HIGHLIGHTS OF 2020

EDQM ANNUAL REPORT

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

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

Council of Europe, EDQM

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MESSAGE FROM SUSANNE KEITEL, DIRECTOR

The year 2020 will unavoidably be associated with the tremendous challenges that the worldwide COVID-19 pandemic imposed in all areas of our lives. Operating on the front lines of public health protection, the EDQM immediately drew up contingency plans for all its branches of activity to continue fulfilling its mission despite the necessary restrictions on travel, shipping and contact between individuals. Enabling the EDQM's dedicated staff to carry out their daily tasks – whether from home or on-site when necessary – was the first step. Communication structures were set up, indispensable procedures and processes were adapted and work organisation as a whole was reformed to weather what was to become a prolonged ordeal.

The EDQM ensured the continuity of its **core business activities** through a series of measures designed to enable the European Pharmacopoeia (Ph. Eur.) Commission to respect its work programme; to safeguard the supply of reference standards; to ensure the processing of applications for new, revised or renewed certificates of suitability (CEPs); and to guarantee the quality control of medicines, including the Official Control Authority Batch Release (OCABR) procedure, through the Official Medicines Control Laboratories (OMCL) Network.

In the field of **substances of human origin** (SoHO), the EDQM, through its European steering committees, facilitated information exchanges and fostered co-operation between member states and health authorities to minimise the impact of the pandemic. The importance of ensuring a safe and sufficient supply of tissues from deceased donors and of supporting donation and transplantation programmes quickly became evident, as did the need to foster safe practice within tissue establishments and to minimise the risks related to SARS-CoV-2 for both transplanted patients and staff.

To better **co-ordinate international efforts,** the EDQM strengthened contacts with stakeholders and partners, resulting in frequent meetings online with national pharmacopoeia authorities (NPAs) of Ph. Eur. member states, the pharmacopoeias of the world and industry associations.

Moreover, the EDQM undertook **numerous initiatives** to support competent authorities, manufacturers and developers of medicines (including vaccines) and health professionals, and to contribute to the wider global effort to combat the coronavirus disease by openly sharing knowledge and offering free access to relevant standards, guidance and training.

While many candidate vaccines were still in development, the EDQM laid the groundwork for a smooth OCABR process by publishing three OCABR guidelines outlining the crucial tests to be performed by OMCLs in the European Union (EU) OCABR Network as part of the **independent control of COVID-19 vaccine batches**. The EDQM also published guidance on the control of viral vectored vaccines to support vaccine developers, and granted free access to a Ph. Eur. "vaccines package" detailing quality standards for vaccines.

After the initial shock of lockdown measures, the EDQM swiftly adapted to the new conditions, adopted measures to conform to health restrictions and carried on. Undaunted, the EDQM continued to organise **events and meetings online** and, by the end of the year, had held 43 webinars, attracting over 15 000 participants from more than 100 countries. The "Meet the World Pharmacopoeias" Symposium also went ahead, bringing together over 200 participants from more than 40 countries.

The **Ph. Eur. Commission** and its groups of experts and working parties, with the support of NPAs and the EDQM, demonstrated their commitment to public health protection by adapting their traditional working methods to the new situation. Thanks to their efforts, 29 new monographs and six new chapters were adopted, and 250 texts were revised to incorporate regulatory changes and scientific progress, a key aspect of ensuring constant alignment with state-of-the-art technologies and regulatory developments.

The Ph. Eur. continued to grow in 2020: **Albania** officially became a Ph. Eur. member state in February, and **Mexico** was granted observer status in May. This confirms once again the fundamental importance of the Ph. Eur. not only on a continental scale, but around the globe.

A **fast-track procedure** was offered for the assessment of new CEPs or revisions covering substances of specific importance in the pandemic situation.

Nitrosamine contamination of active substances and medicines continued to be a thorny issue and the EDQM, in collaboration with other health regulatory authorities, pursued its plan to limit the presence of these impurities as much as possible. Two years after the issue was first identified, the overall strategy – involving the reassessment and revision of CEPs, the revision of relevant Ph. Eur. monographs to add limits for *N*-nitrosamine impurities, the establishment of reference standards to enable effective controls, and the creation of programmes for co-ordinated sampling and testing by OMCLs – is coming to fruition. At its 168th session in November 2020, the Ph. Eur. Commission adopted a new general chapter on the analysis of *N*-nitrosamine impurities in active substances. The next step is the rapid implementation of revised "sartan" monographs to align them with the final decision taken by European regulators to control nitrosamines in the medicinal product rather than in the active pharmaceutical ingredient.

The publication of the 20th edition of the *Guide to the preparation, use and quality assurance of blood components* **(Blood Guide)** in the spring of 2020 marked an important milestone in the field of blood transfusion. Later in the year, an important virtual conference, entitled "Keeping up with Reality and Quality: A Challenge for European Blood Establishments", was held to celebrate 10 years of collaboration in the field of blood between the EDQM and the European Commission, and to take stock of developments in the governance framework for SoHO and of the challenges that European blood establishments face in their daily practice.

Resolution CM/Res(2020)3 on the **implementation of pharmaceutical care** for the benefit of patients and health services was adopted by the Council of Europe Committee of Ministers, as part of the effort to improve medication use and the quality of care across Europe by defining a framework for the promotion and implementation of pharmaceutical care in health systems at national level.

Consumer protection remained an important area of activity for the EDQM in 2020, including ensuring the safety and quality of **cosmetics** in Europe. A virtual meeting in June marked the 10th anniversary of the Network of Official Cosmetics Control Laboratories (OCCLs) – which supports laboratories worldwide in developing market surveillance and enhancing product testing capacity – and was an opportunity to take stock of the many achievements over this time.

The Council of Europe Committee of Ministers also adopted Resolution CM/Res(2020)9 on the **safety and quality of materials and articles for contact with food**. This instrument – which is expected to improve the protection of consumers from contaminants potentially released by material in contact with food – refers specifically in its annexes to technical guides published under the aegis of the EDQM.

The year 2020 will long be remembered as the time when the COVID-19 pandemic almost brought the world to a standstill, but also as a time when health authorities and institutions came together on a global scale to pool resources and organise a collective defence against an unseen threat. The proof of the continued relevance of the EDQM's work in public health protection can be found in this report. If 2020 was a trial by fire for health systems worldwide and at all levels, it is fair to say that our organisation withstood the test. None of the EDQM's achievements would have been possible, however, without the invaluable support and contributions of the experts joining us from national, European and international authorities, universities, scientific institutes and industry. Their skill, excellent scientific competence and dedication form the foundation upon which the EDQM is built, and upon which all its future endeavours will continue to rely. To them, and to the devoted staff in Strasbourg, I offer once again my heartfelt thanks.

Susanne Keitel, PhD
Director, EDQM, Council of Europe

EDQM INITIATIVES IN THE CONTEXT OF COVID-19

Availability of and access for patients to safe, good quality medicines is more important than ever in the context of the current COVID-19 pandemic.

Supporting all stakeholders in their efforts to combat SARS-CoV-2

Throughout the year 2020, the EDQM prioritised the continuous supply of its products and services necessary for the release of medicines to the market to support public health protection.

As part of this effort, the EDQM has been openly sharing knowledge since the crisis began, supporting competent authorities, manufacturers and developers of medicines and vaccines, healthcare professionals, universities and research centres in the global campaign to combat the virus.

The EDQM is also part of the international initiative COVAX, which aims to provide solutions for COVID-19 vaccine development, manufacture and equitable supply. See "Co-operation with WHO", page 68.

Readily available reference substances to prevent shortages of medicines

In addition to making the availability of quality medicines more important than ever, the COVID-19 pandemic also created shortages of medicines worldwide, including of those used to treat or alleviate COVID-19 symptoms or used in intensive care units (ICUs). A number of clinical trials using "repurposed" authorised medicines were also initiated around the world.

To help respond to the public health needs thus created, the EDQM has closely monitored substances used in ICUs and in clinical trials and adapted its production planning to avoid any disruption of the supply chain of its reference standards (RSs) due to increased demand.[1]

1. EDQM, "Ensuring the availability of quality standards for medicines in the context of the COVID-19 pandemic", https://go.edqm.eu/News1422020.

Guidance and quality standards

The EDQM has provided support to developers and manufacturers of medicines, including COVID-19 vaccines, in the form of guidance documents, quality standards and training materials, among others, since the beginning of the health crisis.

Ph. Eur. vaccines package

It is important for developers of COVID-19 vaccines to be aware of relevant and applicable guidelines and standards as early as possible in the development process. Many of these developers are universities or small and medium-sized enterprises that may not have in-depth knowledge of the relevant regulatory requirements or how to apply them. Having identified this need and in collaboration with the European Medicines Agency (EMA),[2] the EDQM resolved to give these developers online access to guidelines, resources and pharmacopoeial texts that would assist them in their efforts. To this end, a first series of pertinent supporting pharmacopoeial texts in the field of vaccines[3] was released in June 2020, and the package was updated with an additional 17 texts in November. This gave users access to all the relevant Ph. Eur. documents.

2. EMA, "Guidance for medicine developers and other stakeholders on COVID-19", available at https://go.edqm.eu/EMAguidanceCOVID.
3. EDQM, "European Pharmacopoeia – Free access to supportive pharmacopoeial texts in the field of vaccines for human use during the coronavirus disease (COVID-19) pandemic", https://go.edqm.eu/Pheurvaccinespackage.

Guidance on recombinant viral vectored vaccines

A broad range of technologies were evaluated for the development of COVID-19 vaccines, from conventional approaches to more recent technologies, such as recombinant viral vectored vaccines. Because limited guidance was available in that area, the EDQM drafted a text on the **control of viral vectored vaccines**[4] in order to support vaccine developers working on candidate vaccines based on this technology. This text was intended to support them in designing appropriate analytical strategies for their candidate vaccines, to help ensure the quality and safety of final products, and ultimately to help expedite regulatory acceptance of subsequent marketing authorisation applications (MAAs). Published in November 2020, this work was accomplished by the EDQM in collaboration with the Ph. Eur. Group of Experts on vaccines for human use (Group 15), which is composed of experts from licensing authorities, national control laboratories, academia and industry from Europe and beyond (including the United States Food and Drug Administration, Health Canada and the Therapeutic Goods Administration, Australia).

Ph. Eur. and British Pharmacopoeia supporting pharmacopoeial texts

In April 2020, the Ph. Eur. and the British Pharmacopoeia (BP) worked together to make supporting pharmacopoeial texts relevant to antiviral medicines available on their respective websites.[5] The texts include monographs, general chapters, appendices and supplementary chapters to support those developing, manufacturing or testing relevant substances and products.

Laboratory quality-control programmes for vaccines and medicines

OMCL activities

Since the beginning of the COVID-19 outbreak in Europe, OMCLs have received requests from their national competent authorities (NCAs) to test the quality of different "COVID-19 materials". These materials included unlicensed essential medicines imported from third countries under Article 5 (1) or 5 (2) of EU Directive 2001/83/EC and used for intensive care patients, but quality-control tests were also carried out on *in vitro* diagnostic kits, medical devices (e.g. gloves and masks) and biocides. The EDQM Secretariat fostered communication and data exchange between the members of the OMCL Network in these fields.

A special session at the 2020 OMCL Annual Meeting was reserved for COVID-19 topics, also highlighting the impact of the pandemic on the functioning of laboratories. One part was dedicated to OCABR activities, in particular addressing the preparation of the network for official batch release of future COVID-19 vaccines.

Preparing for OCABR of COVID-19 vaccines

Vaccines licensed in the EU are subject to independent controls (OCABR), including testing by OMCLs before release to the market. To prepare for this important step for newly authorised COVID-19 vaccines, the EDQM mobilised the EU OCABR Network members and facilitated early exchange with manufacturers. This led to the drafting of a recommendation document for manufacturers on early method transfer and an OMCL competency list, based on control techniques for the different categories of COVID-19 vaccine candidates, to help the manufacturers identify OMCLs with the relevant skill sets. Both documents were available to manufacturers on request from July.

In November 2020, the EDQM published three new OCABR guidelines[6] outlining the tests to be performed by OMCLs in the EU OCABR Network as part of the independent control of the first anticipated pandemic COVID-19 vaccines. This was unprecedented since at the time no COVID-19 vaccines had yet received an EU conditional marketing authorisation. These guidelines were made available at an early stage for transparency, to help anticipate the launch of the first vaccines and to allow OMCLs and manufacturers

4. EDQM, "Recombinant viral vectored vaccines for human use", https://go.edqm.eu/Viralvectoredvaccines.

5. EDQM, "Antivirals supportive pharmacopoeial texts for COVID-19", https://freepub.edqm.eu/publications/AUTOPUB_46/detail. BP supportive pharmacopoeial texts include content drawn from the BP 2020, incorporating Ph. Eur. texts: https://freepub.edqm.eu/publications/AUTOPUB_47/detail.

