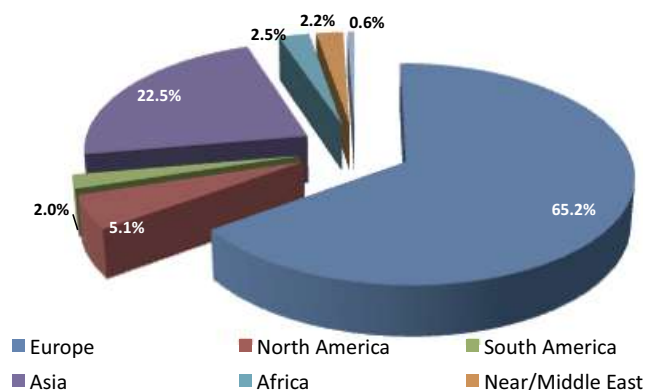
Reference standards for the European Pharmacopoeia

■ At the end of 2015, there were 2,708 reference standards in the Ph. Eur. catalogue.



■ Globalisation of the pharmaceutical industry means that Ph. Eur. RSs are widely used internationally: in 2015, Ph. Eur. RSs were distributed in 112 countries.

Ph. Eur. RS vials distributed by geographical area



New RSs adopted in 2015

■ CRSs used for assay require thorough characterisation in order to assign a quantitative content value. In 2015, the EDQM Laboratory (DLab) established 75 assay CRSs, 32 of which required inter-laboratory studies involving public as well as private laboratories.

■ In 2015, the Ph. Eur. Commission adopted 60 new CRSs and 239 replacement CRSs.

■ The international collaborative studies performed by the BSP in 2015 led to the conclusion of five projects and the adoption of the following BRP/BRR replacement batches by the Ph. Eur. Commission (*see section "The European Pharmacopoeia", page 10*): Rabies vaccine (inactivated) for veterinary use BRP, batch 5; Human Coagulation Factor VIII concentrate BRP, batch 5; set of Hepatitis A virus Detection Antibodies for ELISA-BRR, batch 3; Human Albumin for Electrophoresis BRP, batch 3; and Heparin Low-Molecular-Mass for Assay BRP, batches 9 and 10.

EDQM activities for WHO

International Standards for Antibiotics

■ The project for the establishment of the fourth ISA for Streptomycin was concluded in 2015. This ISA was adopted by the WHO's Expert Committee on Biological Standardisation (ECBS) at its October meeting.

International Chemical Reference Standards

■ In 2015, the ICRS board adopted a total of 5 establishment reports submitted by the EDQM Laboratory: Abacavir sulfate ICRS 2; Paracetamol ICRS 3; Artemether ICRS 3, Rifampicin ICRS 3 and Stavudine impurity F ICRS 1.

General matters and policies

Extended competence in Nuclear Magnetic Resonance (NMR)

■ Thorough characterisation of candidate materials is essential for proper establishment of reference standards. In its continuous effort to improve characterisation, and keeping abreast of constantly evolving technology, the EDQM has further extended its competence in NMR to encompass quantitative application. In addition, a high resolution quadrupole time-of-flight (Q-TOF) mass spectrometer (pictured below) has been acquired and installed.



Collaboration with national laboratories

■ Some RSs (generally for assay/potency tests) are established through a collaborative study involving several laboratories. Continuous collaboration with national laboratories and centres of excellence is fundamental for collaborative studies. Official Medicine Control Laboratories contribute to these studies: at the end of 2015, there were 37 such laboratories in 26 different countries taking part in DLab studies.

Publications, databases and website

■ In 2015, the EDQM finalised the publication of information leaflets for all 2,708 Ph. Eur. RSs, which provide users with additional useful information such as monograph references, scientific information, storage conditions and – when applicable – hazard pictograms and signal words.



■ In addition, 57,000 safety data sheets for Ph. Eur. and WHO RSs, including their translations into 24 European languages (as needed), are accessible directly 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 national authorities of European countries as regards the monitoring and quality control of substances used in the manufacture of medicines.

■ The Certification of Suitability procedure has been set up by the EDQM to evaluate and validate the capacity of Ph. Eur. standards to control the quality of substances used in the production of medicinal products. To apply for a Certificate of Suitability to the monographs of the European Pharmacopoeia (CEP), manufacturers must submit a dossier describing how their product is manufactured and quality-controlled. The EDQM's decision to grant a CEP is based on the evaluation of the data in this dossier. 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 active substances covered by CEPs, to ensure that Good Manufacturing Practices (GMPs) are applied and that the information supplied under the Certification procedure is accurate.

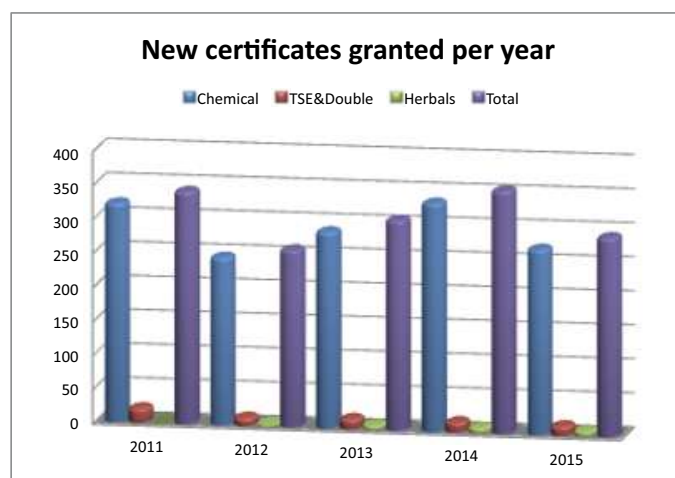
■ An increasing number of licensing authorities worldwide accept CEPs to support (fully or partially) the data related to the quality of APIs used in medicinal products.

Key facts and figures

■ 391 new applications were received in 2015, which is a significant increase over previous years, and in addition the number of requests for revision rose by some 16 per cent (almost 1,900 requests).

■ 291 new certificates and 1,565 revised certificates were issued in 2015.

■ The Certification Division relies on a network of some 100 assessors from 24 different competent authorities for the assessment of applications. There are currently more than 4,200 valid CEPs, covering chemical purity, the risk of transmissible spongiform encephalopathy (TSE) and herbal drug preparations. Overall, over 90 per cent of applications received were dealt with within official timelines.



■ As part of the EDQM inspection programme, 38 manufacturing sites – located mostly in Asia – were inspected with the participation of inspectors from national supervisory authorities. In addition, information on GMP compliance of 42 other sites was obtained by exchanging data with inspectorates from member states and international partners. This led to action being taken on CEPs where relevant. The rate of non-compliance for sites inspected by the EDQM was 18% in 2015. The EDQM inspection programme is fully embedded in the Certification system and it is estimated that about 60% of the sites located in Asia and linked to CEPs have been covered by this programme.

General matters and policies

■ The Certification Division published a number of guidelines and policies in 2015, in order to help applicants in the preparation of their CEP dossier or in their communication with the EDQM.

■ In 2015, the Steering Committee met once, the Technical Advisory Board for chemical purity evaluation met three times, and the Technical Advisory Board for the TSE risk met once. These meetings contribute to addressing the scope of the CEP procedure and related technical issues.

Communication with partners and stakeholders

■ In 2015, the Certification Division continued to be involved in a number of international platforms for collaboration, such as the IGDRP (*see section "2015: A year rich in events and meetings", page 33*), the European Union's Working Group on Active Substance Master File Procedures (ASMF WG), the International API Inspection Programme, the PIC/S and the ICH Q11 Implementation Working Group.

■ In October 2015, a confidentiality agreement was signed between the EDQM and the Medicines Control Council (MCC) of South Africa in order to exchange confidential information about the quality of active substances.

■ As part of the EDQM's collaboration with Australia's Therapeutic Goods Administration (TGA) and the American Food and Drug Administration (USFDA), a total of 3 joint inspections were carried out in 2015.

■ The Certification procedure also features in the EDQM's annual meetings with industry associations as a means of promoting exchanges on the EDQM's work in general and getting feedback from stakeholders about the use of CEPs.

THE EUROPEAN NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES (OMCLs)

Why a European network?

■ Created to prevent substandard medicinal products from reaching patients and compromising the efficacy of their treatments, the OMCL Network continued in 2015 to support the authorities in charge of market surveillance within the framework of controlling the quality of medicines for human and veterinary use.

■ Operating independently of manufacturers and thus without any conflict of interest, 70 OMCLs in 41

member states took part in the Network, which is partially funded by the European Union.

■ This pan-European collaboration offers several advantages, not least the pooling of know-how by experts, access to state-of-the-art technology and selective analytical methods, work-sharing and mutual recognition of test results based on commonly-agreed procedures and guidelines. It also means that national competent authorities do not duplicate their efforts, thus saving time and resources and reducing the cost of testing medicinal products.

Quality Management Programme

■ Efforts to implement, maintain, assess and improve quality management (QM) systems on a harmonised basis were pursued throughout the Network in 2015.

Mutual Joint Audits/Visits (MJAs/MJVs)

■ Designed to assess the compliance of OMCL QM systems with the requirements of ISO/IEC 17025, the Network Quality Management Guidelines and the Ph. Eur., 12 MJAs were carried out on OMCL sites in 2015. Since the QM Programme was launched in December 1997, 130 MJAs, 50 MJVs, 2 Tutorials and 19 Training Visits have been carried out in the OMCL Network.

