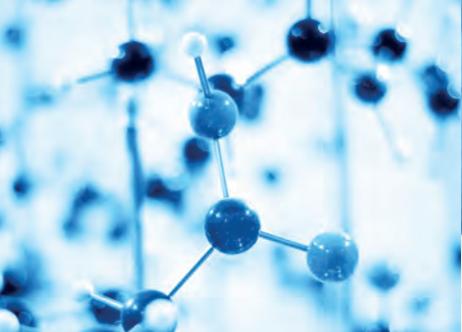


THE EDQM ON THE MOVE



2018 ANNUAL REPORT

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2018 **ANNUAL REPORT**

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

French edition*Rapport annuel 2018*

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MESSAGE FROM DR SUSANNE KEITEL, DIRECTOR

2018 was another productive year for the European Pharmacopoeia (Ph. Eur.) Commission, a testament to its commitment to keeping abreast of new scientific developments and anticipate the need to create standards in some highly complex fields – as demonstrated, for example, by the significant revision of the general monograph *Products of recombinant DNA technology* and the adoption of a new chapter on *Quantification and characterisation of residual host-cell DNA*. Of the 41 new monographs adopted, eight covered active pharmaceutical ingredients (APIs) which are still under patent and are intended for use in medically important indications. Momentum was gained in the development of finished product monographs and the Commission made significant progress with quality standards for live biotherapeutic products, where a new general chapter and two specific monographs have closed the regulatory gap. Finally, the reinstatement of the Gene Therapy Products (GTP) Working Party paves the way for future developments of the Ph. Eur. in this field.

Although human patients are the main focus of the Ph. Eur., much was accomplished in the field of animal health last year. The Ph. Eur. Commission is strongly committed to the principles enshrined in the *European Convention for the protection of vertebrate animals used for experimental and other scientific purposes*. The decision to delete the abnormal toxicity test (ATT) from the Ph. Eur. was taken last year in an effort to further the replacement and reduction of animals used to test human medicines. This achievement was subsequently reflected in other aspects of our work which are partially co-funded by the European Union: guidelines for Official Control Authority Batch Release (OCABR) of vaccines for human use, which contained references to the ATT in the manufacturer's protocol section, were revised to delete any mention of ATT tests. The Biological Standardisation Programme (BSP), which looks into new methods for the quality control of biological medicines, ran 21 projects last



year all aimed at establishing alternatives to the use of animals. The cooperation between the BSP and the Ph. Eur. Commission resulted in another major achievement for animal health in 2018: the replacement of the histamine sensitisation test (HIST) with a standardised CHO cell-clustering assay (in vitro cell-based test) for residual pertussis toxin. The replacement impacted the general chapter on *Residual pertussis toxin* and ten individual monographs on vaccines containing acellular pertussis components.

The development of new reference standards and replacement batches for existing ones was another important activity: Sodium aminosalicylate dihydrate for equipment qualification CRS replaced the former Amoxicillin trihydrate CRS. In addition to simpler and faster sample preparation, the new reference standard allows for a broader spectrum of applications. A brand new set of elemental impurities reference standards was developed in conjunction with the Joint Research Centre (JRC) of the European Commission, the National Metrology Institute of Germany (PTB) and the German Federal Institute for Materials Research and Testing (BAM). These reference standards enable determination of lead, cadmium, mercury and arsenic as elemental impurities in medicinal products, and will efficiently support pharmaceutical manufacturers in the application of relevant public health standards, such as the ICH Q3D Guideline on Elemental Impurities, implemented in the Ph. Eur. via the general monographs *Substances for pharmaceutical use* and *Pharmaceutical preparations*.

Concerning our technical expertise, in 2018 the EDQM laboratory extended its ISO 17025 accreditation to nuclear magnetic resonance (NMR) spectroscopy and quantitative nuclear magnetic resonance (qNMR) spectroscopy, proof of the high level of technical and scientific expertise that underpins the development of the official Ph. Eur. reference standards.

The interest that the work of the Ph. Eur. Commission generates outside its current 39 signatory parties was demonstrated again with a request for observer status to the Commission received from the Republic of Uzbekistan, which was granted during the

March 2018 session. International cooperation remained a priority throughout the year. In addition to the ongoing work with the United States and Japanese Pharmacopoeias in the context of the Pharmacopoeial Discussion Group (PDG) and its substantial support of the International Meeting of World Pharmacopoeias, organised under the auspices of the World Health Organization (WHO), the EDQM provided a forum for the Chinese Pharmacopoeia to present their activities and to illustrate new requirements for excipients in Chinese legislation.

2018 was also marked by the discovery of unexpected impurities in anti-hypertensive medicines containing APIs of the sartan class. This discovery led to the worldwide recall of the medicines concerned. Obviously the news was met with alarm by health authorities and patients alike, and prompted significant questions to be raised throughout the pharmaceutical sector.

The EDQM immediately started work to identify the possible root cause of the problem and did so in close cooperation with national and international authorities and the European Medicines Agency (EMA). All relevant Certificate of suitability (CEP) applications were reviewed and CEP holders requested to address the risk of nitrosamine contamination and take mitigating actions, where necessary. In this context, a number of CEPs were suspended. In just a few weeks, the European network of Official Medicines Control Laboratories (OMCLs), coordinated by the EDQM, developed and delivered test methods, based on different analytical principles, for controlling nitrosamines in sartans. In addition, the Ph. Eur. Commission decided at their November 2018 session to revise the five individual sartan monographs and to include strict limits for these impurities, with further actions on pharmacopoeial texts to be discussed at the March 2019 session. This very unfortunate incident has highlighted the need to review the control system for medicines, from dossier requirements and how dossiers are assessed to GMP inspections and the roles and responsibilities of the different business stakeholders. A “lessons learnt” exercise was triggered at European level at the beginning of this year and will be discussed with international partners from around the world.

Much progress was made across the EDQM’s different healthcare activities: the 7th edition of the Organ Guide with updated information was issued last year to provide professionals with information on the most recent advances in the field, together with technical guidance to ensure the safety and quality of human organs for transplantation. In pharmaceutical care, a new set of Guidelines on Automated Dose Dispensing (ADD) services was finalised, which will guide regulators, suppliers and patients on how to supply ADD services and medicines while ensuring maximal safety for patients. In addition, the adoption of the new CM/Res(2018)1 resolution requiring information on national classifications of medicines will provide impetus for the development of uniform and safe supply conditions for medicines across Europe. The information will be included in our Melclass database and will contribute to the harmonisation of national legislation across Europe. As part of the fight against falsified medicines and medical devices, our Know-X database was revised to facilitate smooth interaction between OMCLs and enforcement authorities involved in the fight against falsified medicines.

The first stone of the EDQM’s secondary site was laid in Metz, north-eastern France, in June. This new site is intended to store contingency stocks of the EDQM’s portfolio of over 3 000 pharmaceutical reference standards and will be key to ensuring the sustainability and continuity of the EDQM’s public health protection mission in the event of any emergency affecting the main EDQM building in Strasbourg.

Last, but far from least, I wish to highlight the outstanding contributions of our experts: joining us from national, European and international authorities, universities, scientific institutes and industry from across the world. It is thanks to their excellent scientific competence that our work is so valuable and relevant. To all of them, as well as to our member states and the dedicated staff at the EDQM, I offer my heartfelt thanks.

Dr Susanne Keitel
Director, EDQM, Council of Europe



QUALITY AND USE OF MEDICINES

In 2018 much was accomplished in the field of setting quality standards for the manufacture and control of medicines in Europe and beyond. Year-on-year, the Ph. Eur. Commission works to provide Ph. Eur. users with the most up-to-date and relevant information possible. The procedure of Certification of suitability to the Ph. Eur. monographs again demonstrated its added value for regulatory authorities and the industry and the work-sharing within the network of European Official Medicines Control Laboratories (OMCLs) allowed members to cover a broad range of products on the market and to address emerging risks to public health.

THE EUROPEAN PHARMACOPOEIA

What it is and how it works

The European Pharmacopoeia (Ph. Eur.) lays down quality standards for the manufacture and control of medicines in Europe and beyond. The texts of the Ph. Eur. are elaborated and revised by a panel of 61 groups of experts and working parties, which may be convened or disbanded by the European Pharmacopoeia Commission, the decision-making body of the Ph. Eur., depending on current regulatory, industrial and technical needs. Since the participation of external stakeholders and users in the Ph. Eur.'s public standard-setting process is vital for the development of authoritative and relevant monographs, these groups comprise representatives from national competent authorities, academia and industry.

The importance of the Ph. Eur. in Europe and beyond

The Ph. Eur., Europe's legal and scientific benchmark for pharmacopoeial standards, is legally binding in 38 European countries and used in over 100 countries worldwide. It delivers crucial information earlier than any other pharmacopoeia in Europe.

To reflect this global status of the Ph. Eur. and keep pace with the far-reaching changes the pharmaceutical world has undergone over the past 50 years which have created a globalised operating environment for medicinal products and their components,

in 2015 the Ph. Eur. Commission reviewed its working procedures to allow the nomination of experts from non-Ph. Eur. member and observer states. This decision was part of a deliberate move to further involve manufacturers from outside Europe in the work of the Ph. Eur. This new policy has been applied for the nomination of Ph. Eur. experts since November 2016. The wide variety of scientific and cultural backgrounds of these experts, all volunteers, testifies to the international scope and reach of the Ph. Eur.

Key facts and figures in 2018

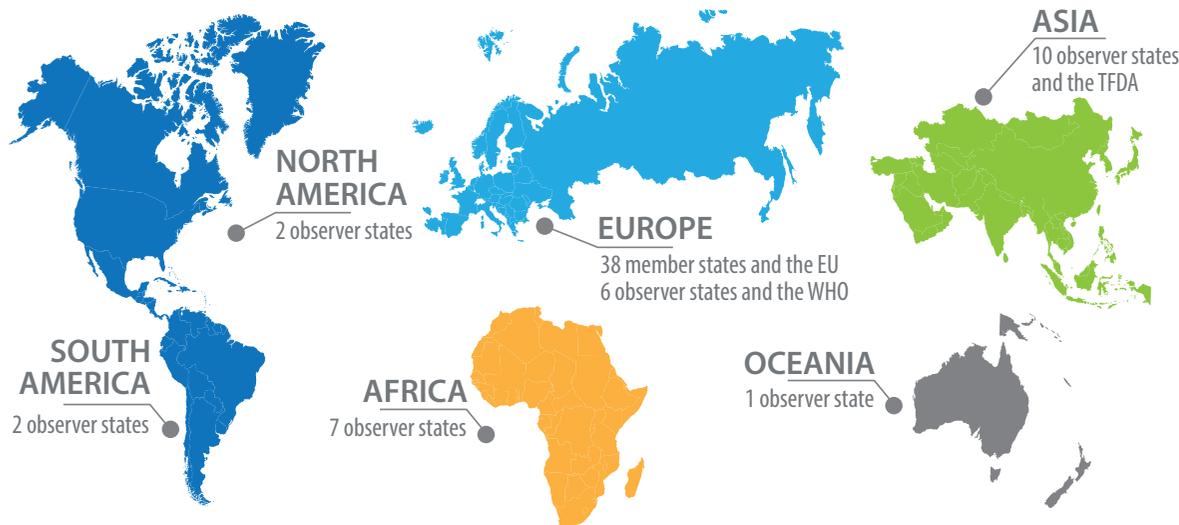
Wide participation

38 member states and the EU are signatories to the Convention on the Elaboration of a European Pharmacopoeia. The Ph. Eur. Commission also has a number of observers, which include countries from all over the world, the Taiwan Food and Drug Administration and WHO. The March 2018 session saw the Republic of Uzbekistan granted observer status, bringing the total to 30. This status will allow the Uzbek authorities to take part in the scientific work of the Ph. Eur. Commission and other

The European Pharmacopoeia Activities in 2018

- ▶ 41 new monographs
- ▶ 8 new chapters
- ▶ and 293 revised texts were adopted
- ▶ the Republic of Uzbekistan became the 30th observer





► Member and observer states of the Ph. Eur. (2018)

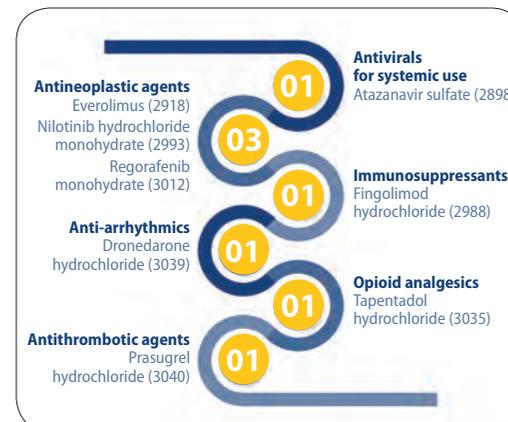
EDQM activities, to benefit from European experience in the field of medicinal products for human and veterinary use, to exchange knowledge with experts from European licensing authorities and inspectorates and to share the work on the development of international quality controls for medicines and the methods of analysis used.

Work Programme 2018

Year-on-year, the Ph. Eur. Commission works to provide Ph. Eur. users with the most up-to-date and relevant information possible, revising existing monographs to incorporate newly developed methods and techniques, and approving new texts for products of high relevance for public health. The work programme for 2018 continued to reflect these efforts: 41 new monographs and eight new chapters were adopted and 293 texts were revised to incorporate regulatory changes and scientific progress.

The Ph. Eur. Commission adopted five monographs on finished products, *Deferiprone oral solution* (2987), *Lacosamide infusion* (2991), *Lacosamide oral solution* (2990), *Deferiprone tablets* (2986) and *Lacosamide tablets* (2989), elaborated under the P4 procedure (single-source products still under patent). These monographs follow on from the decision of the Ph. Eur. Commission in 2014, after the positive results of a pilot phase, to add finished product monographs to its regular work programme. The decision was based on various considerations, including the fact that finished product monographs help OMCLs in their market surveillance tasks and can support the development of generic drugs, an essential point for the sustainability of healthcare systems. Finished product monographs also facilitate the assessment of marketing authorisation applications by regulatory authorities.

The Ph. Eur. Commission also adopted eight new monographs on active substances elaborated under the P4 procedure.