6. European Commission, EDQM, "Guideline for Pandemic COVID-19 Vaccine (Non-replicating Adenovirus-vectored vaccine)", www.edqm.eu/en/ocabr-activities-related-covid-19-vaccines#guidelines.

to take the necessary steps to prepare for OCABR, thus preventing delays in availability while still ensuring their quality and safety. This crucial achievement was made possible through dialogue and co-operation between the EDQM, OMCLs and manufacturers. All these initiatives meant that the EDQM and the OCABR Network were ready when the first COVID-19 vaccines were given a conditional marketing authorisation and were able to ensure that vaccine doses were available for the launch of vaccination in the EU member states.

Online training

To supplement the Ph. Eur. vaccine package, the EDQM compiled a companion list of related training materials on the Ph. Eur. and its texts[7] to support users in applying them. Drawn from selected presentations given at earlier events, the aim was to fast-track understanding of the Ph. Eur. for COVID-19 vaccine developers.

Adapting CEP procedures

Faced with the increasing demand for medicines to treat COVID-19 patients, the EDQM established a **fast-track procedure for Certificates of suitability to the monographs of the European Pharmacopoeia (CEPs)** to respond to users' needs as quickly as possible. This procedure is applied upon request by CEP holders or authorities and on a case-by-case basis for those substances specifically related to COVID-19. The result is a reduction in the time required to assess applications and grant CEPs, helping to increase the supply of much needed APIs.

Paediatric formulations: helping deliver good quality medicines for children

The Ph. Eur. Commission's European Paediatric Formulary (PaedF) Working Party undertook to compile existing knowledge on **paediatric formulations and marketed products that could be useful in the treatment of COVID-19**. In March 2020, stakeholders were asked to support this initiative and to submit information on formulations and products. The resulting tables, which have been updated on a regular basis, currently provide information on dexamethasone and lopinavir/ritonavir.[8]

Illegal and falsified medical products and illegal online pharmacies

The coronavirus pandemic has also created new opportunities for criminals ready to take advantage of the increased demand for medical, personal-protection and hygiene products, including by advertising and offering for sale unauthorised medicines (claiming to prevent or treat COVID-19), as well as falsified vaccines, medicines and test kits.

Initial shortages of medical products and increase in illegal activities

The impact of the COVID-19 pandemic was extensively discussed at both the spring and autumn meetings of the Committee of Experts on Minimising Public Health Risks Posed by Falsification of Medical Products and Similar Crimes (CD-P-PH/CMED). Sharing their experiences, delegates' reports confirmed that criminals never miss an opportunity to exploit a crisis, and most countries had had to counter attempts to profit from shortages of medicines and medical devices. Many found arrangements to resolve such problems through regional co-operation or export regulations. By the autumn meeting, several countries had found that regular reporting by industry and wholesalers to authorities and changes in regulations and legislation had helped in dealing with shortages.

Falsification of medical devices

The pandemic also led to heightened awareness of falsification of medical devices. Such issues already existed previously, but the crisis sparked a dramatic increase in the scale of the illegal market. Unauthorised, substandard and falsified medical devices have been key issues since the beginning of the pandemic, which has also highlighted the differences between regulations governing medicines – perceived as strong – and those on medical devices – seen as weak in comparison.

MEDICRIME Convention

At a time of unprecedented challenges to the health sector, the Council of Europe called on governments to be extremely vigilant against

7. EDQM, "Companion to the COVID-19 vaccine developers package, https://go.edqm.eu/Pheurtrainingvaccines.

8. EDQM, "Products and extemporaneous preparation of paediatric formulations that may be useful in the treatment of COVID-19", https://go.edqm.eu/PaedFormCOVID19.

falsified medical products.[9] The MEDICRIME Convention remains an effective instrument in this regard, enabling states to safeguard public health and target criminals trying to take advantage of the COVID-19 pandemic by offering falsified medical products for sale.

Blood transfusion and organ, tissue and cell transplantation

In the field of substances of human origin (SoHO), the EDQM, through its European Committee on Blood Transfusion (CD-P-TS), European Committee on Organ Transplantation (CD-P-TO) and subordinate working groups, facilitated the exchange of information and fostered co-operation between member states and health authorities **to minimise the impact of the COVID-19 pandemic** in 2020.

Continuity of blood supply

One session (entitled "The COVID-19 pandemic: impact on the continuity of blood supply and lessons learnt", 27 October 2020) of the virtual blood-sector conference held in collaboration with the European Commission (see "2020 – A year rich in events and meetings", page 70) focused on the COVID-19 pandemic and featured key stakeholders from the sector discussing how they managed the crisis to ensure the continuity of blood supply and elaborating on lessons learnt.

National programmes for tissue donation in the context of the pandemic

Two webinars, entitled "Tissue Donation from Deceased Donors during the COVID-19 Pandemic" (April 2020) and "Keep Calm and Use Your QMS to Carry On: Tissue Banking in the New Normality" (July 2020), were also held. They featured leading experts in the field discussing how the pandemic had affected national programmes for tissue donation from deceased donors and daily practices in tissue establishments, and provided a forum to support forward-looking decisions.

9. See www.coe.int/en/web/medicrime/covid-19.

QUALITY AND USE OF MEDICINES

Throughout 2020, the EDQM worked hard to ensure patients' access to good quality medicines through the continuous supply of its reference standards, an increasingly important aspect of public health protection in Europe, given the context of the COVID-19 pandemic.

Activities, programmes and working methods were rapidly adapted to ensure business continuity. The EDQM regularly engaged with all stakeholders, including national, European and international authorities, to keep abreast of developments in public health protection.

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 that compose the Ph. Eur. are elaborated and revised by groups of experts and working parties which may be convened or adjourned by the Ph. Eur. Commission – the decision-making body of the Ph. Eur. – depending on 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 of NCAs, academia and industry.

The members of the currently 61 groups of experts and working parties were appointed for a three-year term at the Ph. Eur. Commission's November 2019 session. Of the 900 applications received and reviewed, the Commission appointed more than 800 members to these groups based on the member profiles listed in each group's terms of reference.

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

As Europe's scientific benchmark for pharmacopoeial standards, the Ph. Eur. is legally binding in 39 European countries and used in over 120 countries worldwide. It delivers crucial information earlier than any other pharmacopoeia in Europe.

The pharmaceutical world has undergone far-reaching changes over the past 50 years, creating a globalised operating environment for medicinal products and their components. To reflect the global status of the Ph. Eur. and keep pace with these changes, experts from non-Ph. Eur. member states also participate in the work of the Commission's expert groups and working parties. This willingness to extend its membership to all interested parties from around the world is part of a deliberate move to further involve both observer states and manufacturers from outside Europe in the work of the Ph. Eur. The wide variety of scientific and cultural backgrounds of these experts, all volunteers, testifies to the international scope and reach of the Ph. Eur.

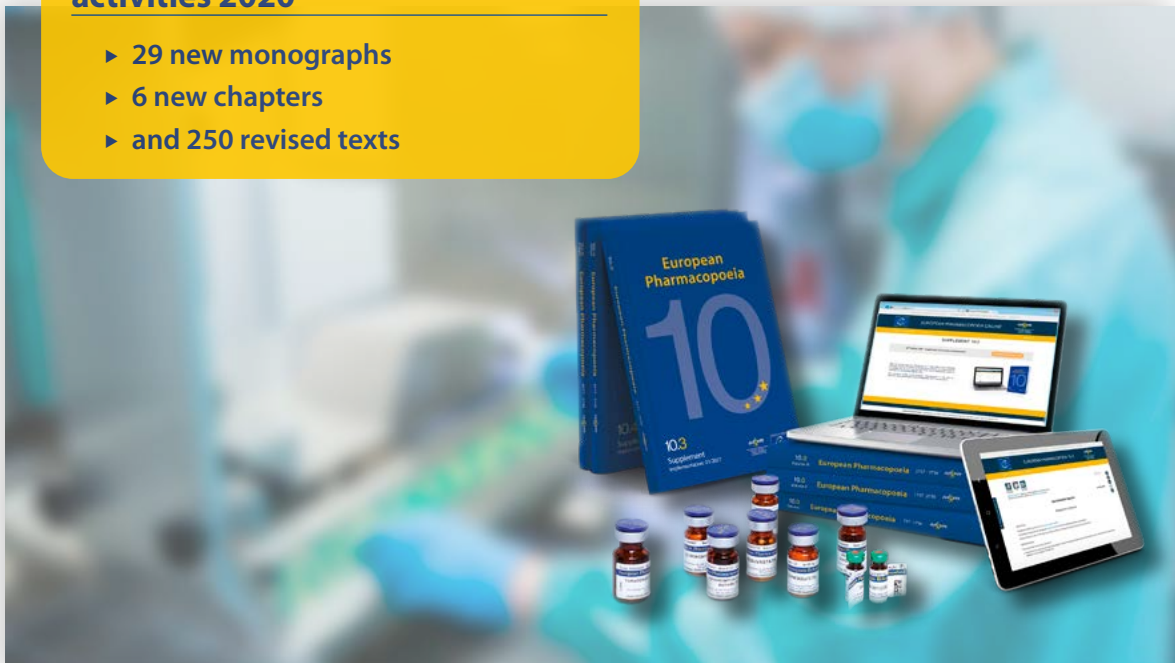
Key facts and figures

Wide participation

The number of Ph. Eur. members and observers continued to increase in 2020. **Albania** acceded to the Convention on the Elaboration of a European Pharmacopoeia (Ph. Eur. Convention) in February 2020, and **Mexico** was granted observer status by the Ph. Eur. Commission in May. Ph. Eur. membership

European Pharmacopoeia activities 2020

- 29 new monographs
- 6 new chapters
- and 250 revised texts



▶ *Members and observers of the Ph. Eur. (2020), to which should be added the EU as a member and the TFDA and WHO as observers*

thus stood at 39 states plus the EU in 2020, and there were 30 observers, including countries from all over the world, the Taiwan Food and Drug Administration (TFDA) and the World Health Organization (WHO).

Observers are entitled to take part in the scientific work of the Ph. Eur. Commission and other EDQM activities, to benefit from European experience in the field of medicinal products for human and veterinary use, to exchange knowledge with European experts and to share in the work on the development of international quality controls for medicines and the analytical procedures used.

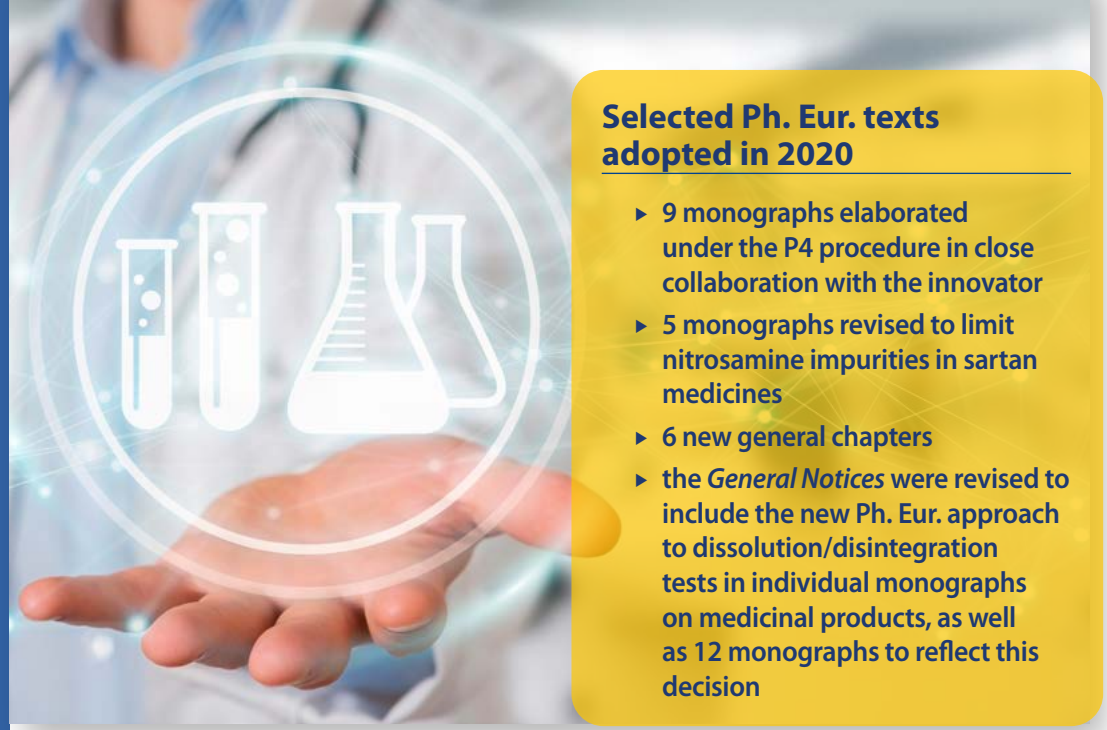
The work programme 2020

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 market relevance. The work programme for 2020 continued to reflect these efforts: **29 new monographs** and **six new chapters** were adopted by the Commission, and **250 texts were revised** to incorporate regulatory changes and scientific progress. These included nine monographs elaborated under the P4 procedure in close collaboration with the innovator: *Regorafenib tablets (3023), Riociguat (3078)* and *Riociguat tablets (3079), Rivaroxaban tablets (3021), Sorafenib tosilate (2931)* and *Sorafenib tablets (3022), Ticagrelor (3087), Ticagrelor tablets (3097)* and *Teriflunomide (3036)*.