OMCL Network QM Guidelines

■ New QM guidelines drafted by experts from the OMCL Network are designed to provide support for laboratories in implementing the ISO/IEC 17025 requirements. In 2015, a new guideline for "*Calibration/Qualification of pH-Meters*" was adopted by the OMCL Network and the guideline for "*Evaluation and reporting of results*" was revised.

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

■ The EDQM has reached out to the EA, with the aim of evaluating the possibility of future cooperation between the two institutions, focusing on exchange of know-how, joint audits by national accreditation bodies (NAB) and EDQM/MJA auditors and mutual participation in meetings as observers. As a result, three joint audits were carried out with the NAB in 2015.

Training Courses/workshops

■ A workshop for experienced MJA auditors was organised to share experience and harmonise approaches for specific topics.

Proficiency Testing Scheme (PTS) studies

■ The EDQM's PTS provides laboratories with an objective means for assessing and demonstrating the reliability of their data.

■ In 2015, five studies were organised in the physico-chemical field, with an average of 56 participants from OMCLs and 44 from other pharmaceutical control laboratories in the private sector (including industry), hospitals and pharmacies taking part. The following studies were run: PTS156 Loss on drying; PTS157 Potentiometric determination of pH; PTS158 Infrared absorption spectrophotometry; PTS159 Dissolution test; and PTS160 Liquid chromatography, assay.

■ Four biological studies were organised involving an average of 20 laboratories: PTS161 Hepatitis C virus-Nucleic Acid Amplification Test (NAT); PTS162 Parvovirus B19 NAT; PTS163 Low-molecular-mass heparins, chromogenic assay (anti-Xa and anti-IIa activity); PTS164 Fibrin sealant – fibrinogen and thrombin potency.

General OMCL Network (GEON) activities

General studies on market surveillance

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

■ In 2015, two MSSs were finalised: MSS044 on Heparin and low molecular mass heparin APIs and finished products, and MSS045 on Eye drops and nasal preparations registered as medical devices (the latter was the first MSS organised within the Network which focused on medical devices).

■ In addition, the testing phase of two MSSs launched in 2014 (MSS046 on Telmisartan APIs and tablets and MSS047 on Pramipexole APIs and tablets) was completed and two new studies, MSS049 on Irbesartan APIs and tablets and MSS048 on Subdivision of tablets, were initiated.

API Working Group

■ Globalisation of the manufacture and trading of active ingredients has created a need for increased control of APIs. The implementation of the Falsified Medicines Directive (2011/62/EU) in the EU in 2013 was an important measure. The involvement of OMCLs in the monitoring of APIs on the European market has been identified as one of the strategic recommendations for the Network in responding to the threat of counterfeiting and in supporting the MEDICRIME convention. The 8th meeting of the API

working group took place in May 2015. The discussions focused on new "Fingerprint" MSSs and the better use of API samples available in the Network for national testing programmes. In this context, the importance of the API testing database as tool for the planning of testing campaigns and sharing of test results was highlighted. The problem of random sampling of APIs was another topic addressed by the group, and it was agreed that improved strategies would need to be developed. Later in the year, two new "Fingerprint" studies on omeprazole and morphine were initiated.

Counterfeit/Illegal Medicines Working Group

■ The Counterfeit/Illegal Medicines Working Group met twice in 2015. One goal of the meetings was to analyse the outcome of past Market Surveillance Studies on Suspicious Illegal Products (MSSIP) and to discuss timelines for new studies (*see also "General studies on market surveillance"*). A collaborative study on non-declared APIs in cosmetics was initiated as the next MSSIP.

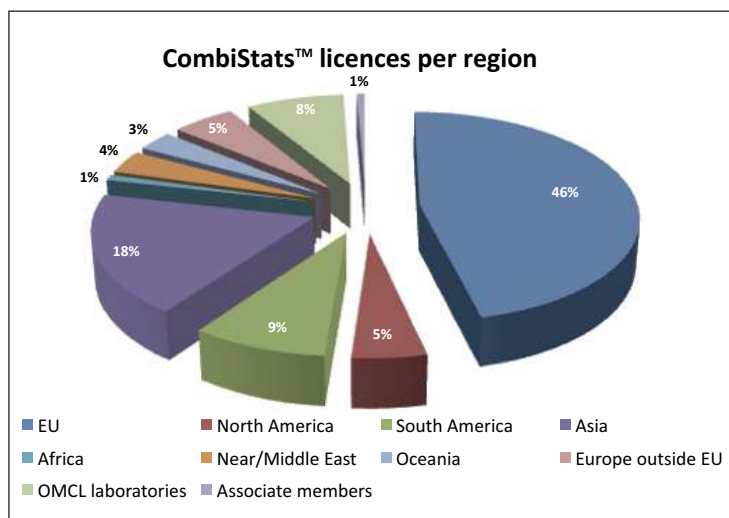
■ Two technical training sessions for OMCL members were organised jointly by the EDQM and the French and Swiss OMCL respectively, in Montpellier in March and in Berne in November; the spotlight in Berne was on testing falsified biologicals.

■ Ways to improve the user-friendliness of the Know-X database, which was launched in March 2014, were discussed. All changes to the database were finalised by the end of 2015 and as of January 2016, 2,500 individual cases had been uploaded onto Know-X by OMCLs.

Gene Therapy Products (GTP) Working Group

■ The OMCL Working Group for GTP was created in 2008 to foster collaboration between OMCLs working in the field of GTPs, in order to save time and resources through sharing knowledge and technologies. Currently, 11 OMCLs are active members of the Working Group.

■ In 2015, the standard methods for the determination of viral and infectious genomes in adeno-associated viral vector (AAV) products were validated. The 7th Annual Meeting of the Working Group was hosted by the Austrian OMCL (AGES, Vienna) in December. The work programme was reviewed and revised to include new vectors (Herpes simplex and retroviral vectors) in view of recent developments in the field and following the positive opinion of the European Medicines Agency (EMA) for a MA for Imlygic® (Herpes simplex virus-based oncolytic virus for the treatment of melanoma).



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

One training course was organised in October, which was also open to participants from industry and the private sector.

The number of users has steadily increased since public release of the software in 2013. By December 2015, 8% of the licences were issued to OMCL laboratories in 25 countries and 92% to non-OMCL users in 45 countries. The pie-chart shows that roughly half of the non-OMCL licences were issued within the EU and the remainder in the rest of the world. CombiStats™ has thus evolved into a common internationally-agreed reference in its domain and contributes to mutual recognition of data and results by all interested parties.

GEON Annual General Meeting

The 20th Annual Meeting of the GEON was held in Brussels from 1 to 5 June 2015. The conference was co-organised and co-sponsored by Belgium's Scientific Institute of Public Health (WIP-ISP), the Federal Veterinary and Agrochemical Research Centre (CODA-CERVA) and the Federal Agency for Medicines and Health Products (FAGG-AFMPS). The meeting brought together more than 240 experts from 61 OMCLs, national medicines agencies and the EU Commission. The Singapore Pharmaceutical Laboratory of the Health Science Authority (HSA) participated for the first time, after the HSA had become an associated member of the Network in May 2014. The programme was organised in nine individual sessions.

EU/EEA-specific activities

Market Surveillance for Products with a Centralised Marketing Authorisation

A contract between the EMA and the EDQM governing an annual Centrally Authorised Products (CAP) Sampling & Testing Programme has been in place since 1999. 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, using a risk-based approach tool.

The programme for sampling and testing CAPs was successfully pursued in 2015 with 33 products for human use (16 biologicals and 17 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 2015, during which 12 branded Irbesartan and Temozolomide products (generic medicinal products and their respective reference medicinal products) were tested.

137 sampling operations were performed within the framework of the 2015 CAP Programme and 34 OMCLs were involved in the testing operations. The controls showed that the vast majority of the products tested were of the expected quality and complied with the authorised specifications for almost all products. One confirmed out-of-specification result as well as several regulatory or technical findings were reported. The EMA handles the follow-up for these observations.

Mutual Recognition Procedure (MRP)/ Decentralised Procedure (DCP) post-marketing surveillance scheme

The OMCLs involved in the programme met twice in 2015 (26th and 27th meeting) to evaluate the programme and discuss ways to optimise collaboration.

The 11th regular programme for the market surveillance of medicinal products authorised in the EEA via the MRP or DCP procedure was carried out. More than 1,000 product-testing projects were added to the 2015 programme, which is an increase over the previous year. The 2015 test reports came from 27 different OMCLs.

Regulatory issues were identified in about 3 per cent of the materials tested (e.g. insufficient details of test method, wrong calculation formula), with one or more out-of-specification results reported in a further 2 per cent of cases. Seven per cent of the tested products were for veterinary use. Two per cent of tested samples were biologicals, which reflects the

general distribution of product types registered via these European procedures. As of December 2015, the database held some 7,300 MRP- and DCP-product testing records, with contributions from 34 OMCLs. During the period 2002 to 2015, a participating member state testing one product received test results for an average of 9 products generated by other member states, which clearly demonstrates the advantages of the Network.

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

■ The activities of the human OCABR network ensure the harmonised application of Article 114 of EU Directive 2001/83/EC by fostering the mandatory mutual recognition of batch release for human vaccines and medicinal products derived from human blood and plasma. Protocol review and testing of the more than 9,000 final lots proposed for OCABR and close to 9,000 plasma pools was carried out by the network to independently confirm their quality before they reached patients.