► Active substances adopted under the P4 procedure

Following the detection of nitrosamine compounds, namely N-nitrosodimethylamine (NDMA) and N-nitrosodiethylamine (NDEA), which are classified as probable human carcinogens, in batches of valsartan and

other sartans, the Ph. Eur. Commission decided to revise the individual monographs concerned at its November 2018 session. The revision will be done in line with the EMA recommendations, as outlined in the press release “Sartan medicines: companies to review manufacturing processes to avoid presence of nitrosamine impurities”, published on 1 February 2019. Five monographs on sartans (*Valsartan (2423)*, *Candesartan cilexetil (2573)*, *Irbesartan (2465)*, *Losartan potassium (2232)* and *Olmesartan medoxomil (2600)*) will have their production and test sections revised for publication in the 10th Edition of the Ph. Eur. (see also “Certification of suitability to the Ph. Eur. monographs” page 21 and “The European Network of Official Medicines Control Laboratories” page 23).

The Ph. Eur. Commission achieved another important milestone in the Live Biotherapeutic Products (LBPs) field, with the adoption of quality standards for LBPs for human use at its 160th session (March 2018). These standards, in the form of a general monograph on *Live biotherapeutic products for human use (3053)* and two general chapters, *Microbial examination of live biotherapeutic products (LBP): test for enumeration of microbial contaminants (2.6.36)* and *Microbiological examination of live biotherapeutic products: test for specified micro-organisms (2.6.38)*, lay down essential quality requirements for users, thus closing a regulatory gap. As their name suggests, LBPs are medicinal products containing living micro-organisms, such as bacteria or yeasts, which have a positive influence on the health and physiology of the host. The most commonly used species are the bacteria

Lactobacilli, *Bifidobacteria*, some streptococcal species and *Bacillus clausii* and the yeast *Saccharomyces cerevisiae var. boulardii*. While many LBPs are available on the European market, until now no Ph. Eur. requirements were available to ensure their quality. These general chapters describe methods for the enumeration of contaminants and for the detection of specified micro-organisms, in addition to providing decision diagrams (in both chapters) describing how to establish a suitable testing method, a supplementary tool to control the quality of LBPs.

One of the original cornerstones of pharmacopoeial testing, the chapter on *Infrared Absorption Spectrophotometry (2.2.24)* is referenced in numerous general texts and more than 1 200 individual monographs. This chapter has been extensively revised by the Ph. Eur.’s Vibrational Spectroscopy and

Analytical Data Modelling (VSADM) Working Party, whose role is to draft and revise general chapters on Chemometrics (i.e. modelling of analytical data, including multivariate data analysis, data mining and chemical imaging), measurement techniques that rely extensively on analytical data modelling (NIR, RAMAN) and on other vibrational spectroscopies (IR).

Another important general chapter, *Absorption spectrophotometry, ultraviolet and visible (2.2.25)*, was extensively revised by the General Methods (MG) Working Party and then adopted at the 162nd session of the Ph. Eur. Commission. The new chapter now also covers UV-Vis detectors for chromatographic systems and process analytical technology applications. In keeping with the REACH regulation, nicotinic acid is now described instead of potassium dichromate (a REACH Annex XIV listed

Ph. Eur. texts for Recombinant DNA technology products adopted in 2018

- ▶ 1 general monograph (0784) revised to take into account current practices and advances in the field.
- ▶ 1 new chapter on Quantification and characterisation of residual host-cell DNA (2.6.35)

substance) for the purpose of controlling absorbance accuracy.

The general monograph on *Products of recombinant DNA technology (0784)* was adopted by the Ph. Eur. Commission at its 160th session after undergoing extensive revision to take into account current practices and advances in the field of recombinant DNA technology. The monograph now covers modified proteins, proteins produced in transgenic animals and plants and recombinant vaccine antigens. Revision work also targeted the Production section, which has been entirely re-structured and modernised in line with the recommendations and guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the EMA and WHO for recombinant proteins. General considerations regarding the testing at the active substance and finished product stages (including identification and assay) have also been included. In short, the monograph has been completely overhauled to ensure that it reflects the advances that have taken place since the original elaboration. The Ph. Eur. Commission adopted a new chapter on *Quantification and characterisation of residual host-cell DNA (2.6.35)*, which describes analytical methods for the quantification of residual host-cell DNA in biological products produced in cell substrates and for the characterisation of its size. This eagerly awaited chapter, deliberately drafted to allow users a certain degree of flexibility, will serve a wide range of recombinant DNA technology products.



► Ph. Eur. Technical Guides adopted (2018)

The Ph. Eur. has always recognised the complexity of biologicals in the development of its texts, and the need for flexibility in monographs had already been the subject of discussions in the 1980s. These debates led, in 1991, to the creation of a Production section in monographs for biological preparations that draws attention to particular aspects of the manufacturing process but is not necessarily comprehensive. While establishing monographs for biotherapeutics, it became evident that additional flexibility was needed to address the structural complexity and naturally occurring heterogeneity, as well as the potential diversity of the compound resulting from different manufacturing processes. During its 161st session (June 2018), the Ph. Eur. Commission approved a new edition of the *Technical Guide for the elaboration of monographs on recombinant DNA proteins and synthetic peptides* that has undergone a general update to take into account the experience gained in recent years, notably on the elaboration of

monographs for complex molecules. The new Guide therefore includes a new section entitled “flexibility”, providing insight into the approach to be followed when tackling biotherapeutic products.

The Ph. Eur. Commission approved revised versions of two other important technical guides:

- the *Guide for the elaboration and use of monographs on vaccines and immunosera for human use*. This guide has undergone a general update to incorporate the experience accumulated over the last decade in elaborating monographs for vaccines and immunosera for human use;
- the *Guide for the elaboration of monographs on radiopharmaceutical preparations*, which contains a new section on the validation of analytical methods used to assess the quality of these medicinal products.

In 2018, the Ph. Eur. Commission continued its commitment to phasing out animal tests, continuously reviewing the *in vivo* tests described in Ph. Eur. texts and applying, whenever possible, the “3Rs” (Replacement, Reduction and Refinement) set out in the *European Convention for the Protection of Vertebrate Animals used for experimental and other scientific purposes*. The decision to replace the histamine sensitisation test (HIST) for residual pertussis toxin testing is a testament to this effort: in November 2018, the Ph. Eur. Commission adopted the replacement of the HIST (test in mice) with a standardised CHO cell-clustering assay (*in vitro* cell-based test). This change affects general chapter 2.6.33 *Residual pertussis toxin* and ten individual monographs on vaccines containing acellular pertussis components. The introduction of a standardised CHO cell-clustering assay for residual pertussis toxin testing is based on the results of two collaborative studies, run under the auspices of the EDQM’s BSP.

The Ph. Eur. Commission also decided to re-activate its Working Party on Gene Therapy products and entrusted it with the revision of general chapter 5.14 *Gene Transfer Medicinal Products for Human Use*, to take into account more recently elaborated pharmacopoeial texts, such as general chapter 5.2.12 *Raw materials of biological origin for the production of cell-based and gene therapy medicinal products*, and to assess the need to revise other general chapters or elaborate new Ph. Eur. texts related to gene therapy to include the latest developments in this fast-moving area.

General matters and policies

Biological Standardisation Programme



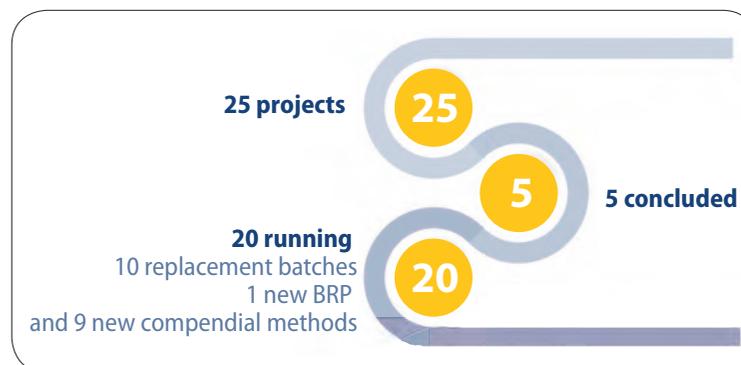
The BSP is a joint Council of Europe/ EU initiative, partly funded by the EU. Its mission is to establish reference materials for biologicals and to develop and validate new analytical methods for the quality control of biologicals, including alternative methods for the replacement of animals in laboratory experiments based on the 3Rs principles (Replacement, Reduction and Refinement).

In 2018, the programme ran 25 projects in different fields, from vaccines for human and veterinary use to plasma-derived and biotechnology products. Five were concluded during the year, leading to the establishment of one new and three replacement reference

standards (see “Pharmaceutical Reference Standards” page 19). One reference standard (Pertussis Toxin BRP) was newly calibrated for use in the CHO cell-clustering assay that will be prescribed instead of an animal test in the monographs on acellular pertussis-containing vaccines.

The EDQM carried forward another ten projects aimed at establishing replacement batches for existing reference standards for biologicals. One important project is underway to establish a new non-endotoxin pyrogen reference standard for use in the *Monocyte activation test (2.6.30)*.

Nine projects focused on the development of new compendial methods, and six of these were dedicated to applying the 3Rs principles to the field of quality control of biologicals. The continued efforts of the BSP to elaborate, validate and implement analytical methods in line with the 3Rs principles were widely acknowledged in 2018.



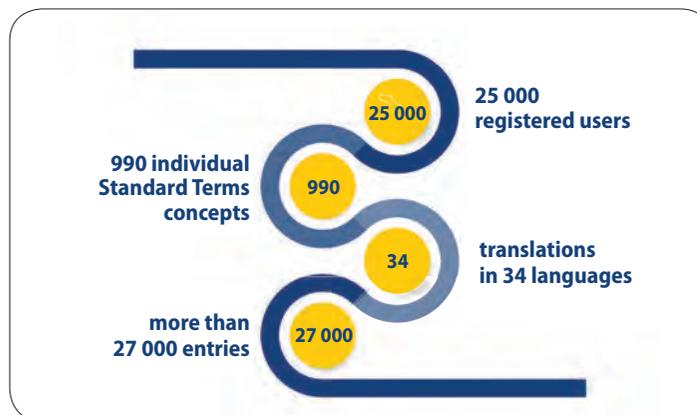
► *Biological Standardisation Programme achievements (2018)*

Standard Terms database



Initially drawn up at the request of the European Commission for use in marketing authorisation applications, the database containing the list of Standard Terms provides users and prescribers with harmonised vocabularies to describe dosage forms, routes of administration, units of presentation, containers, closures and delivery devices for medicinal products. It also includes a mapped terms section, which allows users of external databases across the world to introduce and map their own terms against Standard Terms, and web services (also known as application programming interfaces), which allow registered users to extract data directly from the database for use in their own systems. By the end of 2018, the free, online Standard Terms database had almost 25 000 registered users and held 990 individual Standard Terms concepts with translations in 34 languages, totalling more than 27 000 entries.

Collaboration between the ICH and the Standard Terms Working Party continued in 2018, with five new ICH requests being submitted and assessed. In addition to its established use throughout Europe, interest in the Standard Terms database continued to spread among non-member states, reflecting the growing recognition of the importance of harmonising vocabularies used for the identification of medicinal products worldwide. The Standard Terms database remains at the forefront of the drive for global harmonisation in order to improve the health and safety of patients throughout the world.



► The free on-line Standard Terms Database key figures (2018)

The Pharmacopoeial Discussion Group and other international harmonisation initiatives

Through its active participation in the work of the PDG, the Ph. Eur. continued its efforts to reduce unnecessary duplication of testing and reporting during drug development and routine manufacturing testing. The Group, which has the Ph. Eur., the Japanese Pharmacopoeia (JP) and the United States Pharmacopoeia (USP) as members, together with WHO as an observer, was set up in 1989 to harmonise pharmacopoeial standards across the world. Two PDG meetings were organised in 2018, one virtual (by videoconference) and one face-to-face which was hosted by the EDQM. These meetings focused on strategic direction setting and were combined with technical teleconferences, which allowed geographically distant experts to discuss and resolve targeted technical topics, notably issues related to the monographs on

Carmellose sodium and *Sterile Water for Injection* and to the general chapters on *Elemental impurities* and *Particulate contamination*.

To speed up progress with its work programme, the PDG also continued its strategic review of individual work items and launched a pilot phase trialling a prioritisation scheme for excipient monographs and general chapters. This trial phase concerned ten excipient monographs and five general chapters and will continue in 2019.

Sign-offs of harmonised texts at the 2018 PDG meeting included a new monograph on *Copovidone* and the revision of two monographs, *Microcrystalline Cellulose* and *Wheat starch*.

As a result, 28 of the 31 general chapters and 46 of the 60 excipient monographs on the work programme had been harmonised amongst the PDG Pharmacopoeias by the end of 2018.

Further harmonisation initiatives

The Ph. Eur. is actively involved in a number of other harmonisation initiatives at international level. It attends the International Meeting of World Pharmacopoeias (IMWP), which is organised under the auspices of WHO and brings together pharmacopoeias from around the world to discuss possible ways of strengthening harmonisation and convergence. Amongst the various projects carried out, the Good Pharmacopoeial Practices (GPhP), elaborated jointly by the participating pharmacopoeias, stands out as a basis for improving cooperation and work-sharing among the pharmacopoeias of the world.

The 9th IMWP took place in April 2018 in Da Nang, Vietnam, hosted by the Vietnamese National Institute of Drug Quality Control. This meeting was focused on defining the future policy and strategy of the IMWP, using the results of a survey of national, regional and international member pharmacopoeias to identify future challenges, possible “priority topics” and areas of mutual interest with opportunities for joint activities. Initial discussions were held on models of collaboration, and it was agreed to use the IMWP as a discussion forum to report recent challenges and share any solutions identified; in this context it was decided to set up a system for member pharmacopoeias to exchange information on issues detected with products covered by monographs that necessitate urgent action.

Cooperation with national and European regulatory authorities

Throughout 2018, the Ph. Eur. Commission continued to work closely with national competent authorities and the EMA. This ongoing cooperation is crucial to ensuring continued consistency between the approaches of licensing authorities and the Ph. Eur.; the monographs and chapters of the Ph. Eur. and the EMA scientific guidelines are complementary instruments for ensuring the quality of medicinal products. More specifically:

- ▶ the Ph. Eur. sets legally binding harmonised specifications for pharmaceutical preparations, their constituents and containers; and
- ▶ the EMA delivers guidelines providing advice on the best or most appropriate way to fulfil legal obligations.

Representatives of national authorities are members of the Ph. Eur. Commission and its groups of experts and working parties. National authorities and the EMA also take part in the work of the Ph. Eur. by submitting requests for revision and reviewing draft texts issued for public consultation in *Pharmeuropa online*. Members of EMA working groups (i.e. for which the EMA provides the Secretariat) and members of the EMA Secretariat itself participated in some of the Ph. Eur. Commission’s groups of experts and working parties.