N-*nitrosamine impurities*

At its November 2020 session, the Ph. Eur. Commission adopted revised versions of five monographs – *Candesartan cilexetil (2573), Irbesartan (2465), Losartan potassium (2232), Olmesartan medoxomil (2600)* and *Valsartan (2423)* – in accordance with the EMA human medicines committee's (CHMP) decision to align recommendations for limiting nitrosamine impurities in sartan medicines with recommendations[10] for other classes of medicines.[11]

10. EMA, "EMA finalises opinion on presence of nitrosamines in medicines", https://go.edqm.eu/EMA20200709.
11. EMA, "Nitrosamines: EMA aligns recommendations for sartans with those for other medicines", https://go.edqm.eu/EMA20201113.



Selected Ph. Eur. texts adopted in 2020

- 9 monographs elaborated under the P4 procedure in close collaboration with the innovator
- 5 monographs revised to limit nitrosamine impurities in sartan medicines
- 6 new general chapters
- the *General Notices* were revised to include the new Ph. Eur. approach to dissolution/disintegration tests in individual monographs on medicinal products, as well as 12 monographs to reflect this decision

The Commission also adopted a new general chapter on the analysis of *N*-nitrosamine impurities in active substances (*2.5.42*, previously listed as *2.4.36*)[12] (see "The EDQM's response to nitrosamine contamination", page 38).

At the same session, the Ph. Eur. Commission also decided to further revise the general monographs on *Substances for pharmaceutical use (2034)* and *Pharmaceutical preparations (2619)* as regards the control of *N*-nitrosamines. Once revised, they will be published in *Pharmeuropa* for public enquiry in 2021.

12. EDQM, "Ph. Eur. Commission adopts a new general chapter for the analysis of *N*-nitrosamine impurities", https://go.edqm.eu/News1492020.

Dissolution or disintegration tests

Over the last few years, the Ph. Eur. Commission has been elaborating monographs on medicinal products – immediate-release solid dosage forms (tablets, capsules) – containing **chemically defined active substances**. These monographs included a mandatory test for dissolution or disintegration that could be replaced, in justified and authorised cases, by another procedure and/or submitted with different acceptance criteria in an MAA.

Since the result of a **dissolution test** may be affected by the formulation and/or manufacturing process, the Ph. Eur. Commission launched a substantive examination of users' expectations with regard to this test in monographs on medicinal products. Based on the results of a survey of all users concerned, and on experience gained by other pharmacopoeias elaborating such monographs, the Commission decided at its 168th session that a dissolution or disintegration test must still be included in each medicinal product monograph on an immediate-release solid dosage form. However, users can propose different procedures and/or acceptance criteria in an MAA without justifying the choice not to select the monograph dissolution test or without demonstrating compliance with this test. The medicinal product must nevertheless still comply with the monograph dissolution test when tested, unless otherwise justified by the applicant.

This new policy is described in a revised version of the *General Notices* adopted by the Commission in November 2020 for publication in Ph. Eur. Supplement 10.6 and in the 12 individual monographs on medicinal products revised to reflect this new approach.[13]

Products of fermentation

The Ph. Eur. Commission adopted a revised version of the general monograph on *Products of fermentation (1468)*. In the paragraph on *Down-stream processing*, histamine and other biogenic amines from fish and fishery products used in raw materials were added to the list of substances that must be reduced to a minimum or removed by the process or processes used.

13. EDQM, "New policy for dissolution and disintegration testing in Ph. Eur. monographs", https://go.edqm.eu/News1292020.

3R principles

The Ph. Eur. Commission continued its efforts to promote the 3R principles of **replacing, reducing and refining** the use of animals in scientific procedures. Three monographs on vaccines for veterinary use have therefore been modified:

- *Canine parvovirosis vaccine (live) (0964)* to reduce to a minimum the number of dogs to be used in the safety tests;
- *Equine herpesvirus vaccine (inactivated) (1613)* to stress that an *in vitro* alternative method should preferably be used for the routine batch potency test;
- *Avian infectious bronchitis vaccine (live) (0442)* to allow any suitably validated method to be used to recover the virus from tracheal swabs; although the original method using embryonated hens' eggs can still be employed, the aim is to encourage manufacturers to develop and use suitably validated alternative methods, such as PCR.

Pyrrolizidine alkaloids

The Ph. Eur. Commission also adopted the new general chapter *Contaminant pyrrolizidine alkaloids (2.8.26)* to address the demands of European regulators following reports in some Ph. Eur. member states of contamination of herbal medicinal products (HMPs) and foods with traces of plants containing pyrrolizidine alkaloids (PAs).

The acute toxicity, genotoxicity and carcinogenic potential of PAs have been known for decades. Patient exposure to PAs from HMPs should be as low as possible and must not exceed the maximum daily intake agreed by the competent authority.

This general chapter, which describes 28 target PAs, allows for the use of any procedure consisting of chromatography coupled with tandem mass spectrometry (MS/MS) or high-resolution mass spectrometry that meets the validation requirements given in the chapter. This approach was adopted because there is considerable variation in the composition and matrices of the herbal drugs, herbal drug preparations and HMPs concerned, as well as in the applicable limits, making it difficult to describe all the methods suitable for quantitative analysis of the target PAs.

This general chapter gives an example of an analytical procedure that has been shown to be suitable for the determination of the 28 target PAs in a number of matrices. It also provides verification requirements analysts may need to meet to demonstrate that the analytical procedure used remains valid during routine analysis.

Dosage forms

The Ph. Eur. Commission also adopted several revised versions of dosage form monographs and changes to dosage form testing. These included the general monographs on *Eye preparations (1163)*, revised to include new requirements for sub-visible particle contamination in preparations intended for use in the injured eye or during surgical procedures, and on *Ear preparations (0652)*, with the revision focusing on the applicability of the test for uniformity of mass.

Biotherapeutics

The approach to the elaboration of Ph. Eur. monographs in the field of biotherapeutics has significantly evolved in recent years. In particular, where monographs on complex biotherapeutics are concerned, the emphasis is placed on allowing greater flexibility as a means of better addressing the structural complexity and naturally occurring heterogeneity of these substances, and the potential diversity of the preparation resulting from different manufacturing processes.

In line with its approach of allowing greater flexibility to better address the structural complexity of these substances, and the diversity of different manufacturing processes, the Commission adopted a revised version of *Erythropoietin concentrated solution (1316)*, the first Ph. Eur. monograph on a complex glycosylated molecule that was initially published in the Supplement to the 3rd Edition of the Ph. Eur. in 1999. Following the approach already applied in other monographs for complex biotherapeutics (e.g. *Etanercept (2895)* and *Infliximab concentrated solution (2928)*), glycan analysis has been added to the "Production" section of the revised monograph, which also includes a requirement for consistency of production with respect to glycosylation pattern. An outline of a suitable procedure for glycan analysis is provided as a requirement. A complete and detailed analytical procedure follows, given as an example allowing users to apply another suitable, validated procedure without having to demonstrate its equivalence to the example described, as long as it has been approved by the competent

authority. Furthermore, the system suitability of the example procedure is verified using a dedicated Ph. Eur. reference standard, while the results are assessed against a suitable in-house reference preparation, no single pharmacopoeial reference standard being suitable for all the products. Finally, the acceptance criteria are not expressed as numerical limits, as no universal specification limits are possible for this process-dependent quality attribute. These changes reflect the latest thinking of the Ph. Eur. Commission to bring about a significant improvement in the analytical performance of monographs on biotherapeutics, while simultaneously providing the sought-after flexibility.

Multivariate statistical process control

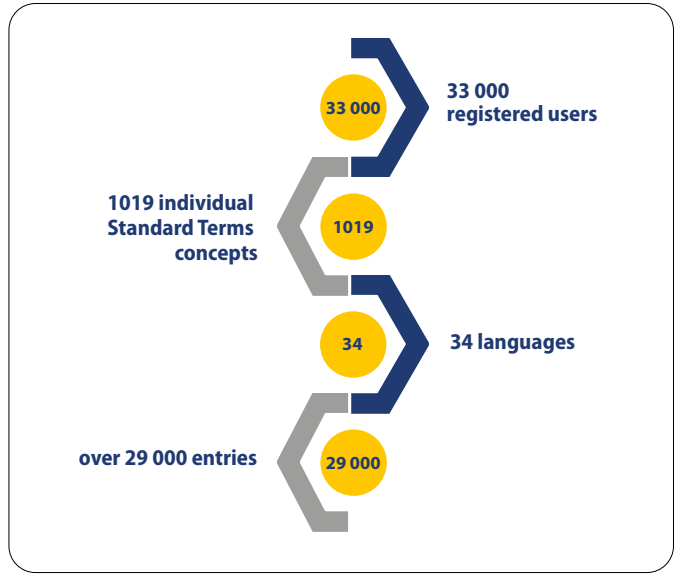
The Ph. Eur. adopted a general chapter (*5.28*) on *Multivariate statistical process control* (MSPC), becoming the first pharmacopoeia to address this topic, as well as a revised version of chapter *5.25* on *Process analytical technology*, which has been updated to refer to the newly elaborated chapter *5.28*. MSPC can be defined as the application of multivariate statistical techniques in order to analyse complex process data with potentially correlated variables. MSPC in combination with automated data collection and analysis may be used to generate control charts based on a multivariate (chemometric) model. These charts can then be used to control and improve manufacturing processes. In combination with a high degree of automation, MSPC may facilitate continuous manufacturing (CM), as well as real-time release testing (RTRT). It can be combined with process analytical technology (PAT), quality by design (QbD) and design of experiments (DoE), in line with relevant guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

Traditional Chinese medicines

Traditional Chinese medicines (TCMs) have been on the Ph. Eur. Commission's agenda since 2005 and monographs setting standards for the safety and efficacy of a number of these herbal drugs have been published in the Ph. Eur., with more in the pipeline.

In 2019, the Commission decided to launch a pilot phase on using semi-quantitative high-performance thin-layer chromatography (HPTLC) as an alternative to liquid chromatography assays in monographs on TCMs that are not subject to marketing authorisations. The pilot study was successfully completed for two of the candidates, Thunberg fritillary bulb (*Fritillaria thunbergii* Miq.: Beimu) and Corydalis rhizome (*Corydalis yanhusuo* W. T. Wang: Yanhusuo).

In 2020, the monograph on Thunberg fritillary bulb, which had been revised in line with this new approach, was adopted by the Commission. A general chapter entitled *Methods of pre-treatment for preparing traditional Chinese drugs: general information (5.18)* was also adopted. Both texts will be published in Ph. Eur. Supplement 10.6.



► *The free online Standard Terms database, key figures (2020)*

Technical guides

The newly drafted "Technical Guide for the elaboration of monographs on medicinal products containing chemically defined active substances" and the new edition of the "Technical Guide for the elaboration and use of monographs for immunological veterinary medicinal products" were also approved by the Commission for publication on the EDQM website.[14] Such documents offer guidance to the authors of monographs and are also a means of communicating the principles for the elaboration of monographs to Ph. Eur. users in industry, licensing authorities, OMCLs, etc. Since the principles applied and guidance

14. See https://go.edqm.eu/techguides.

given for the elaboration of monographs should be the same as those applied by licensing authorities, the technical guides may also serve as guidelines in the elaboration of specifications intended for inclusion in licensing applications.

General matters and policies

Biological Standardisation Programme

Funded by the European Union and the Council of Europe
EUROPEAN UNION
COUNCIL OF EUROPE
CONSEIL DE L'EUROPE
Implemented by the Council of Europe

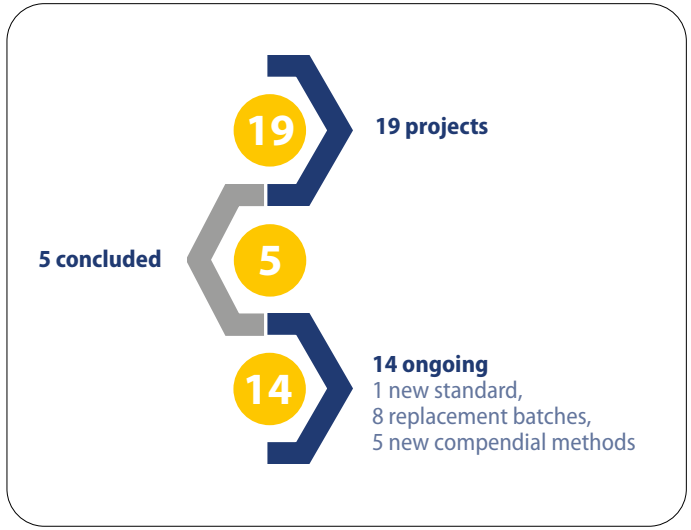
The Biological Standardisation Programme (BSP) is a joint Council of Europe/EU initiative, partly funded by the EU. Its mission is to establish reference materials for biologicals and to develop and validate new analytical procedures for the quality control of biologicals, including alternative methods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

In 2020, the programme ran 19 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 four replacement reference standards (see "Reference standards", page 25) and the validation of a new analytical procedure (ELISA method for quantification of Timothy grass pollen major allergen Phl p 5) as a proposal for inclusion in the Ph. Eur.