■ With more than 90 participants, the turnout at the OCABR sessions of the GEON Annual Meeting in Brussels was the largest in five years. An excellent opportunity for exchanging expertise, these sessions are also a way of optimising resources for common problem solving. The OMCLs also addressed complex technical issues to allow better control of products such as combination vaccines for children and medicinal products for haemophiliacs. The annual workshop on testing oral poliomyelitis vaccine bulks attended by OMCLs and manufacturers and the meeting between vaccine manufacturers and the OCABR Advisory Group were successful opportunities to maintain open communication lines, allowing the system to run smoothly.

■ One new and 4 revised guidelines for vaccines, one revised guideline for blood-derived products and a number of internal network guidelines came into force in 2015.

OCABR of Immunological Veterinary Medicinal Products (IVMPs)

■ This subset of specialised OMCLs and competent authorities focuses on the independent control of immunological veterinary medicinal products according to Articles 81 and 82 of EU Directive 2001/82/EC, as amended.

■ Thirty-one participants from 16 member states took part in the Veterinary Batch Release Network (VBRN) session of the annual meeting. Annual reports demonstrated that active participation in the system is increasing; however, mechanisms need to be found to better share the workload and ensure that competence is maintained.

■ The reactivity of the system was demonstrated by the adjustments to a testing programme agreed for a specific group of vaccines based on the results obtained during OMCL testing. The VBRN advisory group met with the IVMP manufacturers' representatives in February to discuss common issues.

■ One new and 3 revised product-specific guidelines, 1 manufacturers' protocol template for live viral vaccines and the revised EU Administrative Procedure for Application of Article 82 for Official Control Authority Batch Release of IVMPs came into force in 2015.

ANTI-COUNTERFEITING ACTIVITIES

Combating crime to protect public health

■ The EDQM continued to promote cooperation between authorities at national and international levels in the fight against counterfeit and falsified medical products (medicinal products and medical devices, including ingredients). One of the key tools for this is the MEDICRIME Convention, the first and only binding international instrument in the field of criminal law on counterfeiting and falsification of medical products. The experts serving on the Steering Committee 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 aiming at disseminating best practices.

Key facts

■ Efforts focused on encouraging authorities and governments to sign and ratify the Convention. Together with the Parliamentary Assembly of the Council of Europe and the Criminal Law Division of the Directorate General Human Rights and Rule of Law, the EDQM contributed to the publication of a Handbook for Parliamentarians on the Convention, alerting them in particular to the importance of ratification. The handbook was launched at a parliamentary conference in Paris in November. In the same month, the EDQM supported the Criminal Law Division of the Directorate General Human Rights and Rule of Law in organising a regional conference on the MEDICRIME Convention in Cyprus. In 2015, the Convention was signed by Albania, Bosnia-Herzegovina and Croatia and was ratified by Guinea, which meant that the Convention entered into force on 1 January 2016 with the necessary five ratifications.

■ The promotion of the MEDICRIME Convention goes hand-in-hand with activities developed and supported by the EDQM and its experts to implement

Signatures and ratifications of the MEDICRIME Convention

Signatures

■ Albania	17/12/2015
■ Austria	28/10/2011
■ Belgium	24/07/2012
■ Bosnia and Herzegovina...	04/12/2015
■ Croatia	03/09/2015
■ Cyprus	28/10/2011
■ Denmark	12/01/2012
■ Finland	28/10/2011
■ France	28/10/2011
■ Germany	28/10/2011
■ Iceland	28/10/2011
■ Italy	28/10/2011
■ Israel	28/10/2011
■ Liechtenstein	04/11/2011
■ Luxembourg	22/12/2011
■ Morocco	13/12/2012
■ Portugal	28/10/2011
■ Russia	28/10/2011
■ Switzerland	28/10/2011
■ Turkey	29/06/2012

Ratifications

■ Armenia	05/02/2016
■ Guinea	24/09/2015
■ Hungary	09/01/2014
■ Moldova	14/08/2014
■ Spain	05/08/2013
■ Ukraine	20/08/2012

■	Member States of the Council of Europe
■	Non Member States of the Council of Europe

the Convention and its tools in practice. One example is the collection of information and data on counterfeit and falsified products through single points of contact (SPOCs) established at local, national and international levels between health authorities, customs, police and other competent authorities. The EDQM continued to deliver training to such authorities for this particular purpose, in collaboration with:

- ▶ the Asia-Pacific Economic Cooperation (APEC), in the context of the APEC Roadmap for Global Medical Product Integrity and Supply Chain Security – a training event was held in the Philippines for representatives of authorities from 12 APEC member states in January;
- ▶ the EU-funded project “Responding Effectively to the Production and the Trafficking in falsified medicines” (REPT), with which a Memorandum of Understanding was signed, allowing SPOC training events to be organised in 3 countries (Cameroon, Ghana and Jordan) in the last quarter of 2015.

■ In June, healthcare professionals and authorities took part in an expert workshop to discuss the outcome of a study on a screening tool designed to help medical doctors detect symptoms (“signals of harm”) caused by the possible use of counterfeit and falsified medicinal products.

Anti-counterfeiting traceability service for medicines

■ The EDQM continued to support the development of mass serialisation systems as a tool for preventing counterfeit and falsified medicines from contaminating the legal supply chain. To this end, EDQM promotes a harmonised approach in Europe and public governance of all traceability systems in order to prevent any misuse of data.

■ As a result of the agreement signed in 2015 between the EDQM and the EMVO, which is comprised of various European supply-chain operators, the EDQM will directly support the implementation of medicine traceability systems by performing periodic conformity assessments of the EMVS developed in the EU by the EMVO. This will make it possible to determine whether the European system (European hub and national systems) is designed, managed and operated in accordance with the standards described in the Delegated Act on the Unique Identifier² implementing the EU Falsified Medicine Directive (Directive 2011/62/EU).

API Fingerprint Programme

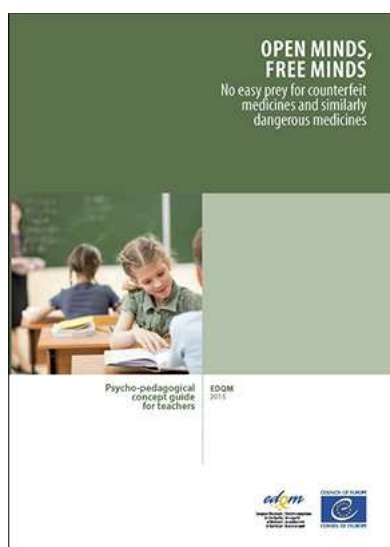
■ The project continued, with the preparation of two new studies to be run in 2016, targeting the APIs omeprazole and morphine. The experience gained through the 2014-2015 study on macrolide antibiotics and statins, which made extensive use of chemometric analysis to cluster sources of APIs, helped to further develop the project.

2. See <https://go.edqm.eu/2016161regu>

Publications, databases and website

■ The EDQM maintains a secure and restricted database called Know-X to store comprehensive information on individual cases of counterfeit and falsified medical products after a criminal investigation has been completed. 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 terms of trend monitoring and follow-up.

■ Know-X also hosts information related to chemical-analytical identification of medicinal products (see section “The European Network of Official Medicines Control Laboratories”, page 15), as well as data on the modus operandi, risk management and prevention measures taken by the competent health or enforcement authorities. The Committee of Experts CD-P-PH/CMED cooperates with the OMCL working group on counterfeit medicines to maintain the database and is also involved in its ongoing promotion and in user training. As of 2015, reports include a section on risk criteria and risk assessment in order to improve risk-oriented approaches in general.



■ In 2015, the EDQM published a concept guide for teachers, which includes a cartoon booklet. It is aimed at supporting training and education in schools, explaining to children and adolescents the risks posed by counterfeit and falsified medical products and encouraging behaviours that will avoid exposure to them.

■ The EDQM and experts from the Committee CD-P-PH/CMED contributed significantly to the publication of a Handbook for Parliamentarians on the MEDICRIME Convention (see “Key facts” above).

Communication with partners and stakeholders

■ Representatives of the EDQM and of the CD-P-PH/CMED participated in IFPMA (International Federation of Pharmaceutical Manufacturers & Associations) conferences in Asia and Africa.

PHARMACEUTICALS AND PHARMACEUTICAL CARE

Optimal use of medicines for improving patients' quality of life

■ The activities in this area are carried out by the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and subordinate bodies.

Key Facts

■ The Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC) completed the study run for the validation of 4 basic sets of indicators for the quality of pharmaceutical care in Europe under the Pharmaceutical Care Quality Indicators Project (PCQIP). The indicators cover the following key areas of the pharmaceutical care process:

- ▶ Adherence to antimicrobial prescribing guidelines in ambulatory care settings;
- ▶ Monitoring of therapeutic plans and medication safety by pharmacists through data linking and exchange of information about therapy and the patient's medical condition in anticoagulant and antibiotic therapy;
- ▶ Structured patient-pharmacist consultations (chronic therapy; poly-pharmacy; polymorbidities) via “My CheckList”;
- ▶ Pharmacist's self-assessment concerning the implementation of the pharmaceutical care philosophy and working methods in community pharmacy settings.