Likewise, the EDQM has observer status in a number of EMA bodies, such as the Committee for Advanced Therapies (CAT), the Herbal Medicinal Products Committee

(HMPC), the joint CHMP/CVMP Quality Working Party (QWP), the Biologics Working Party (BWP), the Immunologicals Working Party (IWP) and the GMP/GDP Inspectors Working Group.

Cooperation with National Pharmacopoeia Authorities

The EDQM organises an annual meeting of National Pharmacopoeia Authorities (NPAs) of Ph. Eur. member states to facilitate and coordinate activities of common interest, and to provide an informal forum for exchanging information. The 2018 meeting was hosted by the Agency for Medicinal Products and Medical Devices (HALMED) in Split (Croatia) in May. Among other topics, discussions focused on the Ph. Eur. work programme and on process improvements.

Cooperation with other stakeholders

Stakeholders’ involvement in the elaboration and revision of Ph. Eur. texts is of crucial importance, and the EDQM strives to ensure regular exchanges with all those affected by its work. In 2018, various bilateral meetings were held with a variety of stakeholders to promote exchanges on all aspects related to the work of the EDQM, and also to ensure that the feedback from users could be taken into account.



PUBLICATIONS, DATABASES AND WEBSITE

The 9th Edition of the Ph. Eur. (with its latest Supplement 9.8) contains 2 406 monographs (including dosage forms), 365 general texts (including general monographs and methods of analysis) and around 2 730 descriptions of reagents.

Pharmeuropa online is the free online publication in which draft Ph. Eur. texts are launched for public consultation. Easily and widely accessible, *Pharmeuropa online* aims to optimise interactions between the Ph. Eur. Commission and its stakeholders: it provides interested parties with enough time to comment on draft texts and ensures access to all stakeholders across the globe. Texts are published on an ongoing basis and comments can be submitted on the basis of four deadlines per year.

► Ph. Eur. 9th Edition (2018)

REFERENCE STANDARDS

Ph. Eur. reference standards

Official reference standards (RSs) are an essential part of the quality standards of the Ph. Eur.: they are needed to apply the tests prescribed in the relevant monographs. Reference standards include Chemical Reference Substances (CRSs), Herbal Reference Standards (HRSs), Biological Reference Preparations (BRPs), Biological Reference Reagents (BRRs) and reference spectra. The official Ph. Eur. reference standards are established and distributed by the EDQM and adopted by the Ph. Eur. Commission; only the official Ph. Eur. reference standards are authoritative in case of arbitration.

The EDQM distributes its reference standards to countries around the world and its portfolio is constantly evolving: new standards are regularly introduced to complement new or revised Ph. Eur. texts, or to replace existing RSs when corresponding stocks run out. The overall lifecycle management of the RS portfolio covers a wide range of tasks: from the procurement of candidate materials, characterisation and establishment, to manufacturing, quality control, quality assurance, release, distribution and monitoring.

EDQM activities for WHO on Reference Standards

The EDQM is an observer to the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSP) and the Expert Committee on Biological Standardisation (ECBS). The tasks entrusted to these Committees include the development of standards and guidelines to promote the quality assurance and quality control of medicinal products around the world. In 2018,

the EDQM Laboratory participated in two collaborative studies organised by WHO for the establishment of two new International Standards: D-Antigen content of sIPV preparations and Adalimumab.

In addition the EDQM is responsible for the establishment and distribution of WHO International Standards for Antibiotics (ISAs), which are essential for the standardisation and quality control of antibiotic drug substances and medicinal products. These

Batches of Ph. Eur. Reference Standards adopted in 2018

- ▶ 107 new RSs
- ▶ 295 replacement RS batches were adopted
- ▶ distributed directly by the EDQM to 118 countries.



standards are supplied across the entire world for microbiological assays performed in the context of the quality control of antibiotics.

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

Key Facts and Figures



► Growth of the Ph. Eur. RS Portfolio (Number of Reference Standards 2014-2018)



► Distribution of Ph. Eur. RSs across the world (2018)

At the end of 2018, there were 2 922 reference standards available in the Ph. Eur. catalogue.

Globalisation of the pharmaceutical industry means that Ph. Eur. RSs are widely used around the world: in 2018, the EDQM distributed Ph. Eur. RSs directly to 118 countries.

RSs adopted in 2018

In 2018, the Ph. Eur. Commission adopted 107 new and 295 replacement RSs.

The RSs used for assays must be thoroughly characterised to assign a quantitative content value. In 2018, the EDQM Laboratory established 101 assay RSs, 62 of which required inter-laboratory studies involving OMCLs and other centres of excellence.

The international collaborative studies performed as part of the BSP in 2018 led to the conclusion of five projects and to the adoption of two new or newly calibrated reference standards by the Ph. Eur. Commission: *Infliximab BRP* and *Pertussis Toxin BRP*. Furthermore, three replacement standards were established: *Bordetella pertussis mouse antiserum BRP*, *Erythropoietin BRP* and *Hepatitis A vaccine ELISA detection antibodies set - BRR* (See also "The European Pharmacopoeia" page 14).

The ECSP adopted the establishment reports submitted by the EDQM Laboratory for five new ICRSs and one ICRS replacement.

The ECBS adopted the Third International Standard for Erythromycin, established by the EDQM, at their meeting in October 2018.

General matters and policies

Extended competence in RS establishment

In line with its continuous efforts to improve characterisation and establishment of reference standards, the EDQM Laboratory has extended the scope of its ISO 17025 accreditation to include nuclear magnetic resonance (NMR) and quantitative NMR spectroscopy.

Collaboration with the ISO

The EDQM also continued its participation as an observer in the activities of the International Organization for Standardization (ISO) Committee on Reference Materials (REMCO).

Collaboration with national laboratories

Continuous collaboration with national laboratories and centres of excellence is fundamental for RSs, such as those for assay/potency tests which are established through inter-laboratory studies. In 2018, the establishment of RSs benefited from contributions from a panel of 39 OMCLs from 27 different countries.

PUBLICATIONS, DATABASES AND WEBSITE

Throughout 2018, the EDQM continued to run and maintain its “Reference Standards Online Database” providing access to all standards officially valid for the uses prescribed in the Ph. Eur. monographs. The database has been further fine-tuned to help users find the standards easily and rapidly: RSs can be searched by code, name, monograph number or CAS number. In addition, RS Batch Validity Statements (BVSs) are available to users to document the validity of the particular RS batch supplied at the time of use. Downloadable Safety Data Sheets and Safety Data Statements, as well as leaflets, are also available in the EDQM’s Online Database¹.



In 2018, the EDQM issued 472 leaflets providing RS users with additional information, such as a chromatogram, assigned value, etc. for a given substance.

In addition, Safety Data Sheets and outer labels have been created or updated for hazardous chemicals in accordance with EU regulations on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and on Classification, Labelling and Packaging (CLP). Safety Data Statements have been created or updated for biohazardous materials within the scope of Directive 2000/54/EC. Safety Data Sheets and labels are provided in 27 languages.

1. The EDQM reference standards Online database can be accessed here: <https://crs.edqm.eu/>

CERTIFICATION OF SUITABILITY TO THE PH. EUR. MONOGRAPHS

The Certification procedure is becoming increasingly recognised worldwide

The Certification of Suitability (CEP) procedure has been set up to evaluate and validate the capacity of Ph. Eur. standards to control the quality of substances used in the manufacture of medicinal products.

To apply for a certificate, manufacturers submit a dossier describing how their substance is manufactured and demonstrating that its quality can be adequately controlled by the Ph. Eur. monographs. The EDQM evaluates the data in this dossier and may then grant a CEP. The procedure centralises the evaluation of data for the benefit of regulatory authorities and industry alike, and contributes to keeping the relevant Ph. Eur. monographs up to date.

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

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

The Certification of Suitability (CEP) to the Ph. Eur. monographs Procedure activities in 2018

- ▶ 285 new applications
- ▶ and 1 768 requests for revision of CEPs were received
- ▶ all requests were dealt with within official timelines.



Key Facts and Figures

In 2018, the EDQM received 285 new applications, including 13 for the risk of transmissible spongiform encephalopathy (TSE) and 59 for herbal preparations; additionally, 1 768 requests for revision of CEPs were received. These figures are stable compared to previous years.

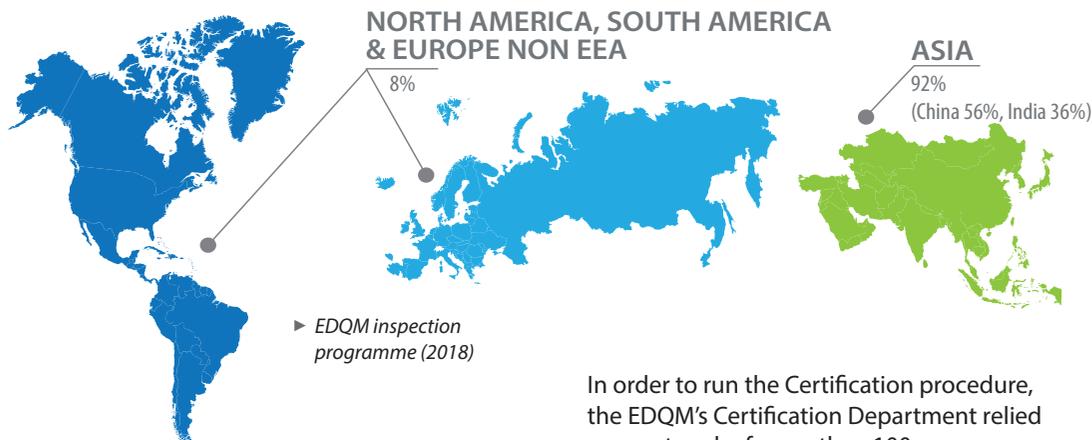
In 2018, a total of 261 new certificates and 1 449 revised certificates were issued. More than 95% of applications, whether new applications or requests for revision, were dealt with within official timelines. Information on adherence to timelines for CEP applications is published on a monthly basis on the EDQM website.

In December 2018, there were more than 5 000 valid CEPs covering chemical purity, TSE and herbal drug preparations.

Following a major quality issue related to the presence of nitrosamines – impurities classified as probable human carcinogens – in valsartan and other sartans, the EDQM reviewed all relevant CEP applications and asked CEP holders to address this risk and update their applications accordingly. This resulted in the suspension of CEPs for a number of sartans containing levels of nitrosamines above tentative limits defined by the EMA's Safety Working Party until corrective actions are taken. The EDQM used its website to regularly communicate information on progress made with the

▶ Total valid and granted CEPs in 2018





reviews and decisions taken on CEPs which posed a potential risk for public health (see also “European Pharmacopoeia” page 12 and “The European Network of Official Medicines Control Laboratories” page 23).

As part of the EDQM inspection programme, 36 manufacturing sites (mainly located in Asia) were inspected in 2018. As part of its collaboration with international partners worldwide, the EDQM also performed two joint inspections with WHO, and contributed to two inspections coordinated by the EMA.

In addition, by exchanging data with inspectorates from member states and international partners, the EDQM obtained information on GMP compliance for 46 other sites. In total 82 manufacturing sites were assessed for GMP compliance.

In response to cases of GMP non-compliance, the EDQM suspended five CEPs and withdrew eight CEPs from the companies concerned in 2018. In one case, actions were taken on CEPs after EU/EEA supervisory authorities issued statements of non-compliance for sites involved in CEP applications.

In order to run the Certification procedure, the EDQM’s Certification Department relied on a network of more than 100 assessors from competent authorities in 25 different countries, and more than 30 inspectors from 10 EU/EEA countries.

General matters and policies

In 2018, the Certification Department published a number of guidelines and policies² to support applicants in their communication with the EDQM, in the preparation of their CEP dossiers and in the use of CEPs in marketing authorisation applications. These include, in particular, the new guideline “How to read a CEP” and the revised “Guideline on requirements for revision/renewal of CEPs”, which triggered updates to other EDQM guidelines.

The EDQM continued to implement its roadmap for the submission of CEP applications in electronic format. The EDQM expects to move towards the exclusive use of the Electronic Common Technical Document (eCTD) format by 2020 (with the exception of TSE dossiers and substances for veterinary use only).

2. Available on the EDQM website <https://go.edqm.eu/CEPgI>

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

As part of the pan-European alert system that was triggered to handle the major quality issue with sartans, the EDQM has been working with the EMA, as well as with European and international competent authorities worldwide, to better understand the root causes of the nitrosamine contamination and to establish remedial actions. This collaboration involved continuous exchange of information on findings and on actions taken, under the established confidentiality agreements, and is now being followed up with a “lessons learnt” exercise at European level.

In 2018, the Certification Department took part in a number of events, conferences and international platforms for collaboration, such as the newly created International Pharmaceutical Regulators Programme (IPRP), the international Active Pharmaceutical Ingredients (API) inspection programme, and the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

The Certification Department continued to work on strengthening co-operation and exchange of information on the quality of pharmaceutical substances with authorities worldwide and promoting the informed use of CEPs as support documentation for the quality evaluation of substances.

THE EUROPEAN NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES



The importance of a network for pan-European cooperation

Throughout 2018, the EDQM continued to coordinate the activities and programmes of its General Network of OMCLs, the GEON. The coordination of the OMCL Network is partly funded by the European Commission.