The EDQM carried forward another eight projects aimed at establishing replacement batches for existing reference standards and one for a new reference standard for biologicals.

Five ongoing projects focused on the development of new compendial methods. Four of these projects are dedicated to applying the 3R principles to the field of quality control of biologicals.

The continued efforts of the BSP to elaborate, validate and implement analytical procedures in line with the 3R principles were widely acknowledged in 2020.



► *Biological Standardisation Programme achievements (2020)*

Standard Terms database

Funded by the European Union and the Council of Europe
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CONSEIL DE L'EUROPE
Implemented by the Council of Europe

Initially drawn up at the request of the European Commission for use in MAAs, the Standard Terms database 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 around 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 2020, the free, online Standard Terms database had almost 33 000 registered users and held 1 019 individual Standard Term concepts with translations in 34 languages, totalling more than 29 000 entries.

In addition to its established use throughout Europe, the Standard Terms database is recommended by the ICH for compiling adverse event reports. Interest continues to spread among non-member states, particularly regarding the harmonised 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 Pharmacopoeial Discussion Group and other international harmonisation initiatives

In a challenging context of increasingly globalised supply chains, the Ph. Eur. continued its efforts to reduce unnecessary duplication of testing and reporting during drug development and routine manufacturing testing through its active participation in the work of the Pharmacopoeial Discussion Group (PDG). The PDG was set up in 1989 to harmonise pharmacopoeial standards around the world, and counts the Ph. Eur., the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP) as members, together with WHO as an observer. Two PDG meetings took place in 2020, both by videoconference due to the COVID-19 pandemic. Discussions focused on a number of strategic aspects of the challenges related to pharmacopoeial harmonisation, including opportunities to enhance the global reach and impact of international harmonisation of quality standards.

Maintaining the Q4B Annexes was also on the agenda, a task assigned to the PDG by decision of the ICH Assembly in November 2018.[15] Subsequent to this decision, the PDG drafted and submitted a detailed proposal to the ICH on how the respective annexes would be maintained. The PDG's proposal, finalised in April 2020, also takes into account the challenging task of including non-PDG pharmacopoeias of ICH regulatory members who wish to declare interchangeability with the Q4B Annexes. To evaluate feasibility, the PDG proposed a proof-of-concept study to the ICH on three of the annexes (Annex 6: Uniformity of Dosage Units, Annex 7: Dissolution, and Annex 8: Sterility) as a pilot phase. The proposal was presented to the ICH Management Committee and Assembly meetings in May 2020.[16] As agreed at these meetings, a complementary mapping document highlighting the various engagement points, where stakeholders, including ICH members and observers, would be able to contribute to the harmonised standards development process, was also elaborated by the PDG and sent to the ICH Secretariat in preparation for the ICH Management Committee and Assembly meetings in November 2020, at which the PDG's proposed pilot phase was adopted.

In addition to this project, the PDG drafted a proposal for a new framework to facilitate the exchange of information between the PDG and other pharmacopoeias of the world. This proposal is another illustration of the PDG's commitment to supporting the expanding recognition of harmonised pharmacopoeial standards with a view to achieving global convergence of quality standards. This new framework sets out new means of co-operation between the world's pharmacopoeias and the PDG. The latter proposed to conduct a one-year pilot phase with the pharmacopoeias participating in the 11th International Meeting of World Pharmacopoeias (IMWP) to test the framework.

As of 2020, 28 of the 31 general chapters and 46 of the 60 excipient monographs on the PDG work programme had been harmonised.

Further harmonisation initiatives

The Ph. Eur. is actively involved in a number of other harmonisation initiatives at international level. For example, it actively supports the 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. Among the various projects carried out, the Good Pharmacopoeial Practices (GPhP) drafted by the IMWP and published on the WHO website stands out as a basis for improving co-operation and work-sharing among world pharmacopoeias.

The 11th IMWP took place in February 2020 at the EDQM premises in Strasbourg (France). Over 50 national and regional pharmacopoeial authorities, including the 39 countries represented by the Ph. Eur., renewed their commitment to strengthening their co-operation.

Pharmacopoeias also shared an update on their respective responses to *N*-nitrosamine contamination of medicines. This exchange, initiated by the EDQM at the 10th IMWP in 2019, was deemed very helpful in facilitating the alignment of action to be taken by the different pharmacopoeias in support of decisions by regulatory authorities. Participants re-emphasised the importance of exchanges between the world pharmacopoeias and agreed to increase meeting frequency by holding regular virtual meetings in addition to the annual face-to-face meetings.

15. ICH, "ICH Assembly Final Minutes, 14-15 November 2018", https://go.edqm.eu/ICH20190108.

16. ICH, "Summary of MC Session Actions and Decisions: ICH Management Committee Virtual Meeting, 13, 25 and 26 May 2020, B. Q4B Maintenance", https://go.edqm.eu/ICH20200716.

The EDQM organised the one-day "Meet the World Pharmacopoeias" Symposium on 20 February 2020 at its premises in Strasbourg, following on the heels of the 11th IMWP. This symposium brought together 67 representatives of pharmacopoeial and regulatory authorities, as well as of the pharmaceutical industry and other stakeholders, and was followed remotely by a further 160 from over 40 countries.

It provided an opportunity to share experience and exchange information on achievements and challenges related to pharmacopoeial convergence, harmonisation and co-operation between world pharmacopoeias and stakeholders. An update on the work of the IMWP, background information on the GPhP and proposed future interactions between the PDG and the IMWP were provided. Pharmacopoeias and representatives of the pharmaceutical industry and trade associations discussed the challenges related to pharmacopoeial convergence and harmonisation, as well as ways to further strengthen work-sharing and co-operation. The feedback received from stakeholders during the symposium provided the IMWP participants with a basis for considering and reflecting on future initiatives and communication strategies.

Due to the COVID-19 pandemic, regular videoconferences organised by WHO took place during the year. Pharmacopoeias discussed their business continuity plans to safeguard essential activities, in particular the provision of documentary and physical (reference) standards to ensure the quality of medicinal products and their ingredients

Co-operation with national and European regulatory authorities

Throughout 2020, the Ph. Eur. Commission continued to work closely with NCAs and the EMA. This ongoing co-operation was crucial to ensuring continued consistency between the approaches of licensing authorities and the Ph. Eur.; EMA scientific guidelines and Ph. Eur. monographs and general chapters are complementary instruments for ensuring the quality of medicinal products. More specifically:

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

In the particular context of the COVID-19 pandemic, the EDQM and the EMA held regular videoconferences (see "EDQM initiatives in the context of COVID-19", page 10).

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 revisions and reviewing draft texts issued for public consultation in *Pharmeuropa online*. Members of EMA working groups (for which the EMA provides the secretariat) and members of the EMA Secretariat itself are observers to some of the Ph. Eur. Commission's groups of experts 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 (GMDP-IWG).

Co-operation with National Pharmacopoeia Authorities

The EDQM organises an annual meeting of the NPAs of Ph. Eur. member states to facilitate and co-ordinate activities of common interest, and to provide an informal forum to exchange information. The 2020 meeting was organised as a virtual conference. Among other topics, discussions focused on the Ph. Eur. work programme and on process improvements.

Owing to the COVID-19 pandemic, the EDQM also organised weekly videoconferences until June, followed by monthly videoconferences (see "EDQM initiatives in the context of COVID-19", page 10).

Co-operation with other stakeholders

Stakeholder involvement in the elaboration and revision of Ph. Eur. texts is of crucial importance, and the EDQM endeavours to maintain regular exchanges with all interested parties. In 2020, a number of bilateral meetings were held with a broad range 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.

These exchanges were organised more frequently due to the COVID-19 pandemic (see "EDQM initiatives in the context of COVID-19", page 10).

► *Ph. Eur. 10th Edition*

PUBLICATIONS, DATABASES AND WEBSITE

The 10th Edition of the Ph. Eur. (with its latest Supplement 10.5) contains 2 447 monographs (including dosage forms), 378 general texts (including general monographs and methods of analysis) and around 2 800 descriptions of reagents.

A new version of *Pharmeuropa online* was launched at the beginning of 2020. The website comprises *Pharmeuropa Bio & Scientific Notes* and *Pharmeuropa Texts for Comment*, the free online forum in which draft Ph. Eur. texts are made available 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 worldwide. Texts are published on an ongoing basis and comments can be submitted on the basis of four deadlines per year.

Two technical guides were published in 2020: "Technical Guide for the elaboration of monographs on medicinal products containing chemically defined active substances" and the new edition of the "Technical Guide for the elaboration and use of monographs for immunological veterinary medicinal products" (see "Technical guides", page 20).

At the end of 2020, a new version the EDQM's free publications website (FreePub: https://freepub.edqm.eu/publications) went live, offering a more user-friendly and visually appealing website.

REFERENCE STANDARDS

The EDQM ensures the supply of its reference standards (RSs) to help safeguard the availability of quality medicines in Europe and beyond, a mission which took on even greater importance as the COVID-19 pandemic developed. Early on, extraordinary efforts were made to adapt and reinforce the functioning of the EDQM laboratory, manufacturing and logistics entities, to protect the health, safety and security of staff while they continued to develop, manufacture and dispatch reference standards.

What are reference standards and why are they needed?

Ph. Eur. reference standards

Official reference standards are an integral part of the Ph. Eur.: they complement the documentary texts for the intended use described and are necessary to apply the analytical tests described in the Ph. Eur. monographs. Reference standards include chemical reference substances (CRSs), herbal reference standards (HRSs), biological reference preparations (BRPs), biological reference reagents (BRRs) and reference spectra. Ph. Eur. reference standards are established and distributed by the EDQM and adopted by the Ph. Eur. Commission; only the Ph. Eur. RSs are official and authoritative in case of arbitration.

Distribution and portfolio

The EDQM distributes its RSs 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 life-cycle management of the RS portfolio covers a wide range of tasks, ranging from the procurement of candidate materials, characterisation and establishment, to manufacturing, quality control, quality assurance, release, distribution and monitoring.

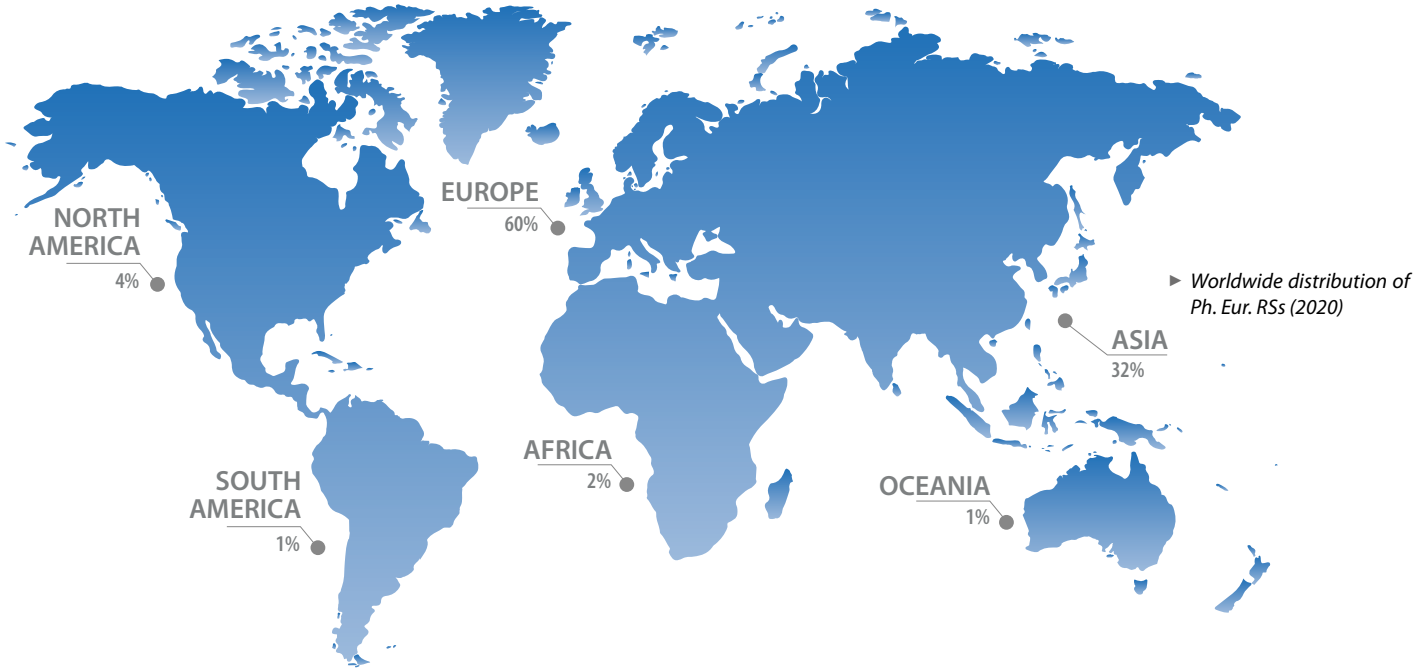
Travel, customs and shipping restrictions imposed in 2020 as a response to the pandemic created significant obstacles to the distribution of RSs. Considering the increasing need for quality medicines during the health crisis, immediate steps were taken to implement measures to keep the EDQM's distribution services fully operational (see "EDQM initiatives in the context of COVID-19", page 10).