■ Validated quality indicators are currently available for implementation in different countries across Europe with different healthcare systems, medical traditions and pharmaceutical care practices. The indicators can support policy-makers, health authorities and healthcare professionals in the evaluation of the quality of pharmaceutical care and pharmaceutical practices. They can thus contribute to the continuous improvement of health outcomes and patients' quality of life as well as to the efficient and effective use of resources. The EDQM will ensure that the outcomes of the PCQIP, which it presented in a workshop held in November, will be disseminated

widely. It will also promote the implementation of the PCQIP approach through partnerships with relevant stakeholders and appropriate policy guidance, to reinforce the harmonisation of quality standards in Europe.

■ The project to prepare the future harmonised “*European Formulary for Paediatric Formulations*” (PaedForm), which is run under the auspices of the CD-P-PH in close cooperation with the Ph. Eur. Commission, aims to address the lack of authorised medicines specifically designed for the paediatric population. The approach chosen, as a first step, was to identify suitable candidate unlicensed preparations in national formularies and to elaborate monographs on the basis of CD-P-PH-approved criteria. In 2015, the Criteria for Inclusion and Evaluation of Monographs, the Criteria for Maintenance and Vigilance of Monographs and the Procedure for the European Paediatric Formulary were elaborated and approved by the CD-P-PH. With the adoption of these documents, the Ph. Eur. PaedForm Working Party can start reviewing national formularies collected from among member states within the framework of the project.

■ In 2015, the guide on the best practices for automated dose dispensing (ADD) systems and their implementation in Europe was finalised, taking into account the discussions at a workshop organised by the EDQM in September, which was attended by experts from national authorities, pharmacies and ADD system operators. The scope of the project is to provide member states with a guidance document on the emerging practice of automated preparation of individual and customised containers or pouches containing different medicinal products prescribed to patients. The guideline proposes a holistic approach, covering aspects ranging from technical requirements and risk assessment to handling medicinal products once they have been removed from their outer packaging and assessing the suitability of ADD for patients on an individual basis.

■ The CD-P-PH/PC finalised a guidance document setting out general quality and safety standards for reconstituting medicinal products to the required dosage strength or form by adding a liquid. This will be followed by an update of the Council of Europe Resolution CM/ResAP(2011)1 on “Quality and safety

assurance requirements for medicinal products prepared in pharmacies for the special needs of patients” and the publication of a new Resolution covering the specific aspect of reconstitution.

■ 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 for classification. Its work is of relevance to all stakeholders in the medication chain, and helps promote access to safe medicines for patients in Europe.

Publications, databases and website

■ The annual update by the CD-P-PH/PHO which generated the 2015 classification recommendations is available on the EDQM website. 2015 also saw completion of the review of the classification of drugs for the treatment of peptic ulcers and gastro-oesophageal reflux disease which will be published on the EDQM website³ in 2016.

■ The Melclass database⁴, which presents the classification status of medicines in member states, was continually updated in 2015. The database was also upgraded and migrated to a web application with a responsive design using state-of-the-art technologies. The upgraded database was launched in January 2016.

Communication with partners and stakeholders

■ The mission and work of the CD-P-PH/PHO, including the PaedForm project, was presented at the 27th DIA Annual EuroMeeting, which was held in April in Paris (France), and at the 11th Symposium of the Medicines and Medical Devices Agency of Serbia (ALIMS), which took place in November in Kragujevac (Serbia).

3. 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>

4. See <https://melclass.edqm.eu/>

HealthCare

The EDQM has continued to work diligently to protect public health by proposing trusted ethical, safety and quality standards for the collection, preparation, storage, distribution and appropriate use of blood components for blood transfusions, and for the transplantation of organs, tissues and cells. It has also continued its work of establishing standards and coordinating controls for cosmetics and food contact materials.

BLOOD TRANSFUSION

Promoting blood safety and quality in Europe and beyond

The EDQM has responsibility for the Council of Europe's activities in the area of blood transfusion, which have been built on three major principles: promoting voluntary and non-remunerated donations, achieving self-sufficiency 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 safety and quality, increasing availability, ensuring optimal use of blood supplies 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. This committee 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 bodies working on specific issues relevant to this field.

Key facts and figures

■ The achievements of the CD-P-TS and its subordinate bodies in 2015 include:

- ▶ publishing the 18th edition of the “*Guide for the Preparation, Use and Quality Assurance of Blood Components*” (commonly referred to as the Blood Guide);
- ▶ 6 Blood Proficiency Testing Scheme (B-PTS) studies;
- ▶ 1 Blood Training Visit (B-TV) and 3 Blood Mutual Joint Visits (B-MJVs), and
- ▶ organising the first training course on QM for Blood Establishments (BEs).

General matters and policies

Risk behaviours having an impact on blood donor management and transfusion safety

■ Working group TS100 has taken over from working group TS057 which elaborated Resolution CM/Res(2013)3 on risk behaviours⁵. The new Group is responsible for continuing to collect data on the incidence and prevalence of sexually transmitted infections in the general population, in blood donors and among individuals with risky sexual behaviours, for use as a scientific basis for future amendments to donor deferral policies. It is also expected to provide advice on the need for future revisions of the Resolution.

QM Programmes

■ The EDQM continued to stimulate interest and encourage participation in the two programmes it established to support BEs in implementing elements of a Quality Management System (QMS): the B-PTS Programme and the Blood Quality Management (B-QM) Programme. Among other things, both programmes are designed to help BEs implement EU Blood legislation, the Blood Guide and the Good Practice Guidelines (GPG, see below).

B-PTS Programme

■ External assessment of the testing capabilities of European BEs continued through the organisation of PTS studies. In 2015, 6 studies were organised with an average of 53 participants per study.

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

Nucleic Amplification Techniques

☐ B-PTS018 - HBV/HCV/HIV

Serology

☐ B-PTS019 – anti-HCV

☐ B-PTS020 – anti-HIV/p24

☐ B-PTS021 – HBsAg

☐ B-PTS022 – anti-HBc

Immuno-Haematology

☐ B-PTS023 ABO, Rhesus, extended phenotyping and irregular antibodies

B-QM Programme

■ This programme proposes tools that enable European BEs to develop, implement and improve their QMS. Strongly supported by the CD-P-TS, the EU Commission and BEs, this programme includes the organisation of 3 types of schemes, all run by experts from European BEs.

- ▶ B-TVs: on-site visit and tailor-made training on technical and QMS topics;
- ▶ B-MJVs: scrutiny of the QMS under development; observation of the level of implementation of minimum standards: the Blood Guide, the GPG, EU blood legislation and standards used in the BE (e.g. ISO Standards, GMP); recommendations on the implementation of the QMS and its improvement;
- ▶ Blood Mutual Joint Audit (B-MJA): checking of the compliance of the QMS with the Guide, the GPG, EU blood legislation and standards used in the BE.

■ In 2015, 1 B-TV and 3 B-MJVs were conducted. In addition, the first European Training Course on QM for BEs was organised in April, and involved 36 participants.



Participants in the first European Training Course on QM for BEs.

Publications, databases and website

Guide to the Preparation, Use and Quality Assurance of Blood Components – 18th Edition

■ A dedicated working group is entrusted with the task of updating the Blood Guide to keep abreast of the latest scientific developments and regulatory changes occurring during the two-year period between editions of the guide. For the first time, the *“Good Practice Guidelines for Blood Establishments and Hospital Blood Banks required to comply with EU Directive 2005/62/EC”* (GPG) were published as an integral part of the Blood Guide in the 18th edition. In future, the GPG will be revised together with the Blood Guide to reflect the latest changes in the regulation of the GMP that apply to BEs. The EU Commission is currently evaluating the possibility of giving the GPG official status within EU legislation.

Resolutions on optimal use of immunoglobulins and clotting factors

■ Council of Europe Resolutions CM/Res(2015)2 on immunoglobulin therapies and CM/Res(2015)3 on haemophilia therapies⁶, which emerged from the Kreuth III symposium in 2013, were elaborated by the CD-P-TS and adopted by the Committee of Ministers in April.

European Database of frozen units of rare blood groups

■ An online database has been developed by the EDQM in close collaboration with the CD-P-TS to help BEs source frozen units of rare blood groups. The pilot phase was completed successfully in 2015 and

6. See <https://go.edqm.eu/BTrec>

the CD-P-TS decided to move the database into the operational phase in early 2016.

Communication with partners and stakeholders

EU Commission

■ An intensive and fruitful collaboration with the EU Commission allows optimal use of resources. An excellent example is the data collected in Council of Europe member states during annual surveys and published as the *“Report on the Collection, Testing and Use of Blood and Blood Components in Europe”*. These data have been included by the EU's Directorate-General for Health and Food Safety (DG SANTE) in the recently-published report *“An EU-wide overview of the market of blood and blood components and plasma derivatives focusing on their availability for patients”*. In April and November, the EDQM attended the meetings of the competent authorities on blood organised by DG SANTE, as an observer.

Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S)

■ The EDQM participated in the “21st PIC/S Expert Circle on Human Blood, Tissues and Cells” in the context of the revision of the “PIC/S GMP Guide for Blood Establishments”.

International Society of Blood Transfusion (ISBT)

■ The EDQM has been granted observer status at the ISBT Board of Directors and is also a member of two dedicated ISBT working parties, the Quality Management and the Code of Ethics Working Parties.

ORGAN TRANSPLANTATION AND TISSUES AND CELLS FOR HUMAN APPLICATION

Promoting strict quality and safety standards

Impressive progress has been made in organ transplantation and the clinical applications of tissues and cells in recent decades. However, the demand for organs and for many tissues and cells still far outweighs the available supply. As with all substances of human origin, their use entails risks of disease transmission that must be minimised through appropriate donor screening and selection criteria. Furthermore, only organs, tissues and cells procured and handled using strict quality criteria are likely to function correctly.