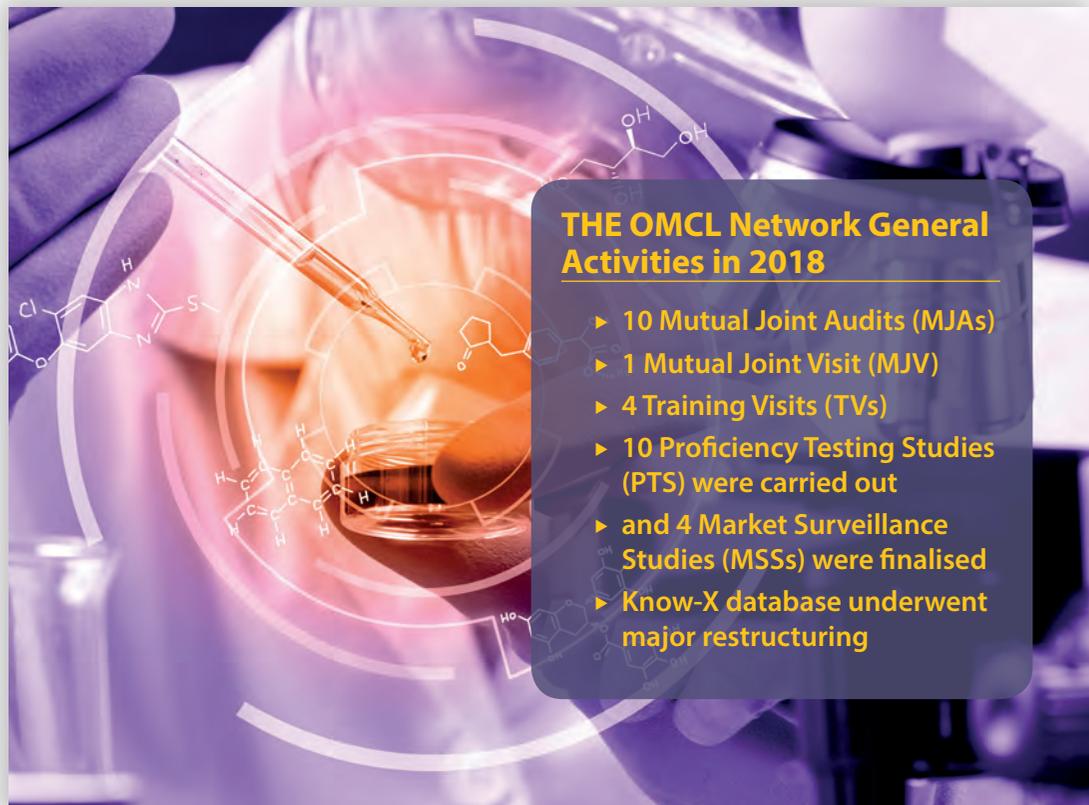
Created to prevent substandard medicinal products from reaching patients and compromising the efficacy of their treatment and potentially their health, the OMCL Network currently brings together official laboratories based in 36 European member states and seven non-European countries. Operating impartially and independently of manufacturers, and thus without any conflicts of interest, this Network facilitates the pooling of resources and information on the latest technologies with a view to saving public money and sharing expertise and best practices across Europe.

The Network operates on the basis of commonly agreed standards, procedures and guidelines, and follows the principle of mutual recognition of test results. Its work gives member states the support they need to monitor the quality of medicines.

In order to support regulatory action in response to nitrosamine contamination in APIs of the sartan class (see also “Certification of Suitability” page 21), the EDQM coordinated the development of determination methods with its network of OMCLs; it also implemented a pan-European risk-oriented sampling and testing programme of APIs and drug products of this class. This resulted in a number of API batches and medicinal products (from several sources) being identified as contaminated.

In 2018 a new video and brochure highlighting the main activities of the OMCLs and their Network were published on the EDQM website³ and made available to the whole OMCL Network.

3. Available on the EDQM website <https://go.edqm.eu/GEON>



THE OMCL Network General Activities in 2018

- ▶ 10 Mutual Joint Audits (MJAs)
- ▶ 1 Mutual Joint Visit (MJV)
- ▶ 4 Training Visits (TVs)
- ▶ 10 Proficiency Testing Studies (PTS) were carried out
- ▶ and 4 Market Surveillance Studies (MSSs) were finalised
- ▶ Know-X database underwent major restructuring

Quality Management programme

In 2018, the Network continued to implement, maintain and assess the Quality Management (QM) programme for its members. The main goals are:

- ▶ to ensure harmonisation of quality management systems (QMS) among OMCLs, and
- ▶ to achieve appropriate quality levels for the mutual recognition of test results among members (e.g. official batch release testing of biologicals, market surveillance and falsified medicines testing).

The activities coordinated by the EDQM in 2018 focused on the implementation of the new ISO/IEC 17025:2017 norm that requires OMCLs to adapt to the new requirements within a transition period of 3 years.

Mutual Joint Audits/Visits and Training Visits

Mutual Joint Audits/Visits (MJAs/MJVs) are used to assess the compliance of OMCL QMSs with the requirements laid down in ISO/IEC 17025, the Network QM guidelines and the Ph. Eur. In 2018, ten MJAs, one MJV and four Training Visits (TVs) were carried out, bringing the total to 179 MJAs, 52 MJVs and 28 TVs/Tutorials since the programme was launched in 1997.

OMCL Network Quality Management Guidelines

QM Guidelines are elaborated by experts of the Network and updated on a regular basis, coordinated by the EDQM Secretariat. They

Status	Guideline/Recommendation documents
Adopted	<ul style="list-style-type: none"> ▶ Qualification of Equipment – Core document ▶ Qualification of Mass Spectrometers ▶ Qualification of Liquid Chromatography Equipment ▶ Qualification of Piston Pipettes ▶ Validation of Computerised Systems
Under revision	<ul style="list-style-type: none"> ▶ Qualification of Balances ▶ Management of Reagents ▶ Qualification of UV/Visible Spectrophotometers ▶ Estimation of Measurement Uncertainty ▶ Qualification of Analytical Columns ▶ Qualification of Infrared Spectrophotometers

▶ *Quality Management Guidelines elaborated (2018)*

are established to support laboratories in the implementation of the ISO/IEC 17025 requirements. The QMS Guidelines and Recommendation documents on the 2018⁴ working programme are listed below.

Training Courses/Workshops

In order to allow OMCLs to share their experience and harmonise best practices, in 2018 the EDQM organised a workshop on “Management of Control Charts to Monitor Laboratory Data and Metrological Topics”. In addition, to support the Network during the transition to the new version of ISO 17025:2017, a two-day training session was organised for OMCL representatives followed by a one-day workshop specifically dedicated to MJA auditors.

4. Available on the EDQM website <https://go.edqm.eu/QAQMgl>

Proficiency Testing Scheme studies

The EDQM Proficiency Testing Scheme (PTS) provides laboratories with an objective means to assess and demonstrate the reliability of their data. In 2018, five studies were organised in the physico-chemical field: “PTS186 Sulfated ash”, “PTS187 Volumetric titration”, “PTS188 Liquid Chromatography”, “PTS189 UV-Vis Spectrophotometry” and “PTS190 Melting point”. On average 103 laboratories (OMCLs and other pharmaceutical control laboratories from industry, hospital pharmacies, universities and pharmacy associations) took part in each study.

A specific PTS programme is also organised by the EDQM in collaboration with WHO. In 2018, two studies were completed: “EQAAS 8.1 Assay by liquid chromatography” and “EQAAS 8.2 Related substances by liquid chromatography”. On average 35 laboratories took part in each study.

Five studies in the field of biologicals were organised in 2018, with an average of 16 participating laboratories for each study. They covered “PTS164 Fibrin sealant: fibrinogen and thrombin potency”, “PTS174 Acellular pertussis vaccine serology”, “PTS183 Unfractionated heparin chromogenic assay”, “PTS191 Parvovirus B19 NAT” and “PTS192 Hepatitis C virus NAT”.

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

The EDQM continued to work with the EA, with the aim of evaluating cooperation opportunities, focusing on exchanges of know-how, mutual participation in meetings as observers and running joint audits with National Accreditation Bodies (NAB) and EDQM/MJA auditors. In 2018, the focus was on the training of auditors for the implementation of the new ISO 17025:2017 standard. One joint audit was carried out.

General OMCL Network (GEON) activities

GEON Annual General Meeting

The 23rd GEON Annual Meeting was held in Sarajevo (Bosnia and Herzegovina) from 14 to 18 May 2018 and was organised with the support of the Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina (ALMBiH). The meeting was attended by more than 230 experts from 38 countries – representing 65 official laboratories and national medicines agencies – including representatives from non-European partners Canada, Israel, Singapore and, for the first time, the Taiwan Food and Drug Administration.



► Participants in the 23rd Annual Meeting of GEON in Sarajevo (Bosnia and Herzegovina)

General Market Surveillance Studies

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

In 2018, four MSSs, *Foreign Matter in Herbal Drugs (MSS051)*, *Hyaluronic Acid-Based Dermal Fillers (MSS050)*, *Zoledronic Acid Preparations for Parenteral Application (MSS055)* and *Meloxicam APIs and Solutions for Injection (MSS056)* were finalised.

Two new MSSs on *Liothyronine APIs and tablets (MSS054)* and on *Pioglitazone tablets (MSS057)* were initiated.

On average nine OMCLs from the GEON participated in each of these studies.

Active Pharmaceutical Ingredients (API) Working Group

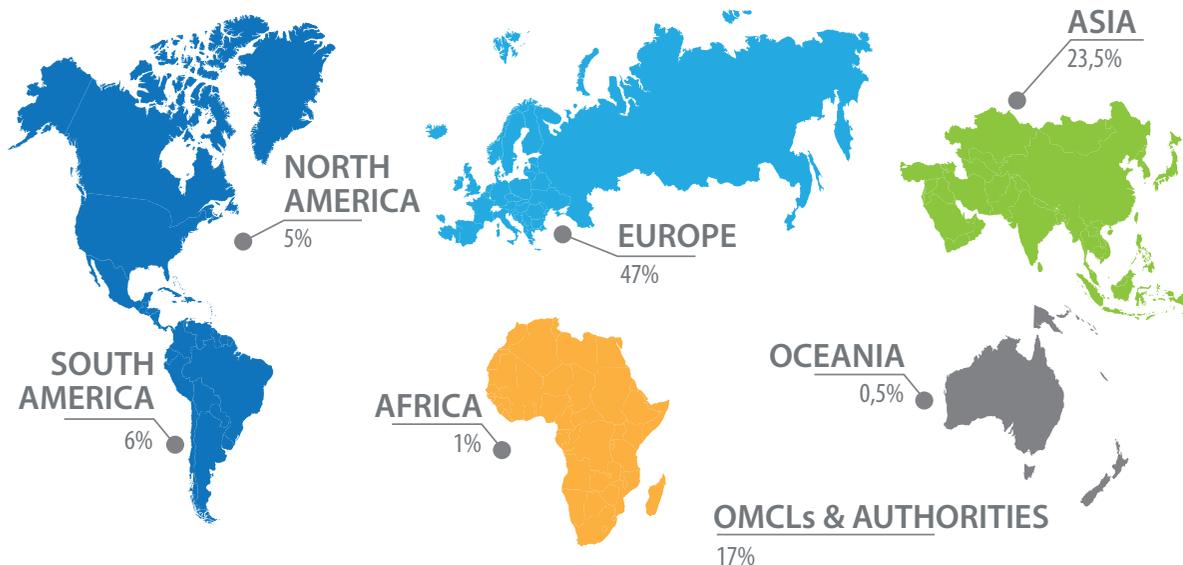
The 12th meeting of the API Working Group took place in November 2018. Discussions focused on strategic topics key to defining

the mid- and long-term objectives of the group. Other important topics were also addressed, including the Fingerprint MSSs on sildenafil and omeprazole, the collaboration with GMP inspectors during the Heparin and the Valsartan cases and ways of improving cooperation with the other programmes.

Following discussions on lessons learnt from the first fingerprint MSSs aimed at improving the testing scheme in preparation for future studies, it was decided to perform the first combined CAP, MSS and API Fingerprint studies on sildenafil. The main purpose of the combined studies is to create synergies for API sample collection and testing.

OMCL Falsified Medicines Working Group

The group met twice in the course of 2018. The second meeting in November 2018 brought together for the first time the Falsified Medicines and API Working Groups in a joint session. A new MSS on *Suspected*



► CombiStats™ licences per region

OMCLs & AUTHORITIES

17%

Illegal Products (MSSIPs) was initiated. It covers the so-called designer molecules (chemical derivatives of INN drugs) in dietary supplements, herbal medicines, medical devices etc.

Two technical training sessions for OMCL members were organised by the EDQM jointly with the Czech OMCLs at SUKL in Prague. They covered LC-MS (TOF), Infrared and Raman Spectroscopy as applied for the analysis of falsified medicines. The training particularly targeted small OMCLs with limited resources.

The EDQM's Know-X database is secure and restricted and stores comprehensive information on individual cases of falsified medical products. The Know-X database underwent major re-structuring to make it more user-friendly (see also "Publications, databases and website" page 30).

Gene Therapy Products Working Group

The OMCL Working Group for Gene Therapy Products (GTP) was created in 2008 to foster collaboration between OMCLs working in the GTP field, and to save time and resources through sharing of knowledge and information on the latest technological advancements. Currently, 11 OMCLs are active members of this working group and collaboration with the US FDA has been initiated.

The validation of standard methods for the determination of viral and infectious genomes in Adeno-Associated Virus (AAV) vector products was continued throughout 2018. Validation of the ELISA method for AAV8 Physical Particles Titre (PPT) is ongoing, while the validation of an ELISA method for AAV2 PPT is almost complete. Work on the standard method for determination of residual mammalian host cell DNA in GTPs was continued in 2018.

A joint meeting was organised with the GTP Working Party of the Ph. Eur. in Rome in order to gather stakeholders' opinions on the future work of EDQM in the GT field.

CombiStats™

CombiStats™ is computer software developed by the EDQM for the statistical evaluation of biological dilution assays in accordance with Chapter 5.3 of the Ph. Eur. Initially designed for OMCLs, CombiStats™ is now also available to other laboratories. The current version 5.0 introduced new features such as equivalence testing, robust regression, 5-parameter asymmetric sigmoid curves and password protection of datasheets. The online manual, a tutorial and other background information for CombiStats™ are available on the EDQM website⁵, while

5. These publications are available on the EDQM website <https://go.edqm.eu/combistats>

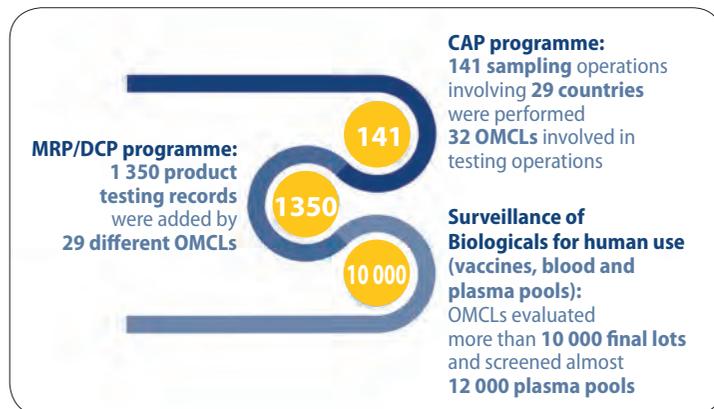
training courses for users are organised at the EDQM once a year.

In 2018, 659 licences were issued and CombiStats™ was used in 31 countries in Europe and 27 countries in the rest of the world. CombiStats™ has thus evolved into a common internationally agreed reference in its domain and contributes to the mutual recognition of data and results by all interested parties.