EDQM activities for WHO reference substances

The EDQM is an observer to the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) 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

Batches of Ph. Eur. reference standards adopted in 2020

- 92 new RSs
- 312 replacement RS batches
- Distributed directly by the EDQM in 123 countries



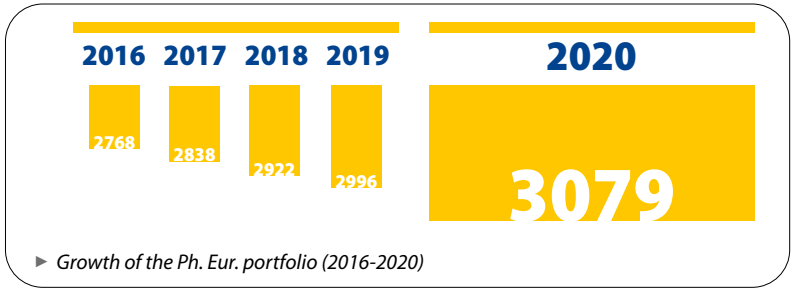
► *Worldwide distribution of Ph. Eur. RSs (2020)*

medicinal products around the world, with a focus on diseases prevalent in developing countries and on countries with a less stringent regulatory system.

The EDQM is responsible for establishing, manufacturing, monitoring and distributing WHO International Chemical Reference Substances (ICRSs). ICRSs are used in conjunction with the monographs and texts of the International Pharmacopoeia, which is published and maintained by WHO and used worldwide, notably in countries with a less robust regulatory system. The ICRS catalogue consists of 244 reference substances.

In 2020, the ECSPP adopted the establishment reports submitted by the EDQM Laboratory for five new ICRSs and one replacement ICRS.

The EDQM is also responsible for establishing, manufacturing, storing and distributing WHO International Standards for Antibiotics (ISAs), which are essential for the standardisation and quality control of antibiotic drug substances and medicinal products. These standards are supplied around the entire world for microbiological assays performed in the context of the quality control of antibiotics. The ISA catalogue consists of 23 reference standards.



► *Growth of the Ph. Eur. portfolio (2016-2020)*

Key facts and figures

There are currently 3 079 RSs in the Ph. Eur. RS portfolio, which is constantly evolving to complement new or revised Ph. Eur. texts, or to replace existing RSs when corresponding stocks run out.

In 2020, the EDQM distributed Ph. Eur. RSs directly to 123 countries.

Ph. Eur. RSs adopted in 2020

At the three sessions held in 2020, the Ph. Eur. Commission adopted 404 batches of RSs based on establishment reports submitted by the EDQM. This figure includes the reference standards for medicines for which demand increased due to COVID-19 (for example, dexamethasone). It also includes seven new RSs specifically developed to complement the new Ph. Eur. chapter on the control of nitrosamines, N-*nitrosamine impurities in active substances* (*2.5.42*).[17]

As a result of the international collaborative studies performed as part of the BSP in 2020, the Ph. Eur. Commission adopted one new RS, Human Albumin for Molecular Size Distribution Test BRP.

Three replacement batches of RSs were also adopted: Pertussis Toxin BRP, Human Coagulation Factor VIII concentrate BRP and Somatropin/Desamidosomatropin resolution mixture CRS (see also "The European Pharmacopoeia", page 16).

General matters and policies

Continuous support to all users

Regulations in some countries require access to Ph. Eur. reference standards be maintained even after they are withdrawn from the official catalogue. The EDQM has therefore modified its policy and, subject to the availability of stock, it now keeps RSs available for an additional period of six months after their suppression from the Ph. Eur. to allow users to comply with their country's regulatory framework.[18]

Collaboration with the ISO

As in previous years, the EDQM participated as an observer at the ISO Committee on Reference Materials (REMCO), providing advice and suggestions on the ISO REMCO standards and guides drafted or revised in 2020.

Collaboration with national laboratories

The EDQM Laboratory can count on a number of OMCLs to establish Ph. Eur. assay standards requiring collaborative studies. In 2020, 26 laboratories participated in EDQM Laboratory CRS collaborative studies, representing 24 countries.

Scientific events related to RSs

In 2020, the EDQM Laboratory actively contributed with a virtual presentation to the "Measurements, Standards, Quality and Safety Therapeutics and Diagnostics International Workshop" held in Nanjing (China) from 10 to 12 November.

PUBLICATIONS, DATABASES AND WEBSITE

Throughout 2020, the EDQM continued to run and maintain its Reference Standards Online Database, providing access to all standards officially valid for the use prescribed in the Ph. Eur. monographs. 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. The EDQM Reference Standards Online Database can be accessed at https://crs.edqm.eu.

Downloadable Safety Data Sheets (SDSs) and Biological Safety Data Statements, as well as leaflets, are also available in the EDQM's online database.

In April 2020, the EDQM released a streamlined, more user-friendly version of the WebStore for Reference Standards,[19] presenting clearer information on shipping conditions of each item and links to the Reference Standards Online Database.

The EDQM issued 577 leaflets in 2020, providing RS users with additional information, such as a chromatogram or assigned value, for a given substance.

In addition, SDSs 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. SDSs and labels are provided in 27 languages.

17. EDQM, "Seven new reference standards available for the analysis of *N*-nitrosamine impurities", https://go.edqm.eu/News1602020.

18. EDQM, "Change in the policy for withdrawing reference standards from sale", https://go.edqm.eu/News0142020.

19. EDQM, "New and improved WebStore for EDQM Reference Standards", https://go.edqm.eu/RSWebStore.

CERTIFICATION OF SUITABILITY TO THE PH. EUR. MONOGRAPHS

Certification procedure widely recognised around the world

The Certification of suitability (CEP) procedure was 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. Extra-European production of pharmaceutical ingredients has become increasingly common as the world's economies continue to evolve, creating challenges for the monitoring and quality control of substances used in the manufacture of medicines.

To apply for a CEP, manufacturers submit a dossier describing how their substance is manufactured and its quality is controlled, demonstrating that the tests described in Ph. Eur. monographs are suitable for that purpose. 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.

Certification of suitability (CEP) procedure activities in 2020 – Applications received

- 361 new applications
- over 1 880 requests for revision

The EDQM also carries out inspections of manufacturing and/or distribution sites of drug substances covered by CEPs. Inspections ensure that Good Manufacturing Practice (GMP) is enforced and that the information supplied under the Certification procedure is accurate.

An increasing number of licensing authorities worldwide accept CEPs to replace (fully or partially) the active pharmaceutical ingredient (API) quality section in MAAs for medicinal products.

211	1 429	> 5 400
new certificates	revised certificates	valid certificates

Total issued and valid CEPs in 2020

Key facts and figures

In 2020, the EDQM received 361 new CEP applications (+18% over 2019), including 343 for chemical purity, 12 for the risk of transmissible spongiform encephalopathy (TSE) and 3 for herbal preparations; more than 1 880 CEP revision requests were received (+4% over 2019).

In 2020, 211 new certificates and 1 429 revised certificates were issued. Processing times were impacted by the COVID-19 pandemic, mainly due to the extended lockdown and because experts from competent authorities were unable to support the EDQM's Certification Department in the assessment of files. As a consequence, delays occurred in the treatment of all kinds of applications and the EDQM took a number of specific measures and developed alternative solutions, which have had a positive impact.

In addition, the Certification Department established a **fast-track procedure** for applications for substances important in the context of the pandemic, to be implemented upon justified requests from companies or from competent authorities (see "EDQM initiatives in the context of COVID-19", page 12).

In December 2020, there were more than 5 400 valid CEPs covering chemical purity, TSE and herbal drug preparations.

The EDQM has continued working closely with the EU regulatory network and international partners on the presence of **nitrosamines** in order to ensure co-ordinated and harmonised approaches on the issue.

In this context, a call for review of CEPs was issued at the end of 2019, and the EDQM Certification Department has since been dealing with the risk assessments and updated applications received from CEP holders. The assessment work was prioritised based on the risk of the presence of these impurities and CEPs have been revised when specific tests on the active substances were deemed necessary (see "*N*-nitrosamine contamination in brief", page 40).

The EDQM inspection programme was also impacted by the COVID-19-related travel restrictions in place from early 2020 onwards. Seven on-site inspections were nevertheless carried out (in India and China), and the EDQM carried out remote assessments for 48 manufacturing sites by exchanging data with inspectorates from member states and international partners. In addition, the EDQM set up a new procedure called **"Real-Time Remote Inspections" (RTEMIS)**. A pilot phase was initiated and two companies in India were invited to take part; the results obtained were satisfactory, both from a technical point of view and in terms of expected outcomes. When more experience has been gained with this new approach to inspections, RTEMIS has the potential to help increase the number of manufacturing sites covered annually.

In 2020, the EDQM suspended and/or withdrew 15 CEPs due to non-compliance with GMP or inability of the CEP holder to meet the requirements of the procedure for the maintenance of their dossier. On the other hand, 11 CEPs were restored following the evaluation of action taken by companies in response to the suspension of their CEP.

Under the Certification procedure, if a Ph. Eur. monograph is not capable of controlling the quality of a substance, a request for revision is submitted to the relevant Ph. Eur. groups of experts for consideration. In 2020, 22 such requests were issued, mainly proposing the addition of specified impurities to the monograph's transparency list, together with a suitable test method.

COMMUNICATION WITH APPLICANTS, PARTNERS AND STAKEHOLDERS

Communication with stakeholders who use CEPs is of crucial importance. That is why the EDQM endeavours to publish regular updates on activities on its website and to maintain regular exchanges with interested parties. In 2020, a number of bilateral meetings were held with a variety of stakeholders to promote exchanges on all aspects of the work of the EDQM and to ensure that the feedback from users could be taken into account.

In 2020, the Certification Department launched a project to create the "**CEP of the future**" that will better fit the emerging needs of stakeholders. An online survey was sent to targeted groups and published on the EDQM website to gather broad feedback from various stakeholders with regard to the content, layout, format and use of CEPs. The feedback received will be reviewed in 2021 and used to devise the "CEP of the future" to meet users' needs in the coming years.

The Certification procedure is based on the participation of assessors and inspectors from national authorities and the EDQM works with a network of about 100 assessors from competent authorities and 30 GMP inspectors. The list of these assessors and inspectors is regularly published on the EDQM website.

The Certification Steering Committee met in November 2020, and the Technical Advisory Board for chemical purity assessment held three meetings over the year.

Throughout 2020, the Certification Department continued to work closely with the EMA and NCAs in Europe and beyond. As far as European authorities are concerned, this continued co-operation is crucial to ensuring consistency between the approaches applied for the assessment of quality information pertaining to active substances, as well as for GMP implementation. The EDQM has observer status in a number of EMA bodies relevant to the Certification procedure, such as the joint CHMP/CVMP Quality Working Party (QWP) and the GMP/GDP Inspectors Working Group. In particular in 2020, the EDQM contributed to the sartans "lessons learnt" exercise[20] and will implement the relevant recommendations.

The EDQM continued to work on strengthening co-operation and exchange of information on the quality of pharmaceutical substances with authorities worldwide and on promoting the use of CEPs as supporting documentation for the quality evaluation of these substances. In this context, a confidentiality agreement was signed in June 2020 with the Saudi Food & Drug Administration, which accepts CEPs to support information on active substances as part of their registration process for medicinal products.

The Certification Department took part in a number of online events and conferences in 2020. This created opportunities to provide stakeholders with updates on the CEP procedure with regard to the assessment of CEP applications or GMP inspections.

The Certification Department also participated in a number of international platforms for co-operation, such as the International Pharmaceutical Regulators Programme (IPRP) Quality Working Group, the international Active Pharmaceutical Ingredients (API) inspection programme and the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

20. EMA, "Lessons learnt from presence of *N*-nitrosamine impurities in sartan medicines", https://go.edqm.eu/EMA20200623.