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, ensuring the highest quality, safety and ethical standards. The Committee is composed of internationally recognised experts from Council of Europe member states, observer countries, the EU Commission, WHO, members of DH-BIO and several professional and non-profit organisations.

Key facts and figures

- The achievements of the CD-P-TO in 2015 include:
 - ▶ Publication of the brochure *"Umbilical Cord Blood Banking. A Guide for the Parents"*;
 - ▶ Release of a position paper on *"Transplantation and Physical Activity"* and participation in the organisation of the European Conference on Transplantation and Physical Activity (Krems an der Donau, Austria, July);
 - ▶ Publication of *"Newsletter Transplant 2015"*;
 - ▶ Publication of the 2nd edition of the *"Guide to the Quality and Safety of Tissues and Cells for Human Application"* (TC Guide);
 - ▶ Adoption of Resolution CM/Res(2015)10⁷ on the *role and training of critical care professionals in deceased donation*;
 - ▶ Adoption of Resolution CM/Res(2015)11 on *establishing harmonised national living donor registries* with a view to facilitating international data sharing and its Explanatory Memorandum;
 - ▶ Elaboration of a consensus position paper on the *long-term consequences of living kidney donation*;
 - ▶ Participation in the organisation of the 17th European Day for Organ Donation and Transplantation (EODD) in Lisbon.

General Matters and Policies

Legislative and policy efforts

Over the years, a set of Resolutions and Recommendations in the field of organs, tissues and cells has been adopted by the Committee of Ministers of the Council of Europe. Although not legally binding, they have had a profound impact on national legislation, strategic plans for donation and transplantation and professional practices.

Despite some progress, there is still a shortage of organs available for transplantation, and most countries are unable to meet their transplantation needs. The Committee of Ministers has tried to improve this situation by adopting Resolution CM/Res(2015)10, which recommends that member states implement measures to ensure that healthcare professionals caring for potential organ donors have clear legal and ethical frameworks to guide their work, specifying which practices facilitating donation after death are permitted.

Building on the concept that living donation is a necessary adjuvant in the pursuit of self-sufficiency in transplantation, but mindful that the protection and proper follow-up of living donors, Resolution CM/Res(2015)11 sets out the general guidelines for the

⁷ See <https://go.edqm.eu/OTrec>

construction of national/international living donor registries, with the view to facilitating international data sharing. An additional Explanatory Memorandum provides a detailed list of the parameters that might be included in any living donor registry.

■ In addition, the CD-P-TO has carefully analysed recent publications describing the development of end-stage renal disease after living kidney donation. As a result, it has elaborated a consensus opinion paper on the long-term consequences of living kidney donation and recommendations on the information that should be provided to living donors about the risks associated with donation. This position paper was endorsed by the European Society of Organ Transplantation (ESOT), the International Society of Nephrology (ISN) and The Transplantation Society (TTS), and was published in *Newsletter Transplant 2015* and the scientific journals *Transplantation* and *Transplant International*.

■ Finally, the CD-P-TO's position paper on "Transplantation and Physical Activity" highlights the importance and benefits of prescribing physical activity as a complementary therapy for transplanted patients and a means of improving their quality of life.

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

■ Experts from all over the world have contributed to working groups elaborating the 2nd edition of the TC Guide and the 6th edition of the "Guide to the Quality and Safety of Organs for Transplantation" (Organ Guide, to be published in 2016). These experts have done a tremendous job of compiling the most recent developments and data to ensure the successful and safe clinical application of human organs, tissues and cells.

■ The EU Commission has been actively involved in the elaboration process. This cooperation ensures that the standards set out under the EU Directives are compatible with and complemented by the Council of Europe Guides and ensures that the same quality and safety provisions are applied throughout Europe. The elaboration of the TC Guide was partially funded by the EU Commission. Several professional associations also actively participated in the elaboration of the Guides, most notably the European Donation and Transplant Coordination Organization (EDTCO), the American Association of Tissue Banks (AATB), the European Association of Tissue Banks (EATB) and the European Society for Human Reproduction and Embryology (ESHRE).

■ A new working group has been created to start the elaboration of the 3rd Edition of the TC Guide, to be published in 2017.

Publications, databases and website

■ The Organ Guide and TC Guide have become the gold standard references in Europe and beyond, providing quality, safety and ethical guidance for professionals in the field.

■ *Newsletter Transplant* is the only official source of international figures on organ, tissue and haematopoietic stem-cell donation and transplantation. This information allows the evolution of donation and transplantation activities to be analysed and policy to be amended accordingly. In 2015, *Newsletter Transplant* compiled information from over 70 countries.

■ The CD-P-TO's brochure "Umbilical cord blood banking. A Guide for Parents" is designed to provide clear, accurate and balanced information about the use of cord blood in medical treatment and to guide parents through their blood storage options. In recent years, a number of cord blood banks have emerged, offering families the opportunity to store the cord blood of their babies for possible future private uses in exchange for substantial fees. Parents nowadays face the dilemma of using these private services, donating their cord blood for public use or discarding it after birth.

COSMETICS AND FOOD CONTACT MATERIALS

Protecting consumer health

■ The work programme for cosmetics and materials that come into contact with food is elaborated by the Consumer Health Protection Committee (CD-P-SC, Steering Committee), which is composed of representatives from national ministries with public health responsibilities. In 2015, more than 200 experts from 34 member states and 4 observers to the European Pharmacopoeia Convention followed or contributed actively to the work. The EU Commission, its Joint Research Centre (JRC) and the European Food Safety Authority can send representatives to the meetings of this Committee and its subordinate expert groups.

■ The work programme defined by the CD-P-SC is put into action by two subordinate Committees of Experts, the Committee of Experts on Cosmetic Products (P-SC-COS) and the Committee of Experts on Food Contact Materials (P-SC-EMB).

■ In the field of cosmetics, work focusses on the European network of Official Cosmetics Control Laboratories (OCCLs). For food contact materials, quality and safety requirements are being harmonised and test methods are being developed and updated.

Key facts

OCCL Network

■ The European Network of national OCCLs was set up in 2010 on a voluntary membership basis. More than 30 OCCLs participate in regular network activities, including laboratories in 16 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 noted in an inventory that is accessible to all Network members. The value added for Network members is to be found in better use of resources and enhanced QM in accordance with international standards in the laboratory. The long-standing experience gained with the OMCL Network is an asset in the coordination of the network.

■ The terms of reference of the OCCL Network were published on the EDQM website in 2015.

■ The OCCL network has established close ties with the EU Commission, the JRC and the European Committee for Standardization (CEN). In 2015, the common approach elaborated jointly in 2014 by OCCLs, the JRC and CEN for the validation of analytical test methods developed by single laboratories was put into practice.

■ An inter-laboratory comparison for measuring amounts of the tooth-whitening agent hydrogen peroxide in dental products using liquid chromatography was successfully completed. Another comparative study focussed on the assay of formaldehyde present in cosmetic products such as face creams, shampoos or toothpastes. Inter-laboratory reproducibility of these analytical methods has been established by the studies and they are becoming reference methods for use in the quality control of cosmetic products.

Quality check for cosmetics: market surveillance studies

■ Following an MSS finalised in 2014 on the quality of cosmetic products that are designed to appeal to children, a detailed report was shared between authorities in 2015. Shampoos, skin creams and make-up used for face-painting, bath products and several other product types were checked for compliance with European regulations. According to the findings, more than one-third of the samples were considered non-compliant and several samples contained relevant amounts of nitrosamines, forbidden colorants or lead.

Proficiency testing scheme

■ Proficiency testing is an essential part of quality control management in each testing laboratory. Analytical studies are carried out on the same samples in different laboratories to verify the laboratories' capacity to quantify, for example, the amount of a prohibited substance, and to ensure that test results are

comparable in Europe. In 2015, the study programme included a test for titanium dioxide in sunscreens. Ten OCCLs took part in the study. Another study focused on the amounts of fluorides in toothpaste; 18 laboratories participated. Both studies were concluded within the year.

■ The EDQM proficiency testing scheme is designed as a benchmarking tool for study participants, who share expertise and improve their technical skills in the field of analytics.

Tattoos and permanent make-up

■ To implement the recommendations of Council of Europe Resolution AP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up, safety and documentation requirements are currently being compiled. This document is expected to be finalised and published in 2016.

Food contact materials and articles

■ The review of existing resolutions and technical documents elaborated under the former Council of Europe Partial Agreement in the Social and Public Health Field (dissolved on 31 December 2008) by the P-SC-EMB Committee of Experts continues. The work has been assigned to rapporteurs who will prepare draft provisions for materials such as cork, ion exchange resins or paper and board. Two working group meetings in 2015 were dedicated to paper and board; these meetings were hosted by the Federal Institute for Risk Assessment (BfR, Germany) and by the Austrian Agency for Health and Food Safety (AGES). Work will continue in 2016.

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 very fruitful and an effective way of dealing with matters of common concern. In November, member states, the EU Commission, the JRC and the EDQM met to review analytical methods stated in EU Directives and to set priorities for the work programme related to market surveillance of cosmetic products.