EU/EEA-specific activities

Market Surveillance for Products with a Centralised Marketing Authorisation

Every year since 1999, the EMA and the EDQM have joined forces on an annual programme for Centrally Authorised Product (CAP) Sampling and Testing. The EMA sponsors the programme and has overall responsibility for it, while the EDQM coordinates the sampling and testing operations. The list of products to be included in the annual programme is prepared by the EMA Secretariat together with the EMA Scientific Committees using a risk-based approach. In 2018, the work programme featured 36 products for human use (19 biologicals and 17 chemical products) and eight products for veterinary use (three immunobiological products and five chemical products). API testing was performed in six cases. In addition to the regular CAP programme, one generics programme was run in 2018, during which seven branded Pioglitazone products (generic medicinal products and their respective reference medicinal product) were tested.



► THE OMCL Network EU/EEA
Specific Activities in 2018

As part of the 2018 CAP Programme, 141 sampling operations were performed in 29 countries, and 32 OMCLs were involved in the testing operations. The results showed that the vast majority of the products tested were of the expected quality and complied with authorised specifications. By December 31, 2018, two “confirmed out-of-specification” results and several regulatory or technical findings had been reported to and followed up by the EMA.

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

The OMCLs involved in the programme met twice in 2018 (32nd and 33rd meetings) to evaluate the programme and discuss ways of optimising collaboration. Progress was made with discussions on common risk-assessment procedures. Increasing numbers of market surveillance studies carried out by the Network now combine the strengths of the CAP generics and MRP/DCP testing schemes in order to optimise the testing coverage of generics available on the European market.

The 14th regular programme for the market surveillance of medicinal products authorised in the EU/EEA via the MRP or DCP was carried out in 2018. About 1 350 product testing records were added to the 2018 programme, which is comparable with 2017. The testing reports for 2018 were submitted by 29 different OMCLs; 11% of the tested products were for veterinary use.

Regulatory issues were identified for around 2% of the materials tested. These mostly consisted of insufficient details on testing methods and labelling issues; one or more out-of-specification results were reported in a further 2.5% of cases.

As of January 2019, the MRP/DCP Product Testing Database, which had been set up in 2007 to record planning, sampling and reporting activities carried out within the OMCL network with respect to market surveillance testing of MRP and DCP products, held some 10 600 records, with contributions from 36 different OMCLs.

Official Control Authority Batch Release of Biologicals for Human Use

The Network for Official Control Authority Batch Release (OCABR) of Biologicals for Human Use implements the harmonised application of Article 114 of EU Directive 2001/83/EC across Europe. Network activity fosters the mandatory mutual recognition of batch release for human vaccines and medicinal products derived from human blood and plasma. OMCLs perform a quality review of every batch through testing and protocol review. During 2018, OMCLs evaluated more than 10 000 final lots and screened almost 12 000 plasma pools for safety, thus independently confirming the products' quality before they reach patients.

The OCABR sessions of the annual meeting in Sarajevo were attended by nearly 80 participants. This meeting is an opportunity to exchange expertise and optimise resources to solve common problems. The OMCLs discussed technical issues and strategies that would lead to better and more efficient control of products such as human clotting factors and childhood vaccines. A breakout session was also organised with the full OCABR network and manufacturers' representatives to develop strategies to handle eventual changes needed in the context of the withdrawal of the United Kingdom from the EU, with the goal of ensuring the availability of these important medicines during the transition period.

In 2018, two new and ten revised guidelines for vaccines came into force, as did the revised EU Administrative Procedure for OCABR and a number of internal network guidelines. The

OCABR advisory group and the drafting group for vaccines both met twice during the year to further the work of the OCABR Network between annual meetings. A workshop to foster harmonised testing for the safety of oral polio bulks was also held for OMCLs and involved manufacturers.

Official Control Authority Batch Release of Immunological Veterinary Medicinal Products

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

Twenty-six participants from 18 member states took part in the Veterinary Batch Release Network (VBRN) session of the OMCL annual meeting. The VBRN network confirmed their testing priorities using a risk-based approach and four OMCLs contributed to the first stage of a pilot phase to better coordinate activities for post-marketing surveillance, in particular for IVMPs that are not selected for OCABR. In anticipation of 3Rs developments for testing inactivated rabies vaccine, the OMCLs reviewed best practices for method transfer. In addition, an analysis of the potential conditions following the United Kingdom's withdrawal from the EU were analysed so that appropriate measures could be taken to ensure batch release.

The VBRN Advisory group met twice during the year to advance important issues. Updates to four internal procedures were adopted by the VBRN



ANTI-FALSIFICATION ACTIVITIES

Combating crime to protect public health

The EDQM continued to promote cooperation among authorities at national and international level in the fight against falsified medical products (medicinal products and medical devices), as covered by the Council of Europe's MEDICRIME Convention, the first and only binding criminal law instrument to address the falsification of medical products at international level. Efforts focused on encouraging authorities and governments to sign and ratify the Convention. Together with the Council of Europe Criminal Law Division of the Directorate General Human Rights and Rule of Law, the EDQM contributed to various regional conferences and workshops promoting the MEDICRIME Convention, which entered into force on 1 January 2016 following its 5th ratification by Guinea.

Key facts

By the end of 2018, the Convention had been ratified by 15 countries and signed by another 13. The Committee of the Parties, which held its first meeting in December 2018, will play an important role in supervising implementation of the Convention by the signatory states. The experts in the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH), together with its subordinate Committee of Experts on Minimising the Public Health Risks Posed by Falsification of Medical Products and

Similar Crimes (CD-P-PH/CMED), continued to develop and promote programmes and projects aimed at disseminating best practices in the fight against falsified medical products.

The promotion of the MEDICRIME Convention goes hand-in-hand with the actions taken by the EDQM and its experts to implement the Convention and its tools. One example is the creation of a Network of Single Points of

Contact (SPOCs) involving health authorities, customs and law enforcement agencies and other competent authorities at local, national and international level, through which information and data on falsified products is collected and shared. The EDQM actively promoted the SPOC model in cooperation with other international organisations such as the Asia-Pacific Economic Cooperation (APEC) and the United Nations Office on Drugs and Crime (UNODC).



Anti-Falsification Activities in 2018

- ▶ in total 15 countries ratified the MEDICRIME Convention
- ▶ first meeting of the Committee of the Parties organised by the Council of Europe
- ▶ third MEDICRIME workshop took place in London (UK)

Credit the U.S. Food and Drug Administration

In March 2018, the third MEDICRIME workshop for Good Distribution Practices (GDP), Good Manufacturing Practices (GMP) and Pharmacy Inspectors took place in London (UK). Jointly organised with the national authority MHRA, this technical workshop was attended by 12 inspectors from the Netherlands, Belgium, France, Ireland and the UK.

Mass serialisation systems for medicines

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

In 2018, by means of conformity assessments, the EDQM continued to monitor that the European Medicines Verification Organisation (EMVO) system, as well as systems at national level, were being developed in accordance with the standards in the Commission Delegated Regulation (EU) 2016/161 on the Unique Identifier, which complements Directive 2011/62/EU on Falsified Medicines. This initiative will help member states develop their role as supervisors of traceability systems.

KNOW-X

HOME SIGN IN

Welcome to Know-X Database

The know-X database is a tool that:

- assists officials by expanding their knowledge and awareness of the problem of falsified medicines
- provides a basis for the exchange of information
- highlights and encourages collaboration between health and law enforcement authorities
- fosters the sharing of analytical information on the testing of falsified and other illegal medicines within the Network of OMCLs.

The database contains details on cases of falsified medical products, technical information on the testing performed, the authorities involved and what actions were taken. The information provided is gathered from various sources (e.g. OMCLs, Health Authorities, regulatory agencies, medical product surveillance authorities, customs and police), and it is intended to provide governments with decision aids for the management and prevention of specific risks.

The EDQM has put in place certain criteria for access to the database. Access can be requested by officials working for:

- a competent health or law enforcement authority in a Council of Europe member state or in a state party to the MEDICRIME Convention that is directly involved in fighting falsified medical products and similar crimes, or
- a member of the European OMCL Network that does not belong to the core testing group.

If you would like more information on this database, please contact the EDQM at knowx@edqm.eu.

PUBLICATIONS, DATABASES AND WEBSITE

The EDQM's Know-X database is secure and restricted and stores comprehensive information on individual cases of falsified medical products (medicines and medical devices). The database is a tool for sharing information which enables health and law enforcement authorities across Europe to act more rapidly in cases of suspect medical products. The information provided in the Know-X database also covers the analytical identification of medicinal products and the related follow-up actions taken by the competent health or enforcement authorities. The CD-P-PH/CMED assists the OMCL Falsified Medicines Working Group with the maintenance of the database; it is also involved in promoting the database and offers training to its users. A new version of the database was launched in July 2018 (see also "The Official Medicines Control Laboratories Network", page 25). A webinar introducing the new functionalities was

organised in December 2018 and was attended by over 60 officials from health, police and customs authorities, as well as from the OMCLs.

Since 2007, the EDQM has organised or contributed to 22 training sessions and six conferences. In total, 514 participants from 62 countries, mostly in Europe but also in other parts of the world⁶, have participated in these programmes on falsified medical products.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Throughout 2018, representatives of the EDQM have participated regularly in the meetings of the EU Heads of Medicines Agencies' Working Group of Enforcement Officers (HMA-WGEO), and have attended a number of conferences with the purpose of raising awareness of the MEDICRIME Convention.

6. Overview of activities related to MEDICRIME: <https://go.edqm.eu/MDCRacts16>

PHARMACEUTICALS AND PHARMACEUTICAL CARE

Optimal use of medicines for improving patients' quality of life

Activities in this area are led by the European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) and its subordinate bodies, the Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC), the Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO) and the Committee of Experts on Minimising Public Health Risks Posed by Falsification of Medical Products and Similar Crimes (CD-P-PH/CMED).

Key Facts

In 2018, much progress was made on the drafting of a Council of Europe resolution for the promotion and implementation of pharmaceutical care in Europe. The resolution will advance patient-centred care, support medicines optimisation and encourage responsible use of resources through the implementation of pharmaceutical care in daily practice in community and hospital settings.

The guidelines on best practices for Automated Dose Dispensing (ADD)⁷ were published following a public consultation among interested parties, including authorities and healthcare professionals.

These guidelines recommend standards and approaches for regulating ADD services across Europe, as well as for supporting ADD providers and national authorities in ensuring that ADD services are provided at a consistently high standard.

The CD-P-PH/PHO issued its annual recommendations on the classification of medicines and their supply conditions (prescription and non-prescription). This work is of relevance to health authorities



Pharmaceuticals and Pharmaceutical Care in 2018

- ▶ publication of the **Automated Dose Dispensing (ADD) guidelines**
- ▶ and the annual **recommendations on the classification of medicines and their supply conditions** (prescription and non-prescription)
- ▶ update of the **Melclass database**
- ▶ and review of the **classification of medicines containing anti-inflammatory and anti-rheumatic active substances.**

⁷ The EDQM publications are available here: <https://register.edqm.eu/freepub>



- *Guidelines on best practices for Automated Dose Dispensing (ADD) (2018)*

and all stakeholders across the medication supply chain, and it helps ensure patient safety and accessibility of medicines in Europe. The annual recommendations of the CD-P-PH/PHO are included in the Melclass database⁸, which provides information on the classification and conditions for supply of medicines.

The Committee of Ministers of the Council of Europe adopted

the revised Resolution CM/Res(2018)1 on the classification of medicines as regards their supply. The Resolution, which supersedes the previous Resolution, ResAP(2007)1, will continue to play a key role in supporting the development of uniform and safe supply conditions for human medicines across Europe.

⁸ The Melclass database is accessible here: <https://melclass.edqm.eu/>

PUBLICATIONS, DATABASES AND WEBSITE

The review of the classification of medicines containing anti-inflammatory and anti-rheumatic active substances was published on the EDQM website.

Throughout 2018, the Melclass database was regularly updated with relevant recommendations from the CD-P-PH/PHO to national health authorities on the classification of medicines and their supply conditions. The Melclass database also contains national information about the classification status and supply conditions of medicines.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Interactions took place in 2018 with international organisations and professional bodies active in the field of public health and pharmacy practice, such as the European Association of Hospital Pharmacists (EAHP) and the Co-ordination Group for Mutual Recognition and Decentralised procedures - Human (CMDh) Non-prescription Medicinal Products Task Force, in order to align efforts aimed at ensuring safe and appropriate use of medicines in Europe.

Resolution CM/Res(2016)2 on good reconstitution practices in health care establishments for medicinal products for parenteral use was presented at the 23rd Congress of the EAHP in Gothenburg (Sweden) to promote its implementation and use.

A workshop was organised at the 47th European Symposium on Clinical Pharmacy in Belfast (United Kingdom) focusing on the development of quality indicators in the area of safe and appropriate use of medicines, and presenting the outcomes of the EDQM Pharmaceutical Care Indicators Project.

Member State	Classification Status
Armenia (AM)	Not subject to prescription
Austria (AT)	Not subject to prescription
Belgium (BE)	Not authorised
Croatia (HR)	Not subject to prescription
France (FR)	Not authorised
Germany (DE)	OTC - Exempted
Hungary (HU)	Not subject to prescription
Ireland (IE)	OTC - Exempted
Italy (IT)	OTC - Exempted
Latvia (LV)	Not subject to prescription
Lithuania (LT)	Not subject to prescription
Netherlands (NL)	Not authorised
Poland (PL)	OTC - Exempted
Portugal (PT)	Not authorised
Romania (RO)	Not subject to prescription
Slovenia (SI)	Not subject to prescription
Spain (ES)	Not subject to prescription
Sweden (SE)	OTC
Switzerland (CH)	Not authorised
The Former Yugoslav Republic of Macedonia (MK)	Not subject to prescription
United Kingdom (UK)	Not subject to prescription

- *Anti-inflammatory and anti-rheumatic active substances in Melclass (2018)*



European Paediatric Formulary in 2018

- ▶ **first texts for public consultation** launched on a new online platform
- ▶ **10 monographs** on the work programme
- ▶ **official launch** will happen once the **two pilot formulations** have been adopted

Following the definition of criteria for inclusion and evaluation of formulations in 2015, a dedicated working party – composed of experts from hospital pharmacies, academia and national authorities from 14 countries – was set up under the auspices of the Ph. Eur. Commission to prepare the content of the formulary. The first step was to prioritise the projected workload, a task that is virtually complete.