THE EUROPEAN NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES

The importance of a network for pan-European co-operation

Funded by the European Union and the Council of Europe

EUROPEAN UNION

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Implemented by the Council of Europe

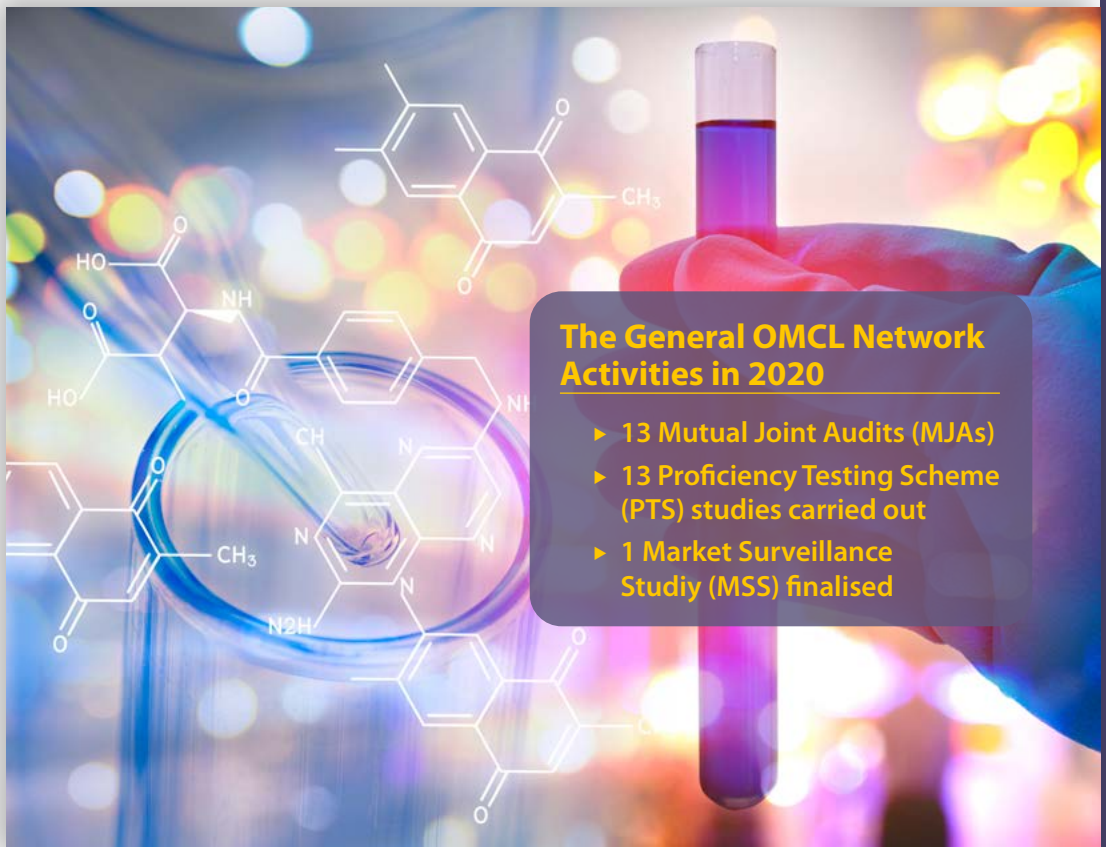
Despite the challenges related to the COVID-19 pandemic, which made it necessary to reorganise and redeploy resources in 2020, the EDQM successfully continued to co-ordinate the activities and carry out the work programme of the General European Network of OMCLs (GEON). The network's secretariat is provided by the EDQM and is partly funded by the European Commission.

The OMCL Network brings together official laboratories based in 36 European member states and in seven non-European partners. Their collective objectives are to ensure the quality of medicines on the market and to prevent substandard and falsified medicinal products from reaching patients and animals and compromising the efficacy of their treatment and potentially their health. Operating impartially and independently of manufacturers, and therefore without any conflicts of interest, the network makes it possible to pool resources and share information on the latest technologies with a view to saving public money and combining expertise and best practices throughout Europe and beyond. 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.

To better integrate independent lab testing activities into the regulatory framework of medicines, the network endorsed four key strategic goals at the 2020 OMCL Annual Meeting: Sharing-Networking, Specialised Centres, Communication Strategies and Funding which will have an impact on the GEON work programme of the coming years.

Mutual Joint Audits/Visits and Training Visits

The system in place within the network to assess the compliance of OMCLs with the quality requirements laid down in ISO/IEC 17025, the network's QM Guidelines and the Ph. Eur. provides for a series of **mutual joint**



audits/visits (MJAs/MJVs). In 2020, 13 MJAs were carried out (including ten distant surveillance and one blank audit). No training visits (TVs) or MJVs took place. Since the QMS programmes were launched in 1997, a total of 193 MJAs, 53 MJVs and 28 TVs/tutorials have been carried out.

In response to the pandemic, the initial 2020 audit programme was significantly revised. Priority was given to OMCLs that do not hold an accreditation certificate issued by their national accreditation body and whose MJA attestation expired in 2020. For these laboratories, further delays in the external verification of the implementation of the new provisions of ISO/IEC 17025:2017 would jeopardise business continuity of their duties at national level and their contributions to the network. Assessments of their quality management systems (QMSs) were carried out remotely by means of videoconference, focusing on the new requirements of the standard.

Harmonising QMSs among OMCLs and achieving appropriate quality levels that enable mutual recognition of test results between members (for example, official batch release testing of biologicals, market surveillance and falsified medicines testing) remain the principal tasks of this programme.

OMCL Network Quality Management Guidelines

Common QM Guidelines are drafted by experts belonging to the network and updated on a regular basis.

Status	Guideline/Recommendation documents
Adopted	▶ Risk-based Auditing Approach ▶ Management of Changes ▶ Management of Environmental Conditions ▶ Management of Samples ▶ Handling and use of non-compendial reference standards in OMCL Network ▶ Validation/Verification of Analytical Procedures ▶ Qualification of Balances ▶ Qualification of GC Equipment ▶ Qualification of UV-visible Spectrophotometers ▶ Qualification of Atomic Absorption / Atomic Emission Spectrometers ▶ Externally Provided Products and Services ▶ Management of Documents and Records
Under revision	▶ Qualification of Automatic Titrators ▶ Management of Volumetric Glassware ▶ Qualification and re-qualification of personnel involved in laboratory activities ▶ Evaluation and reporting of results
Under elaboration	▶ Recommendations on setting expiry period of reagents and reagents prepared and used in the laboratories of the OMCL Network

▶ *Quality Management Guidelines elaborated (2020)*

Under the co-ordination of the EDQM Secretariat, 12 QM Guidelines supporting laboratories in the implementation of ISO/IEC 17025 requirements were drafted or revised and subsequently adopted by the OMCL Network.

Training courses/workshops

In June, the EDQM organised the first workshop on statistical process control dedicated to the OMCL Network. This two-day event was run as a webinar, covering classical control charts (Shewhart charts) and advanced tools (such as control rules, EWMA and CuSum charts) used to monitor and trend laboratory data.

The training on CombiStats™ software, usually given on the EDQM premises, was held as a webinar in October; over 100 participants joined in. Participants learnt how to use the software during the first session; the next session was for advanced users, addressing their questions about assay design, analysis and the interpretation of results.

Proficiency Testing Scheme studies

The EDQM Proficiency Testing Scheme (PTS) provides laboratories with an objective means of assessing and demonstrating the reliability of their data. In 2020, five studies were organised in the physico-chemical field: "PTS204 Potentiometric determination of pH", "PTS205 Water: semi-micro determination", "PTS206 Loss on drying", "PTS207 UV-Vis Spectrophotometry" and "PTS208 Liquid Chromatography". On average, 118 laboratories (OMCLs and other pharmaceutical control laboratories from industry, hospital pharmacies, universities and pharmacy associations) took part in each study.

A collaborative study on assay by UV-Vis spectrophotometry on a sample with a herbal matrix was run in 2020, with the participation of 14 laboratories.

Five studies in the field of biologicals were organised in 2020, with an average of 18 laboratories taking part in each. They covered "PTS209 Hepatitis C virus NAT", "PTS210 Parvovirus B19 NAT", "PTS211 Hepatitis A virus NAT", "PTS212 Seasonal influenza vaccine potency (HA content)" and "PTS213 Human coagulation factor IX potency".

A specific PTS programme was also organised by the EDQM in collaboration with WHO. In 2020, three studies of the External Quality Assurance Assessment Scheme (EQAAS) were launched: "EQAAS 10.1 – Assay by titration", "EQAAS 10.2 – Disintegration test" and "EQAAS 10.3 – Sulphates identification test".

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

The EDQM is an EA-recognised stakeholder and regularly attends the EA/Laboratory Committee (LC) meetings in order to strengthen collaboration with the members of the LC, clarify technical questions of interest to the OMCL Network related to the interpretation of ISO 17025:2017 requirements, and share experience in the field of auditing.

At the request of the EA/LC, the EDQM conducted a survey among OMCLs and national accreditation bodies on joint audits. The feedback confirmed the suitability of the document entitled "Joint EA-EDQM Communication Regarding Cooperation when Carrying out (Joint) Audits/Assessments in OMCLs, EA-INF/15:2017" and provided some proposals to improve future joint audits.

General OMCL Network activities

GEON Annual General Meeting

Originally planned as a face-to-face meeting in Oslo, Norway, the GEON Annual General Meeting was held as a web conference from 12 to 15 May 2020 with a reduced programme (six topic sessions instead of nine). This enabled a wider audience to take part, with about 470 participants joining the different sessions organised over the conference week.

The COVID-19 pandemic, its impact on the work of OMCLs and the co-ordination of the network, as well as the measures taken by the control laboratories and the EDQM (as secretariat of the network) formed the common themes of all six sessions.

► *The GEON Annual General Meeting was held as a web conference from 12 to 15 May 2020*

Furthermore, building on the experience gained from the cases of nitrosamine contamination of medicines, the network agreed that OMCLs need to continue developing screening methods and to focus their testing campaigns on at-risk product groups rather than on individual products. This approach could lead to new concerted programmes.

The group agreed that the network needs to focus on the critical strategic goal of developing specialised centres. While this will allow new challenges linked to the independent quality testing of innovative products (for example, gene therapy products, monoclonal antibodies and auto-injector systems) to be faced, it will require investment in new analytical techniques and additional human resources.

General market surveillance studies

In 2020, a market surveillance study (MSS) on sildenafil APIs and medicinal products (MSS058) was finalised. Twenty-four OMCLs from the General European OMCL Network from 22 European countries, plus Australia and Israel, participated in the study, in which more than 340 samples were analysed and their expected quality confirmed.

Active Pharmaceutical Ingredients Working Group

Two videoconferences were held in 2020, to discuss strategic objectives and the status of ongoing studies and schedule new ones. The API Working Group also worked on a commonly shared API testing plan. In addition, the possibility of using national databases and sharing risk signals from different sources for the establishment of concerted API market surveillance testing programmes is currently under evaluation.

Another topic of interest for the group was the sildenafil fingerprint study (MSSFP004). This study is the first combined Centrally Authorised Product (CAP), MSS and API fingerprint study on a target molecule aimed at concerted collection and testing of API and drug product samples. The outcome of this study and the precedent study on omeprazole (MSSFP003) will be published in scientific journals in 2021.

After having performed several fingerprint studies, the group discussed how to use the experience gained with the application of chemometric methods for quality testing of medicines. One possible practical implementation is to detect API samples suspected of coming from non-authorised sources.

OMCL Falsified Medicines Working Group

The Falsified Medicines Working Group organised two videoconferences in 2020 and finalised an MSS on suspected illegal products (MSSIPs) entitled "Illegal Products containing Non-ATC-INN Molecules". The results of this study will be the subject of a scientific publication, with a summary report published on the EDQM website.

A joint videoconference with representatives from the Customs Laboratories European Network (CLEN) took place on 27 October 2020. The CLEN and OMCL networks have different areas of expertise, different ranges of products to control and different fields of action, but both their programmes provide for the testing of falsified medicines. Participants shared an interest in strengthening collaboration, and this workshop helped to initiate this process at national level. In view of the positive feedback received after the meeting, both partners agreed to go ahead with another joint event, to take place in 2021.

Two hands-on training sessions for OMCL members on cell-based assay of monoclonal antibodies were scheduled in 2020 at the OMCLs at Infarmed (Portugal) and FIMEA (Finland). Due to the COVID-19 pandemic, both sessions had to be postponed to 2021. This was also the case for the 4th Symposium on Falsified Medicines for OMCLs, which was initially scheduled for April 2020.

A new study was launched in the Suspicious Unknown Products (SUPs) programme (SUP0109) in November 2020.

EDQM representatives also take part in the meetings of the EU Heads of Medicines Agencies' Working Group of Enforcement Officers (HMA-WGEO) (see "Co-operation with international partners", page 66) in connection with the promotion of the MEDICRIME Convention.

The activities of the OMCL Falsified Medicines Working Group complement those of the CD-P-PH/CMED regarding the falsification of medical products (see "Anti-falsification activities", page 42).

Gene Therapy Products Working Group

The OMCL Working Group for Gene Therapy Products (OMCL GTWG) was created in 2008 to foster collaboration between OMCLs working in the gene therapy products field and to save time and resources by sharing knowledge and information on the latest technological advancements through meetings and collaborative studies. The working group is currently composed of 11 OMCLs.

Due to the COVID-19 pandemic, the number of laboratory experiments was reduced and resources were re-allocated to more urgent activities. In this context, the pace of the OMCL GTWG activities was reduced. For the same reasons, the annual meeting of the OMCL GTWG was postponed to 2021. Nevertheless, a survey was sent out through the network to gather information on the future needs with regard to resources and financing in the fast-evolving field of gene therapy. The responses to the survey will be analysed in early 2021 and outcomes will be shared with the network.

▶ *CombiStats™ licences per region*

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 available to other laboratories. The current version (6.1) includes features such as equivalence testing, robust regression, five-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 website,[21] while training courses for users are organised once a year.

In 2020, 779 licences were issued and CombiStats™ was used in 27 countries in Europe and 29 countries in the rest of the world. CombiStats™ has thus evolved into a shared, internationally recognised reference tool in its domain, which facilitates 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 in an annual CAP Sampling and Testing programme. The EMA sponsors the programme and has overall responsibility for it, while the EDQM co-ordinates the sampling and testing operations.