Events

■ Within the framework of Luxembourg's presidency of the Council of the EU in the second half of 2015, the EDQM participated in a public EU meeting on Food Contact Materials in September. During this meeting, the EU Commission confirmed to stakeholders that no further EU Regulations and Directives are going to be drafted in the coming years in the field. This regulatory environment underlines the need for Council of Europe/EDQM guidance on the quality of food contact materials to protect consumers from exposure to potentially toxic traces and residues.

Quality management

Committed to continuous improvement

■ Investment in our QM system continued in 2015, with ISO 9001:2008 certification renewed for a number of the organisation's activities. Our ISO 17025:2005 accreditation was also confirmed for 21 analytical techniques. The EDQM's customers and stakeholders can therefore be sure the services provided are of consistent quality and that the organisation is dedicated not just to maintaining but also to continuously improving its QM system.



493-TEST

Cooperation with international partners

The EDQM especially values its cooperation with a range of international partners for all of its activities.

■ The EDQM's activities would not be possible without the support of national pharmacopoeia authorities, national competent authorities, official control laboratories, inspectorates and more than 1,200 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 and the EU Commission and its technical agencies such as the EMA.

COOPERATION WITH NATIONAL AUTHORITIES

■ Representatives of national competent authorities are members of the Ph. Eur. Commission and its currently 72 expert groups and working parties. National authorities also take part in the work of the Ph. Eur. by submitting requests for revisions and reviewing draft texts published in *Pharmeuropa online*.

■ The 2015 annual meeting of the NPAs of Ph. Eur. member states took place in Utrecht, The Netherlands, in June, hosted by the RIVM and attended by 25 of

the 37 member states (*for more details, see section "The European Pharmacopoeia", page 11*).

■ The 20th Annual Meeting of the GEON was held in Brussels from 1 to 5 June 2015. The meeting was co-organised and co-sponsored by Belgium's WIV-ISP, CODA-CERVA and FAGG-AFMPS. The meeting was attended by more than 240 experts from 61 OMCLs, national medicines agencies and the EU Commission (*for more details, see section "The European Network of Medicines Control Laboratories (OMCLs)", page 16*).

■ The Ph. Eur. continued its efforts to reduce duplication of testing and reporting during drug development and quality control through the work of the Pharmacopoeial Discussion Group (PDG) – comprising the Ph. Eur., the JP and the USP as members and WHO as an observer (*for more details, see section "The European Pharmacopoeia", page 10*).

■ The CD-P-TS, CD-P-TO, CD-P-PH and the CD-P-SC continue to receive support from national authorities.

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), created at the end of 2014 and co-chaired by the EMA and a national competent authority, and of the International Standards on Identification of Medicinal Products in the EU (EU ISO IDMP) Task Force group (created in 2015), including the corresponding referentials subgroup.

■ The EDQM also works closely with the EMA as well as national authorities to ensure continued consistency between the approaches of licensing authorities and the Ph. Eur. The EDQM has observer status with 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 Good Manufacturing and Distribution Practice Inspectors Working Group (GMDP IWG), the Biologics Working Party (BWP) and the Immunologicals Working Party (IWP). Members of EMA working groups (i.e. for which the EMA provides the Secretariat) or of the EMA Secretariat itself are observers to some of the Ph. Eur. Commission's Groups of Experts and Working Parties, e.g. 6B (human blood and blood products), 15 and 15V (vaccines and sera for human use and veterinary use) and the BSP Steering Committee.

■ The EDQM and the EMA communicate regularly with regard to the certification procedure: the EMA is a member of the Certification Steering Committee, and channels for regular communication are in place for the inspection programme and its outcomes.

■ The EDQM and the EMA continue to collaborate on operating a long-established CAP Sampling & Testing Programme for products for human and veterinary use (*for more details, see section "The European Network of Medicines Control Laboratories (OMCLs)", page 16*).

COOPERATION ON INSPECTIONS

■ In 2015, the EDQM's Certification Division continued to be involved in the International API Inspection Programme (coordinated by the EMA) and the PIC/S (*for more details, see section "Certification of Suitability to the Ph. Eur. monographs", page 14*), and hosted the 7th meeting of the PIC/S Expert Circle on APIs (*for more details, see section "2015: A year rich in events and meetings", page 33*).

■ The EDQM also participated in the "21st PIC/S Expert Circle on Human Blood, Tissues and Cells" in the context of the revision of the "PIC/S GMP Guide for Blood Establishments".

COOPERATION WITH WHO

■ In 2015, the EDQM continued to collaborate with WHO and to take part in a number of joint meetings and consultations, including:

- ▶ as an observer to WHO's Programme on International Nonproprietary Names (INN), since INN are used in Ph. Eur. monographs;
 - ▶ participation in WHO's ECBS, with WHO participating as an observer in the meetings of the EDQM's BSP Steering Committee, thus guaranteeing a smooth exchange of information;
 - ▶ participation in the ECSPP (*see section "Pharmaceutical Reference Standards", page 11*); and
 - ▶ the sharing of data and joint inspections relating to the certification process for APIs.
- ▶ The EDQM also continued to host WHO as an observer to the Ph. Eur. Commission.

■ In 2015, the EDQM participated in two International Meetings of World Pharmacopoeias organised under the auspices of WHO, one in April in Washington DC (USA) and the other in September in Suzhou City (People's Republic of China) (*for more details, see section "The European Pharmacopoeia", page 10*). In this context, the EDQM actively contributed towards drafting "Good Pharmacopoeial Practices" (GPhP), a WHO initiative which may serve as a basis for future work-sharing and collaboration between the pharmacopoeias of the world (*for more details, see section "The European Pharmacopoeia", page 10*). In September, the EDQM actively participated in an informal consultation on International Standards for biopharmaceutical products organised by WHO.

■ The EDQM is responsible for the establishment, monitoring and distribution of WHO ISA and ICRS (*for more details, see section "Pharmaceutical Reference Standards", pages 11 and 12*).

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

COOPERATION WITH MANUFACTURERS AND INDUSTRY ASSOCIATIONS

■ The EDQM continues to hold annual bilateral meetings with industry associations to promote exchanges on all aspects related to the work of the EDQM and to collect feedback on its activities. In addition, in March 2015, the EDQM organised a stakeholder meeting in which industry associations were invited to present their views on the future of Ph. Eur. texts in the field of biologicals.

2015: A year rich in events and meetings

SYMPOSIA & WORKSHOPS – FOCUSED TOPIC MEETINGS

Symposium: Preparation & Clinical Use of Plasma for Transfusion

Although plasma has been used for decades in intensive care units, surgery and emergency medicine, some questions about this blood component still remain unanswered. In September, the EDQM organised a symposium involving clinicians and blood establishment experts, to discuss the clinical need for plasma for transfusion and the specifications that need to be set to ensure that the plasma is of suitable quality for its intended clinical use. Practices vary between Council of Europe member states, and gaps in knowledge were identified in various areas. The European Committee on Blood Transfusion (CD-P-TS) has undertaken to investigate how those gaps can be filled and how needs can be met in a more consistent manner.

Workshop: Fish Vaccines

In September, the EDQM organised a workshop on “European Pharmacopoeia requirements for fish vaccines” during the 17th International Conference on Diseases of Fish and Shellfish. Organised by the European Association of Fish Pathologists,

the conference attracted both members of the Association and other professionals from a range of disciplines involved in aquatic diseases and related issues and topics. The workshop focused on promoting the Ph. Eur. and its texts and monographs for fish vaccines, as well as *in vitro* methods for potency testing of fish vaccines, and attracted a lot of interest and feedback during the open discussions.

Expert Workshop: Automated Dose Dispensing

The draft guide on the best practices for ADD systems and their implementation in Europe was discussed in a workshop organised by the EDQM in September, which was attended by experts from national authorities, pharmacies and ADD operators.

Symposium: Quality Indicators for Pharmaceutical Use

The EDQM organised a workshop in November to present the outcomes of its Pharmaceutical Care Quality Indicators Project, to obtain feedback and guidance regarding the implementation and use of EDQM quality indicators, and to strengthen the EDQM's role in supporting the harmonisation of quality standards and promoting the safe and appropriate use of medicines in Europe.

TRAINING SESSIONS

■ The EDQM organised two training sessions on the Ph. Eur., in July (Strasbourg, France) and December (Bucharest, Romania). The training session in Bucharest was supported by Romania's National Agency for Medicines and Medical Devices (NAMMD). The programme was designed to enable participants to expand their knowledge and familiarise themselves with the work and procedures of the Ph. Eur. Both sessions focused on chemically defined APIs and included the Certification procedure, providing advice on preparing an application, revisions and the inspection programme.

■ In April, the EDQM organised its first training course on "Best Practices for the Development of Quality Management Systems in European Blood Establishments". Maintaining the high quality and safety of the products and services required by blood donors, patients and the public are of the upmost importance in transfusion medicine. The four-day programme, which was prepared with the input of experts working in blood establishments, aimed to support blood establishments in setting up, developing and further improving their QMS. It covered a variety of topics such as the regulatory framework, process mapping, management of a quality documentation system, the concepts of validation, qualification and risk management, corrective action/preventive action (CAPA) management and continuous improvement processes.



■ The programme also included a visit to the French National Blood Service (*Etablissement Français du Sang*) blood donor centre in Strasbourg. The EDQM would like to thank EFS Alsace for opening the doors of its blood centre to the group and for sharing its experience and know-how. It was very informative and an exciting learning experience which was much appreciated by the delegates.