In October 2018, the EDQM launched the first texts for public consultation on a new online platform. All stakeholders were invited to provide their comments by the end of January 2019 on two general texts introducing the formulary and its general principles and on the first two pilot monographs, *Hydrochlorothiazide 0.5 mg/mL oral solution* and *Sotalol hydrochloride 20 mg/mL oral solution*.

At the end of 2018, ten monographs were on the work programme. The online formulary will be officially launched once the two pilot formulations have been adopted and will be expanded as work progresses.

EUROPEAN PAEDIATRIC FORMULARY

The CD-P-PH and the Ph. Eur. Commission continued with their programme to develop a European Paediatric Formulary. With age-appropriate licensed medicines and dosage strengths often not available for the treatment of children, extemporaneous preparations still play an important role in this field. The European Paediatric Formulary project aims to improve the availability of extemporaneous formulations of appropriate quality across Europe.

The European Paediatric Formulary will be a free, pan-European collection of formulations

for extemporaneous preparations that are currently described in national formularies and formulations that are already well established in European countries. The aim is to give pharmacists and clinicians access to formulations of appropriate quality, allowing preparation of adequate medicinal products when no licensed alternative is available on the market. The European Paediatric Formulary is complementary to efforts of EU and international legislation designed to increase the number of authorised paediatric medicines.





HEALTHCARE

Throughout 2018, the EDQM has continued to protect public health in Europe by proposing trusted and ethical safety and quality standards for the collection, preparation, storage, distribution and appropriate use of blood components for blood transfusion and for the transplantation of organs, tissues and cells. The work related to enhancing and developing standards in the field of food contact materials was also continued, along with the coordination of market studies and proficiency testing schemes in the area of quality control for cosmetics.

BLOOD TRANSFUSION

Promoting blood safety and quality in Europe and beyond

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

The European Committee on Blood Transfusion (CD-P-TS) is the Committee responsible for blood transfusion activities at the EDQM; it elaborates guidelines and recommendations and is supported by its subordinate bodies. It is composed of internationally recognised experts from Council of Europe member states, observer countries, the European Commission, WHO, the US FDA and the Council of Europe's Committee on Bioethics (DH-BIO).

Key facts and figures



The EDQM continued to run the Blood Proficiency Testing Scheme (B-PTS) and the Blood Quality Management (B-QM) Programme. These programmes support Blood Establishments (BEs) in the implementation of current EU blood legislation, the Blood Guide and the Good Practice Guidelines (GPGs). Both programmes have benefited from financial support from the European Commission since 2010.

Nucleic Amplification Technique (NAT)

B-PTS037 HBV, HCV, HIV, NAT

Serology

B-PTS038 anti-HCV
B-PTS039 anti-HIV/p24
B-PTS040 anti-Treponema
B-PTS041 HBsAg/Anti-HBc

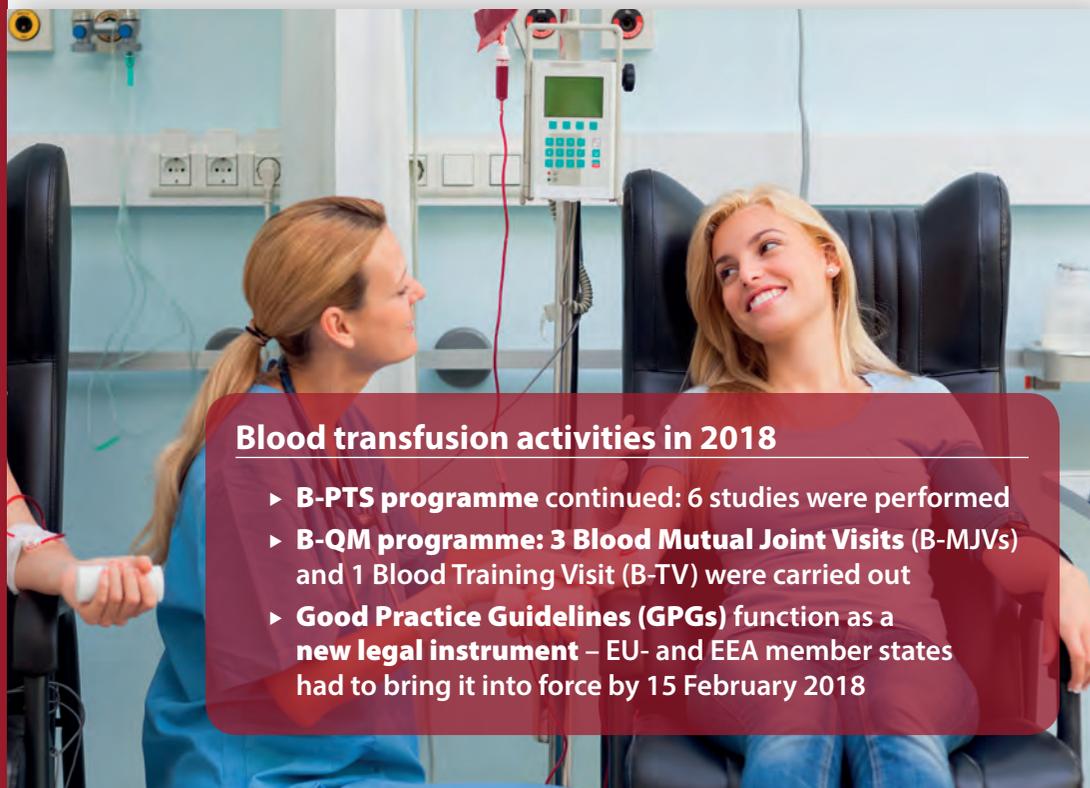
Immuno-Haematology

B-PTS042 ABO, Rhesus, Kell, extended phenotyping and irregular

► B-PTS studies conducted in 2018

Blood transfusion activities in 2018

- ▶ **B-PTS programme** continued: 6 studies were performed
- ▶ **B-QM programme:** 3 Blood Mutual Joint Visits (B-MJVs) and 1 Blood Training Visit (B-TV) were carried out
- ▶ **Good Practice Guidelines (GPGs)** function as a new legal instrument – EU- and EEA member states had to bring it into force by 15 February 2018



Blood Proficiency Testing Scheme (B-PTS)

The external assessment of the testing capability of European BEs continued in 2018 through PTS studies⁹: six studies were organised and an average of 68 laboratories participated in each study.

Blood Quality Management (B-QM) Programme

This programme¹⁰ provides tools enabling European BEs to develop, implement and improve their QMS. The programme offers 3 types of schemes which are all run by experts from European BEs:

- ▶ Blood Training Visit (B-TV): on-site visit and tailor-made training on technical and QMS topics;
- ▶ Blood Mutual Joint Visit (B-MJV): audit to assess the QMS against minimum European standards report findings and issue recommendations;
- ▶ Blood Mutual Joint Audit (B-MJA): audit to check compliance of the QMS against minimum European standards¹¹ report findings and follow-up corrective and preventative actions.

In 2018, 3 B-MJVs and 1 B-TV were carried out.

The proceedings, including recommendations from the conference “Sharing Best practices:

9. <https://go.edqm.eu/BPTS>

10. <https://go.edqm.eu/BQM>

11. *Minimum Standards: the EU blood legislation, the GPG and the Blood Guide. Other standards followed by visited BEs (e.g. ISO Standards, GMP) may also be used.*

Quality Risk Management, Change Control, Validation and Qualification in BEs” which was organised in 2017, were published in 2018.

The 1st European Training Course on Statistical Process Control (SPC) for BEs was organised in 2018 to provide BEs and inspectors with insight into this field; SPC implementation is required by the EU blood legislation and the GPGs.

General matters and policies

Good Practice Guidelines (GPGs)

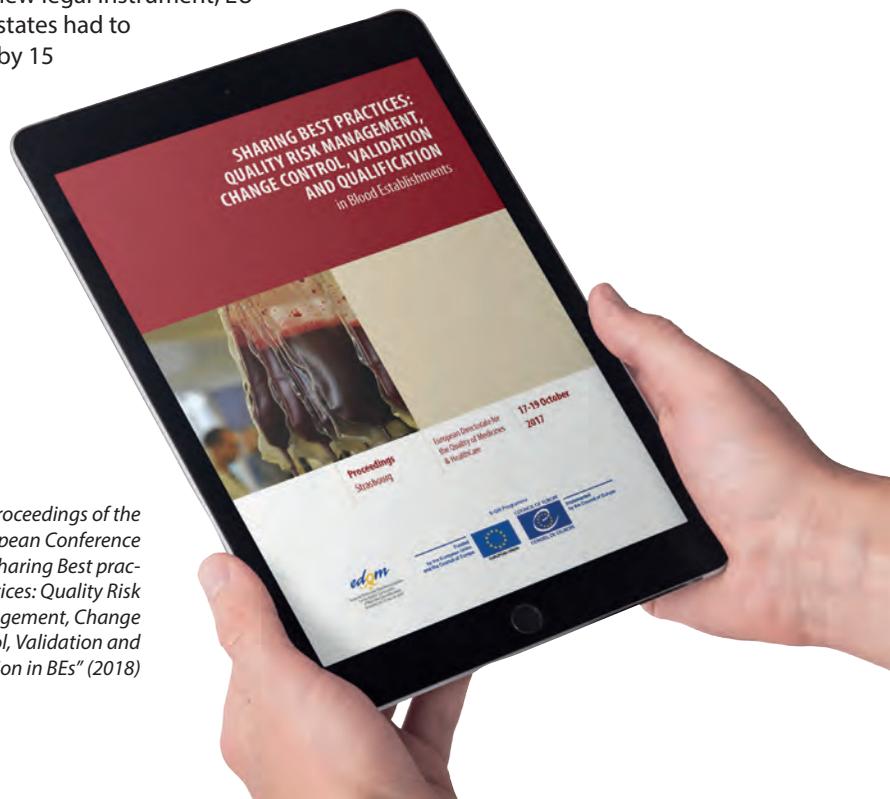
The European Commission included the GPGs issued in the 19th edition of the Blood Guide in Directive 2016/1214. As a result, the GPGs will function as a new legal instrument; EU and EEA member states had to bring it into force by 15 February 2018.

▶ *The Proceedings of the European Conference “Sharing Best practices: Quality Risk Management, Change Control, Validation and Qualification in BEs” (2018)*

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

As required by Resolution CM/Res(2013)3¹², a dedicated working group is responsible for the continuous collection of data on the incidence and prevalence of sexually transmitted infections that might hinder the safety of transfusions. Member states have implemented different deferral policies for men having sex with men and the working group is in the process of running a mapping exercise to identify the aspects lacking harmonisation.

12. Available on the EDQM website <https://go.edqm.eu/BTrec>



PUBLICATIONS, DATABASES AND WEBSITE

The GTS group, the dedicated working group entrusted with updating the “Guide for the Preparation, Use and Quality Assurance of Blood Components” (commonly referred to as the “Blood Guide”)¹³ and ensuring it keeps abreast of scientific developments and regulatory changes, actively worked on the drafting of the 20th edition which will be published in 2020.

The European database of Frozen Blood Units of Rare Blood Groups, the tool that supports blood establishments in their searches for blood with rare phenotypes, has been fully operational since January 2016. To date, six BEs have voluntarily made their lists of frozen units of rare blood groups available to patients in need.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Cooperation with the European Commission

2018 was a year of intense and fruitful collaboration with the European Commission. In particular, this included the analysis of the EU Serious Adverse Reactions and Events (SARE) related to blood components and the continued contribution of the EDQM to the public consultation on the evaluation of the EU blood legislation.

2018 was marked by the signature of a new grant agreement with the European Commission, under which a number of ongoing programmes, as well as new projects, will be conducted.

The EDQM continued to participate as an observer at meetings of the EU competent authorities for blood, which are organised by the European Commission.

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

In the context of the revision of the “PIC/S GMP Guide for Blood Establishments”, the EDQM was invited to join the drafting group responsible for revising the document. Most of the text of the GPGs will be included in the revised PIC/S document for the sake of international harmonisation.

International Society of Blood Transfusion (ISBT)

The EDQM has observer status on the ISBT Board of Directors and is a member of various dedicated ISBT working groups: the Standing Committee of Ethics and the Quality Management Working Party. The EDQM also participated in the annual ISBT congress held in Toronto (Canada) in June 2018.

13. The EDQM publications are available here: <https://register.edqm.eu/freepub>

ORGAN TRANSPLANTATION AND HUMAN APPLICATION OF TISSUES AND CELLS

Promoting quality, safety and ethical standards

The European Committee on Organ Transplantation (CD-P-TO) is the Steering Committee responsible for transplantation activities at the EDQM. Its mandate includes elaborating guidelines and recommendations aimed at improving access to transplantation and strict safety, quality and ethical standards, the collection of international data and monitoring of practices in Europe, and the fight against trafficking. The CD-P-TO is composed of internationally recognised

experts from Council of Europe member states, observer countries, the European Commission, WHO, relevant professional associations and the Council of Europe Committee on Bioethics (DH-BIO).

Key Facts and Figures

Transplantation is a well-established and life-saving therapy. However, supply is unable to keep pace with the demand for organs, and shortages may lead patients to seek their transplant abroad. Patients who have received an organ transplant abroad typically



► *Proceedings of the 2nd Workshop for NFP on Transplant-Related Crimes (2018)*

return to their home country to receive post-transplantation care after the transplantation procedure. The international exchange of information about these patients would facilitate better understanding and analysis of the phenomenon of travel for transplantation, the long-term outcomes and potential risks to both individuals and public health and identification of possible hotspots of illicit practices. For this reason, the EDQM hosts and maintains the “International Database on Travel for Transplantation”, and National Focal Points (NFP) in each country are requested to provide information about all patients who received a kidney transplant abroad. In 2018, the second data collection exercise took place, gathering data from 2016. In addition, the Proceedings of the 2nd Workshop for NFP on Transplant-Related Crimes, which was held in Strasbourg in November in 2017, were published.



Organ Transplantation and Tissues and Cells for Human Applications 2018

- publication of the 7th edition of the “**Guide to the Quality and Safety of Organs for Transplantation**”
- the “**Newsletter Transplant 2018**”
- and the booklet “**Donation of oocytes, a guide for women to support informed decisions**”.



► *Donation of oocytes, a guide for women to support informed decisions* (2018)

The CD-P-TO published several position papers to support member states and healthcare professionals in policy decisions and clinical practices. They addressed issues such as the Global Kidney Exchange concept, kidney exchange programmes in Europe, illicit and unethical activities with human tissues and cells¹⁴ and vascularised composite allotransplantation¹⁵.