The CAP Regular programme covers an annual list of products prepared by the EMA Secretariat together with the EMA Scientific Committees and using a risk-based approach, whereas the CAP Generics programme was amended in 2019 in order to enlarge the number of tested products and include three programmes on generics every year.

A new Biosimilar test programme was introduced in 2019 in response to the increasing number of biosimilars. Three projects will be conducted over a five-year period (2019-2024), covering filgrastim, etanercept and rituximab products.

21. See www.edqm.eu/en/combistats.

Authenticity checks on products distributed in parallel can be performed in the framework of the Parallel Distribution programme. The list of products that are of interest is provided on a yearly basis by the EMA Secretariat.

In order to address the high percentage of APIs produced outside the EU/EEA and used in medicines for the European market, an ad hoc CAP API programme has become part of the co-operation agreement with the EMA.

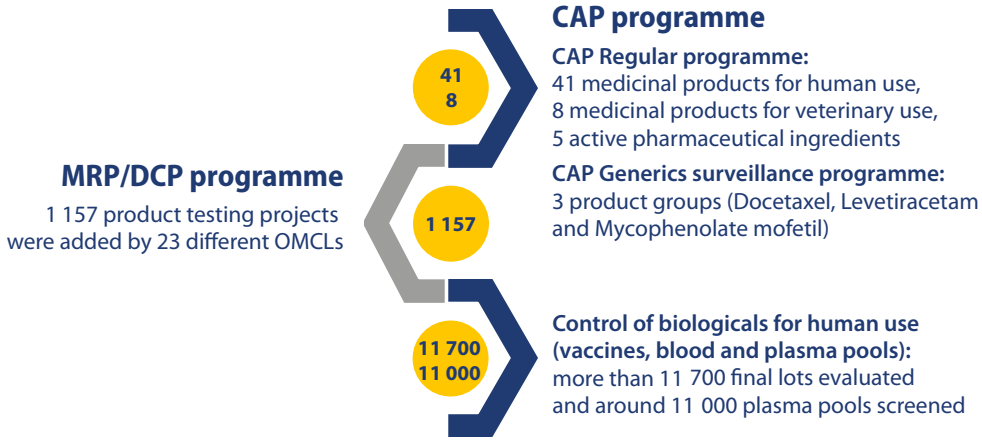
The results of the CAP Sampling and Testing programme showed that the vast majority of the products tested were of the expected quality and complied with authorised specifications.

By 31 December 2020, no out-of-specification results had been found, but a few regulatory or technical findings had been reported to and followed up by the EMA.

Mutual Recognition Procedure/ Decentralised Procedure post-marketing surveillance scheme

The 16th regular programme for the market surveillance of medicinal products authorised in the EU/EEA via the Mutual Recognition Procedure (MRP) or Decentralised Procedure (DCP) was carried out in 2020. Some 1 157 product testing projects were covered in the 2020 programme. This slight decrease compared to previous years could be related to the COVID-19 pandemic, which has led to scheduling changes and a resetting of priorities in different network laboratories. Testing reports for 2020 were issued by 23 different OMCLs and 11% of the tested products were for veterinary use.

► *The OMCL Network EU/EEA specific activities in 2020*



Regulatory issues were identified in around 3.4% of projects. The percentage of projects reporting out-of-specification results is gradually increasing. A few serious findings were also reported in 2020.

By the cut-off date of 31 December 2020, the MRP/DCP Product Testing Database, which was set up in 2007 to improve co-operation on planning, sampling and reporting of testing activities carried out within the OMCL Network on MRP and DCP products, held more than 13 300 records, with contributions from 36 different OMCLs. Database access is restricted to OMCLs and health authorities.

The OMCLs involved in this activity met once in 2020 via videoconference (36th meeting) to evaluate the programme and discuss ways of optimising collaboration. Progress was made on the development of a common risk-assessment model. MRP and DCP product assessment results are now available in the database and will support planning of market surveillance testing activities in the member states.

Official Control Authority Batch Release of biologicals for human use

The Network for 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.

The OCABR human biologicals annual meeting – held virtually on 14 and 15 May in three sessions with a focus on blood products, vaccines and common issues – provided an opportunity to exchange expertise and optimise resources to solve common problems.

In an extension of global co-operation, representatives from the Taiwan Food and Drug Administration (TFDA) and the Krasnoyarsk branch of the Roszdravnadzor OMCL (Russia) participated as observers for the first time in the closed OCABR sessions, based on their respective memoranda of understanding signed with the network in 2019.

In 2020, the OCABR Network signed a new memorandum of understanding on confidential information exchange on batch release activities for vaccines with the Australian Therapeutic Goods Administration (TGA), thus making the TGA an observer and allowing its representatives to participate in the 2021 annual meeting.

Priority activities in 2020 included maintaining regular batch release to ensure a steady supply of essential medicines – such as childhood vaccines and human clotting factors – to the public, together with preparing for the batch release of COVID-19 vaccines. Thanks to early co-ordination within the network, including development of an emergency strategy and careful contingency planning by OMCLs, no impact was seen at the level of batch release carried out in 2020. OMCLs evaluated more than 11 700 final batches and screened around 11 000 plasma pools for safety, thus independently confirming the products' quality before they reached patients.

In addition to the two regular meetings each of the OCABR Advisory Group and the OCABR Vaccine Drafting Group, numerous ad hoc meetings were held with the Advisory Group and involved OMCLs, as well as meetings with stakeholders from industry and other organisations, such as the Coalition for Epidemic Preparedness Innovations (CEPI) and WHO, to foster exchange and define strategies in preparation for OCABR of COVID-19 candidate vaccines. This resulted in the establishment of tools such as guidance for early method transfer in emergencies and a competency list provided to manufacturers to help them identify OMCLs to carry out OCABR. Further activities, including the development of three critical product-specific guidelines, are highlighted in the section "EDQM initiatives in the context of COVID-19" (page 11).

In addition, three new and 31 revised guidelines for vaccines came into force in 2020, as did a revision to the EU Administrative Procedure for OCABR.

A workshop to foster harmonised testing for the safety of oral polio bulks was maintained in November for OMCLs and manufacturers in a virtual format, and resulted in recommendations for improved guidance to be submitted to WHO.

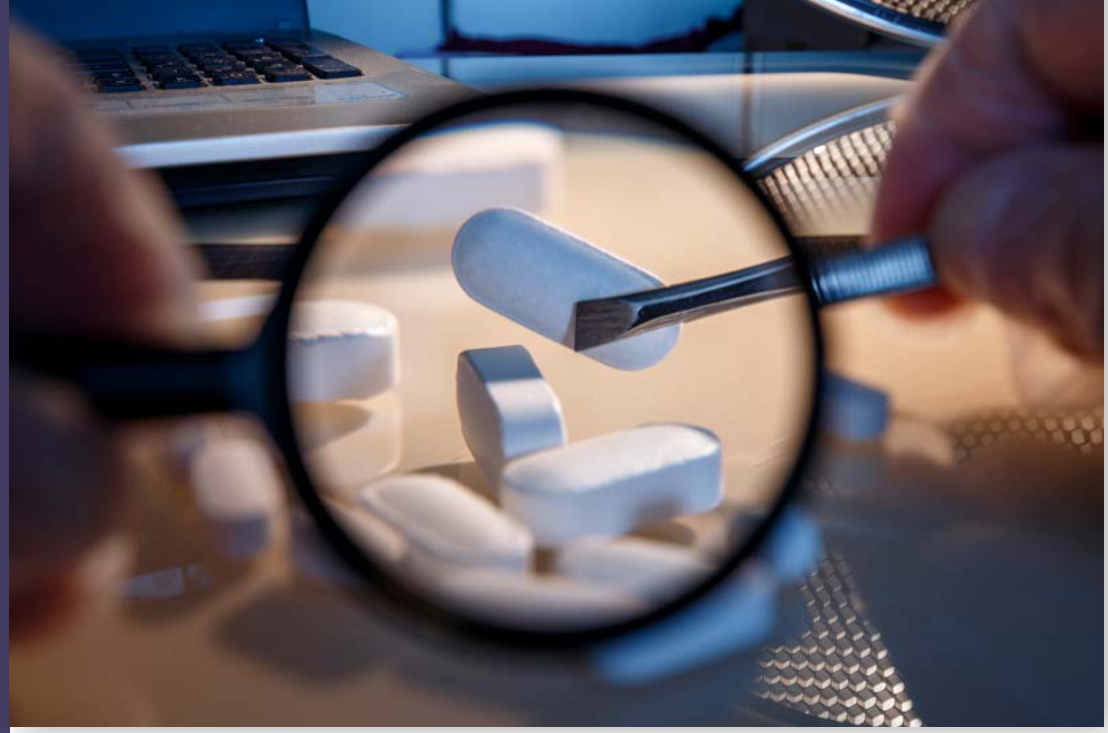
The EDQM supported the human OCABR Network and stakeholders for the post-Brexit transition through surveys and communication on dedicated pages of the EDQM website.

Official Control Authority Batch Release of immunological veterinary medicinal products

A subset of specialised OMCLs, together with NCAs, 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.

The Veterinary Batch Release Network (VBRN) Advisory Group met twice during the year to advance important issues and held additional ad hoc meetings to deal with urgent topics related to COVID-19 emergency resource management and the establishment of related tools, which were communicated to the VBRN members. The regular Official Batch Protocol Review (OBPR) and OCABR activities for IVMPs were largely unaffected thanks to the OMCLs' effective planning. On the advice of the Advisory Group and with the agreement of the network, the 2020 annual meeting was replaced with different written procedures and the regularly scheduled elections for the Advisory Group were postponed to 2021, due to restrictions imposed during the COVID-19 pandemic.

The pilot phase to better co-ordinate activities for post-marketing surveillance was extended with the contribution of data from four OMCLs in 2020.



THE EDQM'S RESPONSE TO NITROSAMINE CONTAMINATION

In line with its mandate to promote and protect public health in Europe by ensuring access to good quality medicines and healthcare, the EDQM has been working actively at various levels to address the issue of nitrosamine contamination since 2018, when *N*-nitrosodimethylamine (NDMA) and *N*-nitrosodiethylamine (NDEA) were detected in certain active substances and medicines. It regularly informs all stakeholders, from national authorities to manufacturers, on the state of the works and on initiatives taken.

The EDQM has also been **co-operating continually with regulatory authorities at international and EU level**. Details of EDQM initiatives concerning nitrosamine contamination can be found below. Information and updates are regularly published on the EDQM's dedicated web page.[22]

22. See https://go.edqm.eu/Nitrosamines.

Ph. Eur. strategy

Revising relevant Ph. Eur. monographs to add limits for *N*-nitrosamine impurities

On 2 April 2019, the European Commission adopted a legally binding decision on nitrosamine impurities in medicines[23] containing the five active substances initially concerned (valsartan, candesartan, irbesartan, losartan and olmesartan).

In response, the Ph. Eur. Commission decided to revise the corresponding monographs. Published in the 10th Edition of the Ph. Eur. in June 2019 and in force as of 1 January 2020, the five revised Ph. Eur. monographs – *Candesartan cilexetil (2573)*, *Irbesartan (2465)*, *Losartan potassium (2232)*, *Olmesartan medoxomil (2600)* and *Valsartan (2423)* – include the interim limits for these impurities (NDMA and NDEA) described in the Annex to the European Commission decision. These interim limits were applicable for a two-year transitional period, during which batches containing NDMA or NDEA above the interim limits, or both nitrosamines at any quantifiable level, were not to be allowed on the market.

On 13 November 2020, the EMA announced that its human medicines committee (CHMP) had aligned recommendations for limiting nitrosamine impurities in sartan medicines with recommendations it had issued for other

23. European Commission, Decision No. (2019)2698, *Official Journal of the European Union*, C180 24.05.2019, https://go.edqm.eu/OJC18020190524.

classes of medicines.[24] The main change concerned the limits for nitrosamines: where they previously applied to active substances, they applied instead to the medicinal products, as sources of nitrosamine contamination in medicines other than by the API had been identified in the meantime.

The Ph. Eur. Commission decided to adapt its strategy accordingly and further revised the monographs on the five active substances initially concerned by deleting the texts under the "Test" section and rewording the "Production" section. The revised monographs will be published in the Ph. Eur. Supplement 10.6 (July 2021).

The Ph. Eur. Commission also decided not to pursue the revision of the general monograph *Substances for pharmaceutical use (2034)*, as initially proposed in *Pharmeuropa* 32.1. This general monograph will still be revised, but the wording will be reviewed to align it with the CHMP's latest recommendations. The general monograph *Pharmaceutical preparations (2619)* will also be revised. The two revised general monographs will be published in *Pharmeuropa* for public enquiry in 2021.