■ One training session on CombiStats™ (see section "The European Network of Official Medicines Control Laboratories (OMCLs)", page 16) was organised in October (Strasbourg, France) and was open to industry and private sector participants.

WEBINARS

■ The EDQM organised a number of webinars throughout the year on several compelling topics which sparked high interest among users (over 1,100 webinar participants from 75 countries worldwide) and allowed the EDQM to reach a wide audience.

■ In March, the EDQM organised a webinar on "Biologicals of the twenty-PhEur-st century", with the aim of showing how the Ph. Eur. embraces current developments, how it has adapted its texts to remain up-to-date with recent advances in science and medical practice, and the challenges that remain ahead. The presentation focused on how monographs and general chapters are elaborated, gave an overview of the main texts with a special focus on biotech products and highlighted the flexibility of Ph. Eur. texts, with examples of Quality by Design (QbD) approaches for biologicals and how the development of biosimilars is being fostered.

■ A webinar on "Reverse Osmosis in the Ph. Eur. Monograph for Water for Injections (WFI)" was held in April. The presentation covered the history of water monographs, the actions that were taken by the Ph. Eur. towards the revision of the WFI monograph and the consequences of the revision on other Ph. Eur. texts covering quality of water.

■ Later in the year, the Certification Division organised a webinar on "How to prepare a successful CEP application". The webinar focused on different sections of the Common Technical Document (CTD) and provided guidance in the form of examples or common misunderstandings, and advice on how to minimise these mistakes. The goal was to help applicants reduce common errors and obtain faster approval of applications for a CEP.

■ Finally, a webinar on "Glass containers for pharmaceutical use" was held in December to provide background information on the recent revision of this general chapter, which was published in July 2014 and came into force in January 2016. The webinar

also highlighted the fact that this general chapter is again under revision, so users are encouraged to provide their input.

PARTICIPATION IN KEY INTERNATIONAL MEETINGS

■ In 2015, the EDQM was invited to participate in several important international meetings and events worldwide.

■ The EDQM contributed to the elaboration of the programme and attended the 22nd International Workshop on Surveillance and Screening of Blood-Borne Pathogens, co-organised by the International Plasma Fractionation Association (IPFA) and the Paul-Ehrlich-Institut (PEI), in Prague (Czech Republic).

■ The EDQM participated in two meetings of the IGDRP, which was established in 2015 following a three-year pilot launched in 2012; the first meeting was held in Pretoria (South Africa) in June, and the second in Seoul (Republic of Korea) in November. The IGDRP promotes worldwide collaboration and convergence in generic drug regulatory programmes in order to address the challenges posed by increasing workloads, globalisation and complexity of scientific issues.

■ In September, the EDQM also participated in an informal consultation on International Standards for biotherapeutic products organised by WHO, and had the opportunity to promote the value of setting pharmacopoeial standards for this important class of products.

■ Representatives of the EDQM and of the Committee of Experts CD-P-PH/CMED participated in the first Moroccan conference (Rabat, December) on medicines and health products, in order to develop the cooperation with officials of target countries for the implementation of the MEDICRIME Convention.

■ The EDQM participated in the ICH Steering Committee meeting (Fukuoka, Japan) in June and the ICH Assembly meeting (Jacksonville, FL, USA) in December, in addition to continued participation in the Implementation Working Groups (IWGs) for ICH Q3D and Q11.

■ Other important international meetings and events included:

- ▶ International Drug Regulatory Regulators Meeting (Hyderabad, India) in January;
- ▶ IPEC Europe Annual General Meeting (Nice, France) in February;
- ▶ APV/IPEC Europe Excipient Conference (Barcelona, Spain) in September;
- ▶ Drug Information Association (DIA) EuroMeeting 2015 (Paris, France) in April, which included a session dedicated to the EDQM's 50th anniversary;

- ▶ DIA CMC Forum Japan 2015 (Tokyo, Japan) in June;
- ▶ Fifth anniversary conference of the ALMBiH (Sarajevo, Bosnia and Herzegovina);
- ▶ 17th All-Russian Conference "State regulation in the field of pharmaceuticals and medical devices" (Moscow, Russia) in October; and
- ▶ Innovation & Quality (IQ) Consortium 2015 Annual Symposium (Washington DC, USA) in October.

■ In October, the EDQM also attended the International Pharmaceutical Federation (FIP) World Congress in Dusseldorf (Germany) and was granted the status of Predominantly Scientific Observer Organisation at the FIP Council meeting.

MEETINGS HELD IN PARTNERSHIP WITH THE EDQM

■ In May, the EDQM hosted the 21st Formal Meeting of the Homeopathic Medicinal Products Working Group (HMPWG). The EDQM has participated as an observer at HMPWG meetings for over 10 years, and some of the experts on the HMPWG are also involved in the Ph. Eur. working parties on Homeopathic Manufacturing Methods (HMM) and on Homeopathic Raw Materials and Stocks (HOM). This exchange and cross-collaboration provides the EDQM with a valuable platform to discuss regulatory and scientific issues relating to these medicinal products.

■ In June, the EDQM hosted a meeting of the ICH Q3D IWG.

■ In August, the EDQM took part in a second Multicentre International Workshop on data integrity organised together with the USFDA in three different cities in China (the first series of workshops was held in India in November 2014). This was an excellent opportunity to train more than 1,000 industry representatives and regulators on inspectors' expectations with regard to this important topic.

■ In October, the EDQM hosted the 7th meeting of the PIC/S Expert Circle on APIs, which attracted delegates from 40 different PIC/S participating authorities, applicants, partners and non-members from across Europe, the Americas, Australia, Asia and Africa. The overall objective of the meeting was to strengthen international co-operation and share experiences in the field of API inspections. Topics discussed included: data integrity; chemical reference standards; genotoxic impurities; a risk assessment for the selection of sites to be inspected or re-inspected; ICH Q7; and the most common deficiencies encountered during API inspections.



INTERNATIONAL FAIRS & EXHIBITIONS – EXPANDING OUR GLOBAL PRESENCE

As global trade in active substances for pharmaceutical use, generics and finished pharmaceutical products continues to grow, international trade shows provide a good way for the EDQM to remain in contact with local manufacturers, associations and stakeholders and represent an occasion to showcase its latest products and services.

This year, the EDQM participated in three pharmaceutical fairs: CPhI China (Shanghai), CPhI Europe (Madrid) and CPhI India (Mumbai). While this was an opportunity for the EDQM to provide information about its activities, several meetings had also been pre-arranged between visitors to the show and Certification Division staff. These were intended to inform applicants about the practical aspects of the Certificate of Suitability (CEP) procedure and to

assist them by clarifying misunderstandings and contributing towards resolving any difficulties they may be experiencing.

In June, the EDQM was invited to participate in a symposium organised by the China Chamber of Commerce for Import and Export of Medicines and Health Products (CCCPMHPIE). Over 120 participants, mainly from China, attended the event, and the presentations focused on the Ph. Eur. and the Certification procedure.

In addition, the EDQM participated in the 25th Regional Congress of the ISBT, which was held in London (United Kingdom) in conjunction with the 33rd Annual Conference of the British Blood Transfusion Society. This event attracted healthcare professionals involved in blood transfusion and transfusion medicine, who discussed the latest developments in the field of transfusion medicine. The 18th Edition of the EDQM's *"Guide for the Preparation, Use and Quality Assurance of Blood Components"* was heavily promoted at the fair, and visitors were able to collect information on the EDQM's activities in this area and learn more about the EDQM's Blood-PTS Scheme and B-QM.



PUBLIC AWARENESS CAMPAIGNS

Organ Transplantation

On 24 March, a "Walk against Organ Trafficking" was organised along part of the pilgrimage route to Santiago de Compostela (the Way of St James, Spain), in the context of a meeting of the European Committee on Organ Transplantation (CD-P-TO). This initiative was led by CD-P-TO experts and involved representatives from organisations such as WHO, the Spanish National Transplant Organization (ONT) and Swisstransplant. Upon arrival at the Cathedral in Santiago, a special church celebration (Jubilee Ceremony) took place in presence of the walkers and members of the general public.



■ The aim of the walk was to heighten public awareness of organ trafficking and to promote the fight against it. It was particularly significant as it was organised the day before the opening for signature of the Council of Europe's new Convention against Trafficking in Human Organs, and a high-level international conference which was held in Santiago (25-26 March). The Convention, which was adopted by the Committee of Ministers on 9 July 2014, aims to harmonise the penal system in Europe for more effective prosecution of individuals and criminal organisations responsible for trafficking.

■ The 17th European Day for Organ Donation and Transplantation (EODD) took place on 10 October in Lisbon (Portugal). The day was sponsored by the Portuguese Ministry of Health, the Portuguese Institute for Blood and Transplantation (IPST) and the Portuguese Transplantation Society (SPT). The day opened with an official ceremony which was attended by a number of representatives and the chairman of the IPST Directive Board, the President of the SPT, members of the CD-P-TO, EDQM/Council of Europe, donors, transplant recipients and their families and Lisbon's City Mayor.

■ The slogan chosen for the EODD was "Art & Transplantation", and several activities were organised throughout the city for children and their families to enjoy. The event was also promoted online and via social media channels such as Twitter and YouTube. Once again the EDQM organised an information stand, this year alongside the IPST. The initiative was again supported widely in Europe: a Thunderclap campaign was launched by the Pulmonary Hypertension Association (PHA) Europe and reached 100,000 followers in one month; requests were made by several countries (e.g. Bosnia-Herzegovina and Croatia) to translate the brochure for local distribution; the video clip was translated and used in Slovakia and Portugal;



and the logo featured on Germany's federal health ministry website. A number of other celebrations took place simultaneously throughout Council of Europe member states.