A scientific article on the evolution of deceased organ donation activity

14. Available on the EDQM website <https://go.edqm.eu/transplantreports>
15. Thuong M, Petruzzo P, Landin L, *et al.* Vascularized composite allotransplantation - a Council of Europe position paper. *Transpl Int.* 2019 Mar;32(3):233-240. Epub 2018 Nov 26.

was published in the scientific journal *Transplantation* on behalf of the CD-P-TO¹⁶.

A scientific article on a Council of Europe-steered international cooperative project in the Black Sea region was published in the scientific journal *Transplantation Proceedings* on behalf of the CD-P-TO¹⁷.

16. Weiss J, Elmer A, Mahillo, B. *et al.* Evolution of Deceased Organ Donation Activity Versus Efficiency Over a 15-year Period: An International Comparison. *Transplantation.* 2018 Oct;102(10):1768-1778
17. Available on the EDQM website <https://go.edqm.eu/TOBSA> Arredondo E, López-Fraga M, Chatzixiros E, *et al.* Council of Europe Black Sea Area Project: International Cooperation for the Development of Activities Related to Donation and Transplantation of Organs in the Region. *Transplant Proc.* 2018 Mar;50(2):374-381.

The 7th edition of the “Guide to the Quality and Safety of Organs for Transplantation” was published¹⁸. It contains updated information to provide professionals involved in organ donation and transplantation with a useful overview of the most recent advancements in the field.

Monitoring of practices in the member states is imperative for the sake of transparency and benchmarking. For this reason, the CD-P-TO has produced the Newsletter *Transplant* on a yearly basis since 1996, and it has evolved into a unique source of official information. The work is coordinated by the Spanish National Transplant Organisation (ONT). This newsletter summarises comprehensive information on donation and transplantation activities, management of waiting lists, organ donation refusals and authorised centres for transplantation activities, from

18. The EDQM publications are available here: <https://register.edqm.eu/freepub>



► *Guide to the Quality and Safety of Organs for Transplantation 7th edition* (2018)

almost 70 countries worldwide. In the 2018 edition, for the first time, some of the data for both organ donors and recipients has been collected disaggregated by gender. This is in line with the commitment of the CD-P-TO to take due account of a gender perspective in the performance of its tasks and to strive to achieve gender mainstreaming in all its policy areas.

The CD-P-TO, in collaboration with the European Society of Human Reproduction and Embryology (ESHRE), prepared the booklet "Donation of oocytes, a guide for women to support informed decisions". This guide supports potential oocyte donors, who may be facing questions of whether oocyte donation is safe, about future implications and, in the end, whether it is the right choice for them.¹⁹

Every year the EDQM supports the organisation of the European Organ Donation Day (EODD). The main objectives are to raise public awareness and encourage public debate, to establish trust among the public towards responsible, ethical, non-commercial and professional organ donation and transplantation, and to engage policy-makers and the medical community. EODD is also an opportunity to honour all organ donors and their families and to thank transplantation professionals. The 2018 EODD was organised in Chisinau (Republic of Moldova) together with the Transplant Agency of Moldova (see "Public Awareness Campaigns" page 49).

19. Available at <https://go.edqm.eu/oocytesbooklet>

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Cooperation with the European Commission

Under the framework of its standing cooperation with the European Commission, the EDQM performed the international annual vigilance exercise on Serious Adverse Reactions and Events (SARE) in the EU in the fields of tissues and cells.

EDQM representatives attended EU Competent Authorities' meetings in the fields of organs and of tissues and cells, as well as key meetings of relevant EU-funded projects, such as ARTHIQS, EuroGTP-II, VISTART and GAPP, to enhance the cooperation between the two institutions and avoid duplication of efforts.

Cooperation with professional associations

Key professional associations in the field of organ, tissue and cell transplantation participate in the work of the EDQM, most notably through the elaboration and dissemination of technical guidance and information for the public.

EDQM representatives were involved in the elaboration of the 2018 Edition of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.



COSMETICS

The European Committee on Cosmetics and Consumer Health (CD-P-COS) is tasked with responding to emerging risks for human health arising from the use of cosmetics. It also deals with the safety of tattoo inks and permanent make-up and promotes the principles laid down in Council of Europe Resolution ResAP (2008)1. By the end of 2018, 32 member states of the Council of Europe had appointed national representatives to the CD-P-COS. Activities on the work programme focus on fostering collaboration between member states and observers.

The European Network of Official Cosmetics Control Laboratories (OCCLs) contributes to consumer health protection by strengthening market surveillance and enforcement of European regulations by the competent authorities. Participation is open to members and observers of the Ph. Eur. Convention. The European OCCL Network was set up on a voluntary basis in 2010. Currently, more than 40 OCCLs participate in network activities, including laboratories from 19 member states of the EU, facilitating better use of resources and enhanced quality management in accordance with international standards. The long-standing experience of the EDQM with the OMCL Network is an asset for the coordination of the OCCL Network.

Key facts

OCCL Network

Most sunscreens on the market indicate the level of protection against harmful effects of UV radiation. This so-called sun protection



Cosmetics in 2018

- ▶ sunscreen testing: efforts were pursued to **implement a common testing strategy** to replace protocols involving humans
- ▶ national data were collected on **tooth-whitening products** and a report on their compliance was shared with national authorities
- ▶ **fragrances in shower gels or body lotion** that can cause allergic reactions were the focus of a **PTS study**

factor (SPF) is typically set based on data from human studies. In 2018, efforts were pursued to implement a common testing strategy for control laboratories using methods that could replace protocols involving humans.

Protection of healthy volunteers in cosmetics testing

The CD-P-COS supported the launch of a survey amongst member states to collect information on the protection of healthy volunteers in studies related to the use, quality and effects of cosmetics. The subject will be further pursued in 2019 to explore possibilities for a common position for member states.

Quality check for cosmetics: Market Surveillance Studies

In response to the discovery of some alarming components in cosmetic products, the EDQM has been collecting national data on the quality of shampoos for children, creams and make-up, lotions and other products for several years. In 2018, national data was collected on tooth-whitening products and a report on their compliance with EU Regulation No 1223/2009 was shared with national authorities.

Proficiency Testing Scheme (PTS) studies

Proficiency testing is an essential part of the QMS in testing laboratories. Analytical studies are carried out on identical samples in different laboratories to verify each laboratory's ability to quantify, for example, the amount of prohibited substance, and to ensure that test results are comparable across Europe.

Even small amounts of certain fragrances in shower gels or body lotion can cause allergic reactions. These substances were the focus of a PTS study which was concluded in 2018. The participating laboratories mainly employed gas chromatography-mass spectroscopy (GC-MS).

Tattoos and permanent make-up

In order to implement the recommendations of Council of Europe Resolution ResAP(2008)1, the EDQM compiled safety and documentation requirements for tattoos and permanent make-up in a report which was finalised and published in 2017. In 2018, the work on the safety of tattoos and permanent make-up was made available to the European Chemicals Agency (ECHA) for the preparation of related restriction proposals.

FOOD CONTACT MATERIALS AND ARTICLES

The European Committee for Food Contact Materials and Articles (CD-P-MCA) focuses on the safety of packaging, containers, utensils and other materials and articles intended to come into contact with food; it defines harmonised measures that supplement EU and national legislation.

The work programme is aimed at harmonising quality and safety requirements across Europe, as well as the development and updating of testing methods.

The published Technical Guides are used as reference documents by manufacturers, safety evaluators and control laboratories²⁰.

Key facts

By the end of 2018, 27 member states of the Council of Europe had appointed national representatives to the CD-P-MCA. Two subordinate working groups support the work: one focusing on food contact materials made from paper and board and the other on printed food contact materials.

Throughout 2018, the national experts continued to review resolutions and technical documents elaborated in the past; the Agency for Health and Food Safety (AGES, Austria) and the National Institute for Public Health (NIPH, Czech Republic) both hosted expert meetings aimed at updating the provisions for paper and board.

Food contact materials made from metals and alloys have been addressed in a practical guide for manufacturers and regulators, which was first published in 2013. Experts from competent authorities, official and private control laboratories and industry have proposed amendments for the second edition of the guide (under preparation).

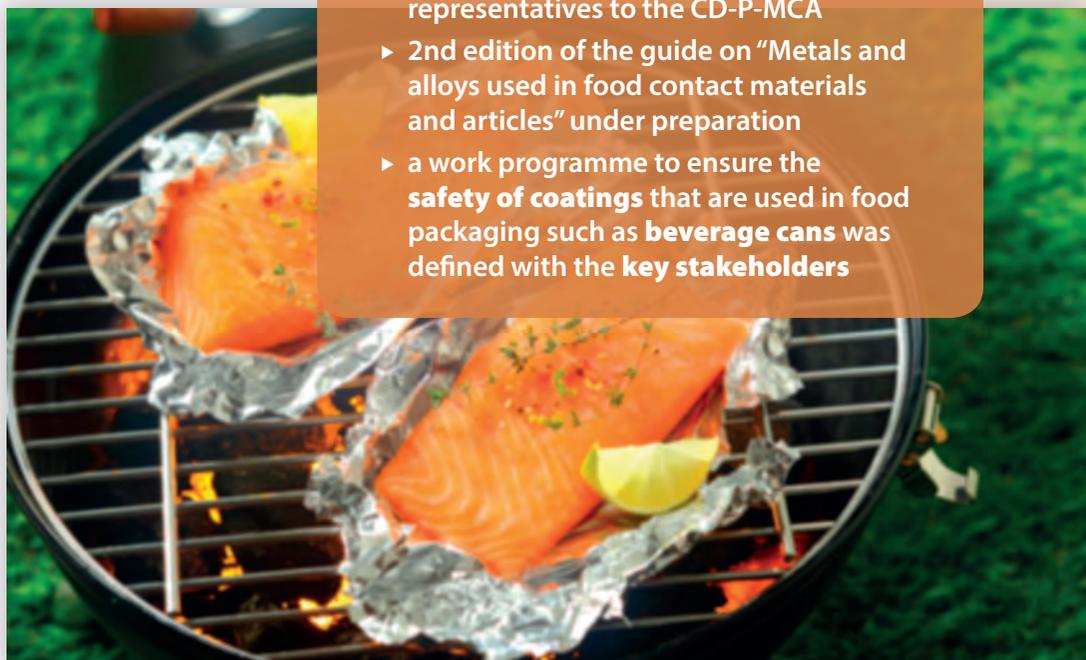
The EDQM, national authorities and the Scientific Network on Food Contact Materials coordinated by the European Food Safety Authority (EFSA) joined forces and defined a work programme to ensure the safety of coatings that are used in food packaging such as beverage cans. This work is expected to be finalised in 2019.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Representatives of the European Commission, its Joint Research Centre (JRC) and EFSA attend the meetings of Steering Committees and subordinate working groups. The EDQM exchanges information on market surveillance with the working groups of the Platform of European Market Surveillance Authorities for Cosmetics of the European Union (EU PEMSAC), notably in response to large numbers of products that do not comply with the European regulations on cosmetics.

Food Contact Materials in 2018

- ▶ 27 member states had appointed national representatives to the CD-P-MCA
- ▶ 2nd edition of the guide on “Metals and alloys used in food contact materials and articles” under preparation
- ▶ a work programme to ensure the **safety of coatings** that are used in food packaging such as **beverage cans** was defined with the **key stakeholders**



20. The EDQM publications are available here: <https://register.edqm.eu/freepub>



QUALITY MANAGEMENT SYSTEM

Investments in the EDQM's QMS continued to be a priority in 2018 with a specific focus on Ph. Eur. reference standards. As a result, the EDQM successfully passed audits by official certification and accreditation bodies.

The scope of the EDQM's ISO 9001 certification has been extended to the establishment, manufacturing, storage, distribution and monitoring of Ph. Eur. reference standards.

The scope of its ISO/IEC 17025 accreditation was also extended to nuclear magnetic resonance (NMR) spectroscopy and quantitative nuclear magnetic resonance (qNMR) spectroscopy in 2018. The new accreditation for NMR spectroscopy, awarded by the Belgian Accreditation Body (BELAC), means that the EDQM laboratory is now in a position to generate ever more accurate and technically valid results for its Ph. Eur. reference standards.

The EDQM is committed not only to maintaining, but also to continuously improving its standards for quality throughout all its activities; its customers and stakeholders can rest assured that the goods and services provided are of consistent quality.

2018: A YEAR RICH IN EVENTS AND MEETINGS

SECONDARY SITE

On 11 June, Ms Gabriella Battaini-Dragoni, Deputy Secretary General of the Council of Europe, and Ambassador Jean-Baptiste Mattei, Permanent Representative of France to the Council of Europe, in the presence of a number of key local dignitaries and Permanent Representatives of the Council of Europe, laid the first stone of the EDQM's secondary site. The new site, which is located in Metz (France), is intended to store contingency stocks of the EDQM's portfolio of over 3 000 pharmaceutical reference standards; it will be key for ensuring the

sustainability and continuity of supply, particularly in case of problems affecting the main site in Strasbourg.

The new building will have three main areas: one dedicated to logistics – storage, preparation and delivery of reference standards, another for informatics and pharmaceutical support, and a technical area on the upper level. It will be operational in the first half of 2020.

SYMPOSIA AND WORKSHOPS – FOCUSED TOPIC MEETINGS

Symposium IPC-EDQM on “Drug Standards and Regulatory Updates” (26-27 April, Mumbai)

In April, the EDQM joined forces with the Indian Pharmacopoeia Commission (IPC) to organise a symposium to discuss the quality control of medicines in the context of the pharmaceutical legislation and regulatory requirements that exist in Europe and India.

The two-day programme covered the roles of the EDQM/Ph. Eur. and the IPC in the quality control of medicines, including harmonisation activities, practical advice on using and interpreting the Ph. Eur. general chapters and monographs, and an overview of the policies and processes used to establish pharmaceutical reference standards. There were also sessions on the certification procedure and its inspection programme.

■ The EDQM was grateful for the support and commitment of the IPC and the Indian authorities to sharing scientific know-how and expertise with the aim of protecting public health worldwide.

► Ms Gabriella Battaini-Dragoni, Deputy Secretary General of the Council of Europe at the Ceremony to lay the first stone of the EDQM's secondary site in Metz (France)





► *Speakers' panel at the IPC-EDQM symposium in Mumbai (India)*

Ph. Eur. - ChP Joint Workshop on “What’s new in the field of excipients in China?” (18 September, Strasbourg)

In September, the EDQM jointly organised a workshop with the Pharmacopoeia of the People’s Republic of China (ChP) on the new Chinese regulations on excipients and their implications for the pharmaceutical sector in Europe. The programme provided an insight into how standards for pharmaceutical excipients are established, assessed and approved by the ChP. Technical and risk management requirements that are applicable to excipients, as well as quality control methods, were also covered.