■ The EDQM also participated in the 17th Congress of the ESOT and the 24th Congress of the EATB. Both events provided the EDQM with an opportunity to talk with scientists and professionals who are working in these fields and learning about recent advances.



OFFICIAL VISITS

■ In January, the EDQM opened its doors to the Permanent Representations of the Council of Europe. The visit allowed the delegations to better understand the organisation's different activities and to grasp how they impact public health policy and the quality control of medicines in Europe and beyond.

■ The same month, the EDQM welcomed a delegation from the Ghanaian Food and Drugs Authority. The delegation met with the Certification Division to get an insight into the Certification procedure for pharmaceutical substances and to share our know-how and experiences.

■ Later in the year, French members of the Parliamentary Assembly of the Council of Europe were received, and again the focus of the visit was a general presentation of our activities.

■ In June, the EDQM received an official delegation from the Korean Food and Drug Administration (Republic of Korea). This visit concentrated on the EDQM's work in the area of OCABR and the batch release of human biologicals.

■ In November, a delegation from the Chinese National Institutes for Food and Drug Control (NIFDC) and the China Food and Drug Administration (CFDA) visited the EDQM. Topics discussed included quality control and standardisation, with a focus on the activities of the EDQM laboratory and the OMCL Network.

■ Later that same month, representatives from the East African Community made a study visit to the EDQM to have an exchange about the establishment and use of RSs and the activities of the OCML Network.

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. Following the ratification of the Convention by Ukraine in December 2012, the Commission now has representatives from 38 signatory parties to the Convention (37 states and the European Union). The 28 observers from all over the world highlight 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 member states. Currently, 72 expert groups and working parties established by the Commission carry out the Ph. Eur. work programme. By the end of 2015, 2,302 quality standards and 354 general texts including methods of analysis had been elaborated, adopted and implemented. These texts are constantly being revised to keep pace with technical and scientific progress 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 professionals working with medicines, and has become the gold standard reference in the sector.

THE BIOLOGICAL STANDARDISATION PROGRAMME (BSP) STEERING COMMITTEE

— The BSP focusses on the standardisation of 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 the 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 as well as the EDQM Director.

NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES (OMCL) ADVISORY GROUPS

— The role of this Network is to ensure that the quality of medicines marketed in the member states is consistent and to contribute to the mutual recognition of the results of quality control testing of medicines by these states. Major decisions are taken by the annual plenary meetings of the OMCL Network. Advisory groups prepare and ensure the implementation of the annual work programme. There are two levels of collaboration within the network:

- ▶ General activities which are open to all of the member states of the Ph. Eur. Convention and the observer states (the latter following an auditing and accreditation process). General activities cover work in the area of QM systems, such as audits and proficiency testing studies (PTS), as well as MSSs and contributing towards combating counterfeit and illegal medicines. These activities are prepared and followed-up by the General OMCL Advisory Group.
- ▶ Activities restricted to the EU and the European Economic Area (EEA) that relate to products with a centralised marketing authorisation (CAP), products authorised according to the 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 some 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, currently, three Technical Advisory Boards (TAB). This Steering Committee is composed of representatives of European licensing authorities and inspectorates. It takes decisions on general policies, 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 (CD-P-TS)

■ This Steering Committee addresses ethical, legal and organisational issues related to blood transfusion with a view to ensuring the safety, quality and optimal use of blood, protecting donors and recipients and avoiding wastage. It supervises the work of a number of individual projects and Working Groups, including 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 (CD-P-TO)

■ 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 (CD-P-PH)

■ The activities of this Steering Committee include contributing to improving public health and reducing health inequalities through the development of harmonised provisions and practices including the rational use of medicines; minimising public health risks posed by counterfeit medical products; and contributing to the multisectorial and multidisciplinary follow-up mechanism ensured by the Committee of the Parties to the MEDICRIME Convention. The Committee also supervises the programmes of activities of 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 (CD-P-SC)

■ The CD-P-SC is responsible for managing the work programme and the decision-making process in the areas of cosmetics and food contact materials. The Committee has two subordinate bodies which examine health-related issues and evaluate their risks, and they draft reports and recommendations for regulatory approaches:

- ▶ Committee of Experts on Food Contact Materials (P-SC-EMB).
- ▶ Committee of Experts on Cosmetic Products (P-SC-COS). The P-SC-COS interacts with the European network of Official Cosmetics Control Laboratories (OCCLs).

GLOSSARY

3Rs	Reduction, Refinement and Replacement of animal testing
AATB	American Association of Tissue Banks
ADD	Automated Dose Dispensing
AGES	Austrian Agency for Health and Food Safety
ALIMS	Medicines and Medical Devices Agency of Serbia
APEC	Asian-Pacific Economic Cooperation
API	Active Pharmaceutical Ingredient
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 Establishments
BfR	Federal Institute for Risk Assessment (Germany)
BRP	Biological Reference Preparation
BRR	Biological Reference Reagent
BSP	Biological Standardisation Programme
BWP	Biologics Working Party
CAP	Centrally Authorised Product
CCCPMHPIE	China Chamber of Commerce for Import and Export of Medicines and Health Products
CEN	European Committee for Standardization
CEP	Certificate of Suitability to the Monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use (EMA)
CODA-CERVA	Federal Veterinary and Agrochemical Research Centre (Belgium)
CRS	Chemical Reference Substance
CVMP	Committee for Medicinal Products for Veterinary Use (EMA)
DCP	Decentralised Procedure
DG SANTE	EU Directorate General for Health and Food Safety Health
DH-BIO	Council of Europe's Committee on Bioethics
EATB	European Association of Tissue Banks
ECBS	WHO Expert Committee on Biological Standardization
ECSP	WHO Expert Committee on Specifications for Pharmaceutical Preparations
EDQM	European Directorate for the Quality of Medicines & HealthCare
EDTCO	European Donation and Transplant Coordination Organisation
EEA	European Economic Area
EMA	European Medicines Agency
EMVO	European Medicines Verification Organisation
EMVS	European Medicines Verification System
EODD	European Day for Organ Donation & Transplantation
EPAA	European Partnership for Alternative Approaches to Animal Testing

ESHRE	European Society for Human Reproduction and Embryology
ESOT	European Society of Organ Transplantation
EU	European Union
EU ISO IDMP	International Standards on Identification of Medicinal Products in the EU
FAGG-AFMPs	Federal Agency for Medicines and Health Products (Belgium)
FIP	International Pharmaceutical Federation
GDP	Good Distribution Practice
GEON	General European Network of Official Medicines Control Laboratories
GMP	Good Manufacturing Practice
GPhP	Good Pharmacopoeial Practices
GPG	Good Practice Guidelines
GTP	Gene Therapy Products
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HRS	Herbal Reference Standards
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 Drug Regulators Programme
INN	International Nonproprietary Name (WHO)
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IPEC	International Pharmaceutical Excipients Council
IPFA	International Plasma Fractionation Association
IPST	Portuguese Institute for Blood and Transplantation
ISA	International Standard for Antibiotics
ISBT	International Society of Blood Transfusion
ISN	International Society of Nephrology
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
MA	Marketing Authorisation
MJA	Mutual Joint Audit
MJV	Mutual Joint Visits
MRP	Mutual Recognition Procedure
MSSIP	Market Surveillance Studies on Suspicious Illegal Products
MSS	Market surveillance studies
NAB	National Accreditation Body
NAMMD	National Agency for Medicines and Medical Devices (Romania)
NIFDC	Chinese National Institute for Food and Drug Control
NMR	Nuclear Magnetic Resonance
NPA	National Pharmacopoeia Authorities
OCABR	Official Control Authority Batch Release

OCCL	European network of national Official Cosmetics Control Laboratories
OMCL	Official Medicines Control Laboratory
PaedForm	Paediatric Formulary
PCQIP	Pharmaceutical Care Quality Indicators Project
PDG	Pharmacopoeial Discussion Group
PEI	Paul Ehrlich Institute
Ph. Eur.	European Pharmacopoeia
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PTS	Proficiency Testing Scheme
Q3D	Code for the ICH guideline on Elemental Impurities
QbD	Quality by design
QMS	Quality Management System
QWP	Quality Working Party (EMA)
RIVM	National Institute for Public Health and the Environment (The Netherlands)
RS	Reference Standard
SPOCs	Single points of contact
SPT	Portuguese Transplantation Society
TC	Tissues & Cells
TGA	Therapeutic Goods Administration (Australia)
TTS	The Transplantation Society
USFDA	United States Food and Drug Administration
USP	United States Pharmacopoeia
VBRN	Veterinary Batch Release Network
WHO	World Health Organization
WIV-ISP	Scientific Institute of Public Health (Belgium)

This publication presents the work carried out in 2015 by the European Directorate for the Quality of Medicines & HealthCare, Council of Europe, highlighting its particular achievements.

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The Council of Europe is the continent's leading human rights organisation. It comprises 47 member states, 28 of which are members of the European Union. All Council of Europe member states have signed up to the European Convention on Human Rights, a treaty designed to protect human rights, democracy and the rule of law. The European Court of Human Rights oversees the implementation of the Convention in the member states.