The workshop was transmitted live over the internet and an online Q&A tool was deployed to gather questions, allowing offsite participants the opportunity to interact

directly with the speakers and have their particular queries answered.

TRAINING SESSIONS

In May, the EDQM organised a Ph. Eur. training session in Zagreb (Croatia). This training, which was organised under Croatia’s Chairmanship of the Council of Europe, focused on European regulations for medicines, reference standards and the certification procedure and its inspection programme. The event was particularly significant as it marked Croatia’s first time chairing the Committee of Ministers and its 20-year long collaboration with the EDQM/ Ph. Eur.

The EDQM was grateful to the Croatian Ministry of Health and its Agency for

Medicinal Products and Medical Devices (HALMED) as well as the Croatian Pharmacopoeia for their support and active involvement. The event was very successful with nearly 140 participants. All the presentations are available to download from the EDQM website²¹.

The EDQM also organised two training sessions on CombiStats™, the computer software developed by the EDQM for the statistical evaluation of biological dilution assays in accordance with chapter 5.3 of the Ph. Eur. Both sessions included a two-hour practical workshop that allowed the participants to put into practice some of the principles covered in the course.

WEBINARS

When it comes to expanding the EDQM’s impact and reach, and to communicating with its stakeholders, webinars have proved extremely useful. With webinars, the EDQM’s voice and its public health goals are conveyed globally. The EDQM organised a number of free webinars in 2018, all of them focusing on various aspects of the Certification Procedure (CEP).

21. Training resources available here : www.go.edqm.eu/pheurtraining

The first focused on the “Top 10 deficiencies found in CEP new applications” and was designed to help applicants understand and become familiar with CEP application requirements and improve the quality of their dossiers, in order to facilitate granting of their CEPs and avoid delays.

Following the publication of the revised EDQM guideline on requirements for revision/renewal of CEPs, a second webinar was organised in September to present the content of the guideline and outline the changes in the acceptability and classification of some revisions. It also covered the revision process and what supporting documentation should be provided in the submitted file.

In November, a webinar was organised on “How to read a CEP”; it provided participants with a clearer understanding of the content of a CEP. Topics covered included the aim and scope of a CEP, and how to interpret information included in each type of CEP.

Altogether, over 2 300 participants connected to these webinars, which were always followed by a live Q&A session, allowing participants to raise specific issues on subjects covered in the presentations. All webinar recordings were posted on the EDQM website and made available for later access.²²

22. Available on the EDQM website <https://pheur-training.go.edqm.eu/pheurtraining> and <https://go.edqm.eu/CEPtraining>



► EDQM booth at CPhI India in New Delhi (India)

INTERNATIONAL FAIRS & CONGRESS – EXPANDING GLOBAL PRESENCE

The EDQM participated in three pharmaceutical fairs in 2018: CPhI China (Shanghai), CPhI Worldwide (Frankfurt) and CPhI India (Mumbai). These trade fairs unite every sector of the chemical and pharmaceutical market and offer the EDQM a very cost-effective way of meeting new and existing customers and staying up to date with the latest industry trends. In addition, the EDQM organised personalised one-to-one sessions with CEP staff during each of the fairs, allowing CEP applicants or users of CEPs to get advice and clarification on any aspect of the CEP procedure.

The 18th “International Conference of Drug Regulatory Authorities” (ICDRA), aimed at promoting the exchange of information between drug regulators and developing collaborative approaches to issues of common concern, was held in Dublin, Ireland, in September 2018. The conference, which is held every two years, was jointly organised by the Irish Health Products Regulatory Authority (HPRA) and WHO and co-sponsored by the EDQM. The EDQM gave presentations on issues relating to active pharmaceutical ingredients, e.g. risk-based inspections and the potential for work-sharing, the regulation of biosimilars and advanced therapies.

PUBLIC AWARENESS CAMPAIGNS

Organ, Tissue and Cell Transplantation

The 19th European Day for Organ Donation and Transplantation (EODD) was organised in co-operation with the National Transplant Agency of the Republic of Moldova on 13 October in Chisinau (Republic of Moldova). The event, which has been organised by the EDQM/Council of Europe in a different country every year since 1996, aims to raise public awareness of the need for organs and to promote the principle of voluntary and non-remunerated donation.

Organ, tissue and cell transplantation is one of the great medical success stories of modern times; in many cases, it is the only life-saving treatment for end-stage organ failure. Every year, EODD provides an opportunity to inform the public about donation and transplantation of organs, tissues and cells.

Blood Transfusion

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

- ▶ *Participants at the 19th European Day for Organ Donation and Transplantation celebrations (EODD) Chisinau (Republic of Moldova)*



LIST OF COMMITTEES COORDINATED BY THE EDQM



THE EUROPEAN PHARMACOPOEIA COMMISSION

The Ph. Eur. Commission was set up in 1964 in accordance with the Convention on the Elaboration of a European Pharmacopoeia. The Commission has 39 members, all signatory parties to the Convention (38 member states and the EU). The participation of 30 observers from all over the world confirms the importance of the work of the Ph. Eur. Commission at international level. The Commission sets out the work programme and adopts the quality standards for medicines and their components to be applied in the territories of its member states. A total of 61 expert groups and working parties established by the Commission carry out the Ph. Eur. work programme. The texts are regularly revised in order to keep pace with the latest technical and scientific advances in the development, production and quality control of medicines. The Ph. Eur. is essential for the protection of public health. It is intended for use by healthcare professionals working with medicines, and has become the gold standard reference in the sector.

THE BIOLOGICAL STANDARDISATION PROGRAMME (BSP) STEERING COMMITTEE

The BSP focuses 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 Ph. Eur. Groups of Experts 6 (Biological and biotechnological substances), 6B (Human plasma and plasma products), 15 (Human vaccines and sera) and 15V (Veterinary vaccines and sera), as well as co-opted experts and delegates from the European Commission, EMA, BWP, IWP and WHO and the EDQM Director.

GEON ADVISORY GROUPS

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

- ▶ general activities involving all of the member states of the Ph. Eur. Convention and the observer states. These activities cover work in the area of QMS, such as audits and proficiency testing studies, as well as MSSs, and contribute towards combating falsified and illegal medicines. General activities are prepared and followed up by the General OMCL Advisory Group;
- ▶ activities restricted to the EU and the European Economic Area (EEA) concerning products approved via the centralised procedure (CAP), the mutual recognition or decentralised procedures (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 intervals between the annual meetings of each specific network.

CERTIFICATION OF SUITABILITY TO PH. EUR. MONOGRAPHS STEERING COMMITTEE

A Network of about 100 assessors and 30 national inspectors participates in the work required for the evaluation of API quality dossiers and the inspection of manufacturing sites. The activities associated with the procedure for certification of suitability to Ph. Eur. monographs are guided by a Steering Committee and three Technical Advisory Boards (TABs). This Steering Committee is composed of representatives of European licensing authorities and inspectorates, the European Commission, the EMA and a number of quality-relevant working parties of the EMA, the chair of the Ph. Eur. Commission and the EDQM Director. It takes decisions on general policy, examines and comments on matters brought to its attention by the Technical Advisory Boards, adopts guidelines and the inspection programme and co-ordinates questions among 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

The CD-P-TS addresses ethical, legal and organisational issues related to blood transfusion in order to ensure the safety and quality of transfusions and the protection of donors and recipients, and to promote the optimal use of blood and minimal wastage. It is supported by subordinate bodies, including the ad hoc Working Group on the “Guide to the Preparation, Use and Quality Assurance of Blood Components”.

EUROPEAN COMMITTEE ON ORGAN TRANSPLANTATION

The CD-P-TO 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 is supported by subordinate bodies, including 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

The CD-P-PH is in charge of activities in the field of the classification of medicines as regards their supply, pharmaceutical practices and pharmaceutical care, and combatting falsified medical products and similar crimes. It is supported by three subordinate committees: the CD-P-PH/PHO, the CD-P-PH/PC and the CD-P-PH/CMED.

EUROPEAN COMMITTEE ON COSMETICS AND CONSUMER HEALTH

The CD-P-COS was formed in early 2018 to respond to emerging risks for human health arising from the use of cosmetics. It replaces part of the former Committee on Consumer Health Protection (CD-P-SC), which was dissolved by decision of the Committee of Ministers at the end of 2017, and is composed of representatives from national ministries with public health responsibilities. Activities on the work programme focus on collaboration between member states and observers from third countries.

EUROPEAN COMMITTEE FOR FOOD CONTACT MATERIALS AND ARTICLES

The CD-P-MCA was formed in early 2018. It replaces part of the former Committee on Consumer Health Protection (CD-P-SC), which was dissolved by decision of the Committee of Ministers at the end of 2017, and is composed of representatives from national ministries with public health responsibilities. Activities on the work programme focus on the safety of food contact materials and articles and defines harmonised measures that supplement EU and national legislation. It is supported by two subordinate bodies: the working group on food contact materials made from paper and board and the working group on printed food contact materials. The published Technical Guides are used as reference documents by manufacturers and other business operators, safety evaluators and control laboratories.

GLOSSARY

3Rs	Refine, Reduce, Replace (animal testing)	CD-P-PH/PHO	Committee of Experts on the Classification of Medicines as Regards their Supply
AAV	Adeno-Associated Virus	CD-P-SC	European Committee on Consumer Health Protection
ADD	Automated Dose Dispensing	CD-P-TS	European Committee on Blood Transfusion
AGES	Austrian Agency for Health and Food	CD-P-TO	European Committee on Organ Transplantation
API	Active Pharmaceutical Ingredient	CEP	Certificate of Suitability to the Monographs of the European Pharmacopoeia
B-MJA	Blood Mutual Joint Audit	CHMP	Committee for Medicinal Products for Human Use (EMA)
B-MJV	Blood Mutual Joint Visit	CHO	Chinese hamster ovary
B-PTS	Blood Proficiency Testing Scheme	ChP	Chinese Pharmacopoeia
B-QM	Blood Quality Management	CLP	Classification, Labelling and Packaging
B-TV	Blood Training Visits	CM	Committee of Ministers
BE	Blood Establishment	CMDh	Coordination Group for Mutual Recognition and Decentralised procedures – Human
BRP	Biological Reference Preparation	CRS	Chemical Reference Substance
BSP	Biological Standardisation Programme	DCP	Decentralised Procedure
BVS	Batch Validity Statement	DH-BIO	Council of Europe's Committee on Bioethics
BWP	Biologics Working Party	DNA	Deoxyribonucleic acid
CAP	Centrally Authorised Product	EAHP	European Association of Hospital Pharmacists
CAT	Committee for Advanced Therapies	ECBS	WHO Expert Committee on Biological Standardization
CD-P-COS	European Committee on Cosmetics and Consumer Health	ECHA	Chemicals Agency of the European Union
CD-P-PH	European Committee on Pharmaceuticals and Pharmaceutical Care	ECSP	WHO Expert Committee on Specifications for Pharmaceutical Preparations
CD-P-PH/CMED	Committee of Experts on Minimising the Public Health Risks Posed by Falsification of Medical Products and Similar Crimes	eCTD	electronic Common Technical Document
CD-P-PH/PC	Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care	EDQM	European Directorate for the Quality of Medicines & HealthCare
		EEA	European Economic Area
		EFSA	European Food Safety Authority
		EMA	European Medicines Agency

EMVO	European Medicines Verification Organisation	IVMP	Immunological Veterinary Medicinal Products
EODD	European Day for Organ Donation and Transplantation	IWP	Immunologicals Working Party
ESHRE	European Society for Human Reproduction and Embryology	JP	Japanese Pharmacopoeia
EU	European Union	JRC	Joint Research Centre of the European Commission
GC-MS	Gas chromatography-mass spectroscopy	MJA	Mutual Joint Audit
GDP	Good distribution practices	MJV	Mutual Joint Visit
GEON	General European Network of Official Medicines Control Laboratories (OMCLs)	MRP	Mutual Recognition Procedure
GMP	Good Manufacturing Practice	MSS	Market Surveillance Studies
GPG	Good Practice Guidelines	MSSIP	Market Surveillance Studies on Suspected Illegal Products
GPhP	Good Pharmacopoeial Practices	NAB	National Accreditation Body
GTP	Gene Therapy Products	NAT	Nucleic acid Amplification Technique
HALMED	Agency for Medicinal Products and Medical Devices	NFP	National Focal Point
HIST	Histamine sensitisation test	NMR	Nuclear Magnetic Resonance
HMA-WGEO	EU Heads of Medicines Agencies' Working Group of Enforcement Officers	NPA	National Pharmacopoeia Authorities
HMPC	Herbal Medicinal Products Committee	OCABR	Official Control Authority Batch Release
HRS	Herbal Reference Standards	OCCL	Official Cosmetics Control Laboratory
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use	OMCL	Official Medicines Control Laboratory
ICRS	International Chemical Reference Substance	ONT	Spanish National Transplant Organisation
IMWP	International Meeting of World Pharmacopoeias	P4	Procedure 4
INN	International Non-proprietary Names	PDG	Pharmacopoeial Discussion Group
IPC	Indian Pharmacopoeia Commission	PEMSAC	Platform of European Market Surveillance Authorities for Cosmetics
ISA	International Standard for Antibiotics	Ph. Eur.	European Pharmacopoeia
ISBT	International Society of Blood Transfusion	PIC/S	Pharmaceutical Inspection Co-operation Scheme
ISO/IEC	International Organization for Standardization/ International Electrotechnical Commission	PPT	Physical Particles Titre
		PTS	Proficiency Testing Scheme
		QM	Quality Management

QMS	Quality Management System
QWP	Quality Working Party (EMA)
REACH	Regulation (EC) No 1907/2006
RS	Reference Standard
SARE	Serious Adverse Reactions and Events
SPF	Sun Protection Factor
SPOC	Single Point of Contact
SUKL	State Institute for Drug Control of the Czech Republic
TAB	Technical Advisory Boards
TSE	Transmissible spongiform encephalopathy
TV	Training Visits
US FDA	United States Food and Drug Administration
USP	United States Pharmacopeia
VBRN	Veterinary Batch Release Network
WGEO HMA	Working Group of Enforcement Officers of the Health and Medicines Agencies of the European Union
WHO	World Health Organization This publication presents the work

This publication presents the work carried out in 2018 by the European Directorate for the Quality of Medicines & HealthCare, Council of Europe, highlighting its particular achievements.

www.coe.int

The Council of Europe is the continent's leading human rights organisation. It comprises 47 member states, including all 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.