Ph. Eur. general chapter on the analysis of *N*-nitrosamine impurities

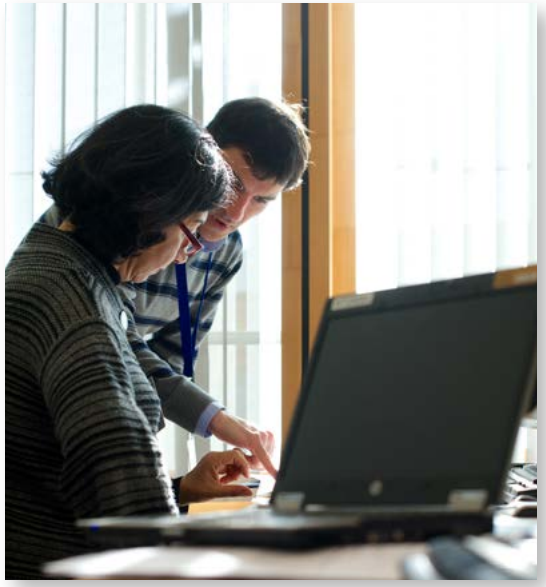
At its 168th session in November 2020, the Ph. Eur. Commission adopted a new general chapter providing analytical procedures to control relevant *N*-nitrosamine impurities in active substances (2.5.42, previously listed as 2.4.36).[25] It is largely based on the work conducted by the OMCL Network (see "OMCLs' work on sampling strategies and testing methods", page 41).

This general chapter should be seen as an analytical toolbox that proposes three procedures relying on sophisticated instruments (GC-MS, LC-MS/MS and GC-MS/MS). It was considered important to include a varied set of procedures using different instruments, thus covering the diverse needs of many quality-control laboratories in Europe and beyond.

The general chapter focuses mainly on the analysis of seven *N*-nitrosamine impurities in the five monographs mentioned above:

- *N*-nitroso-dibutylamine (NDBA);
- *N*-nitroso-diethylamine (NDEA);
- *N*-nitroso-diisopropylamine (NDIPA);
- *N*-nitroso-dimethylamine (NDMA);
- *N*-nitroso-dipropylamine (NDPA);
- *N*-nitroso-ethyl-isopropylamine (NEIPA);
- *N*-nitroso-*N*-methyl-4-aminobutyric acid (NMBA).

Users may apply the given procedures to other substances, however, or to medicinal products after having demonstrated their suitability for the intended purpose with additional validation.



Ph. Eur. reference standards

To support the implementation of the newly adopted Ph. Eur. general chapter on the analysis of *N*-nitrosamine impurities in active substances, seven reference standards were established in 2020 (*N*-nitroso-dibutylamine, *N*-nitroso-diethylamine, *N*-nitroso-diisopropylamine, *N*-nitroso-dimethylamine, *N*-nitroso-dipropylamine, *N*-nitroso-ethyl-isopropylamine and *N*-nitroso-*N*-methyl-4-aminobutyric acid) to cover the impurities mentioned above.[26] They are available from the EDQM.

24. EMA, "Nitrosamines: EMA aligns recommendations for sartans with those for other medicines", op. cit.

25. EDQM, "Ph. Eur. Commission adopts a new general chapter for the analysis of *N*-nitrosamine impurities", op. cit.

26. EDQM, "Seven new reference standards available for the analysis of *N*-nitrosamine impurities", op. cit.

Action on CEPs

Contacting all CEP holders concerned

In September 2019, the EMA initiated a review under EU Article 5(3) of Regulation (EC) No. 726/2004 for human medicinal products containing active substances manufactured by chemical synthesis; in June 2020, the scope of the review was extended to include all chemical and biological human medicines.

The EDQM therefore issued a similar call for review to CEP holders in October 2019 and took the opportunity to remind any CEP holders, through this extension of scope in June 2020, to fulfil their responsibilities before the end of July 2020 in this regard if they had not already done so.[27] The data collected is currently being assessed, with priority being given to high-risk substances.

Reviews of CEPs for active substances

The EDQM applies the principles laid down in the CHMP Opinion for the Article 5(3) of EU Regulation (EC) No. 726/2004[28] and the acceptable intakes published by the EMA for NDMA, NDEA and other nitrosamines to support its assessment of the control strategies proposed by manufacturers of active substances covered by CEPs and to ensure the appropriate limits are being applied whenever necessary.

Irrespective of the substance, **all new or renewed CEPs granted since the beginning of 2019 have been subject to the evaluation of the presence of nitrosamines.** The limits are based on the acceptable intakes for nitrosamines listed by the EMA. If no such limit is described in these CEPs, either the risk was considered to be nil or, if a risk was identified, the manufacturing process includes appropriate controls to ensure that these impurities are not present in the active substance and data to demonstrate this absence has been provided to the EDQM.

The EDQM continues to ensure that this assessment is performed for any revisions to a CEP manufacturing process in which the synthetic route or sourcing strategy has been modified. In addition, any changes to the regulatory decisions and/or Ph. Eur. monographs are taken into account during the CEP assessment procedure.

Specific reviews of CEPs for several active substances, notably ranitidine hydrochloride, metformin and rifampicin, were also launched after nitrosamine impurities were detected in medicinal products containing them.

Ranitidine hydrochloride – All CEPs for ranitidine hydrochloride are currently suspended, as the EDQM was informed of the presence of low levels of NDMA in medicinal products containing this active substance. Remedial action is ongoing and the CEPs will only be restored once it is complete.

Metformin – The EDQM reviewed the CEPs for this active substance and concluded that the presence of nitrosamines was not related to the active substance but to the medicinal product: no action has therefore been taken with regard to CEPs for metformin.

Rifampicin – The presence of nitrosamine impurities in this active substance is still under investigation and appropriate action will be taken as necessary.

Controls for nitrosamine impurities have also been introduced on some CEPs. This step was taken after review and assessment of the different synthesis routes used for the corresponding substances and the data provided by the CEP holders.

CEPs for sartan active substances

Today, all of the currently valid CEPs for the five sartans containing a tetrazole structure comply with the requirements of the respective Ph. Eur. monographs, including with the newly revised monographs adopted by the Ph. Eur. Commission in November 2020.

Conducting GMP inspections of manufacturing sites for the APIs concerned

The EDQM has continued to play an active role in the inspection programmes for API manufacturers, including re-inspections of manufacturing sites of sartan APIs to confirm that appropriate measures regarding the manufacturing process and GMP have been taken.

International co-operation

In addition, the EDQM has co-operated continuously with regulatory authorities at national, international and EU level on this issue and will continue to do so to ensure

27. EDQM, "Announcement to all CEP holders for synthesised APIs regarding presence of nitrosamines", https://go.edqm.eu/News0632019.
28. EMA, Article 5(3) opinions, https://go.edqm.eu/ECReg7262004. See "Nitrosamine impurities in human medicinal products".

a co-ordinated, harmonised approach to decision-making and the implementation of decisions. Moreover, the EDQM will also put into practice the recommendations issued as part of the sartans "lessons learnt" exercise.[29]

OMCLs' work on sampling strategies and testing methods

Co-ordinated sampling and testing

In spite of the challenges related to testing nitrosamines, notably the need to develop highly sensitive and independent detection methods, provide broad coverage of *N*-nitrosamines and test different types of APIs and medicinal products, the OMCL Network, co-ordinated by the EDQM, developed analytical procedures for the determination of NDMA, NDEA, NDIPA, NEIPA, NDBA, NMBA (derived from the use of *N*-methylpyrrolidone) and 1-methyl-4-nitrosopiperazine (MeNP, an impurity found in certain rifampicin samples).

These allowed all members of the European Network of OMCLs with the necessary equipment at their disposal to ensure efficient and targeted controls of medicinal products at risk of containing nitrosamine contaminants. This was a crucial step in providing strong technical support to regulatory authorities.

An overview of publicly available methods developed by the OMCL Network and partner, organisations can be found on the EDQM website.[30]

The analytical procedures of the OMCL Network/EDQM were also used as a starting point for the development of general methods for the Ph. Eur. (see "Ph. Eur. strategy", page 38). The methods used by the OMCLs and international regulatory laboratories from other regions are currently being compared in an inter-laboratory study.

The original purpose of testing activities was to measure levels of contamination in active substances and medicinal products of the sartan class following quality defect alerts and to analyse samples received from targeted GMP inspections. The OMCLs have also actively contributed to the root cause analysis of "nitrosamine cases" (for example, in metformin medicinal products).

In this context, the OMCL Network, with the support of the EDQM, has developed a common format for communicating sampling plans and testing results among participating laboratories.

In the meantime, proactive market surveillance testing of at-risk APIs and medicinal products has been initiated at national and network level (for example, CAP Sampling and Testing Programme).

The data generated by the network are shared on a regular basis with the European Medicines Regulatory Network (EMRN) and international regulators.

29. EMA, "Lessons learnt from presence of *N*-nitrosamine impurities in sartan medicines", op. cit.

30. See Ad hoc projects of the OMCL Network, www.edqm.eu/en/ad-hoc-projects-omcl-network.

ANTI-FALSIFICATION ACTIVITIES

Combating pharmaceutical crime to protect public health

The EDQM continued to promote co-operation among authorities at national and international level in the fight against falsified medical products (medicines and medical devices) and related crimes, as covered by the Council of Europe's MEDICRIME Convention,[31] the first and only binding criminal law instrument to address the falsification of medical products at international level.

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 EDQM continued its close co-operation with the Council of Europe Criminal Law Division of the Directorate General Human Rights and Rule of Law in promoting the MEDICRIME Convention. These awareness-raising activities complement the practical activities of the OMCL Network throughout the participating states (see "OMCL Falsified Medicines Working Group", page 34).

31. Council of Europe Convention on the Counterfeiting of Medical Products and similar Crimes involving Threats to Public Health, CETS No. 211.

Key facts

By the end of 2020, the MEDICRIME Convention had been ratified by 18 countries and signed by another 14. The convention's Committee of the Parties held its third plenary meeting in December 2020 and invited both the Chair of the CMED Committee and the EDQM to present their activities. The Committee of the Parties will play an important role in monitoring implementation of the convention by the states parties.

An example of the EDQM's support of the MEDICRIME Convention is the promotion of co-operation between relevant authorities through the Network of Single Points of Contact (SPOCs). This network of experts from health authorities, customs and law-enforcement agencies and other competent authorities at local, national and international level enables the sharing and collecting of information and data on falsified products. The support and maintenance of this network is an integral part of the CD-P-PH/CMED work programme.

The COVID-19 pandemic affected the CD-P-PH/CMED regular training programme. Two workshops planned for 2020 to raise awareness on issues of falsified medical products and promoting co-operation had to be cancelled – one for GDP, GMP and Pharmacy Inspectors, and one for police, health and customs officers. Instead, the committee made extensive use of virtual meetings to share information on new

emerging risks due to COVID-19 and issued a statement on the EDQM website.[32]

As a follow-up to a 2019 workshop focusing on enforcement action against illegal activities regarding borderline products, the informal expert network was invited to an online meeting in December 2020. The impact of the COVID-19 pandemic was high on the agenda, but further discussions took place on the future and needs of this network. Some 40 participants from 23 countries attended. A follow-up workshop is planned for 2021.

Mass serialisation systems for medicines

In the context of the implementation of the EU Falsified Medicines Directive, the EDQM continued to support EU member states on specific aspects related to the safety features for the packaging of medicinal products for human use. EDQM experts joined the inspection of the Swedish Medicines Verification Organisation (e-VIS) that was conducted by the competent authority of Sweden. Furthermore, the EDQM continued to participate in the Safety Features Working Group Meeting organised by the European Commission.

32. EDQM, "Impact of COVID-19 crisis – National authorities in Europe report shortages of medical products and increase in illegal activities", https://go.edqm.eu/News0752020.

PUBLICATIONS, DATABASES AND WEBSITE

The EDQM's Know-X database,[33] a secure and restricted tool, stores comprehensive information on individual cases of falsified medical products (medicines and medical devices). The database is a platform for sharing information, which enables health and law-enforcement authorities across Europe to act more rapidly in cases of suspect medical products. It also features a Rapid Alert function allowing users to alert others to new cases in real time. The information provided in the Know-X database also covers the analytical identification of medicinal products and the related follow-up action taken by the competent health or law-enforcement authorities. The CD-P-PH/CMED and the OMCL Falsified Medicines Working Group work together on the maintenance of the database, and continue to work on improvements; they also co-operate in promoting the database and offer training to users.

33. "EDQM Know-X database: www.edqm.eu/en/edqm-know-x-database.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Throughout 2020, representatives of the EDQM took part 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 on the MEDICRIME Convention.

Dedicated discussions with partner organisations, such as the European Commission and WHO, made it possible to combine efforts to better fight the issue of falsified medical products in the context of the COVID-19 pandemic.

PHARMACEUTICALS AND PHARMACEUTICAL CARE

Optimal use of medicines for improving patients' quality of life

The European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) is in charge of activities in the area of safe medication use and patient care, supported by 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

Resolution CM/Res(2020)3 on the implementation of pharmaceutical care for the benefit of patients and health services was adopted by the Committee of Ministers of the Council of Europe on 11 March 2020.[34] This resolution defines a framework to promote and implement the concept of pharmaceutical care in health systems at national level with a view to advancing patient-centred care, supporting medicine optimisation and encouraging responsible use of resources.

On 25 November 2020, a webinar on this resolution was held to raise awareness and promote the implementation of pharmaceutical care in national healthcare systems. The webinar illustrated the content of the resolution and provided some practical examples of how pharmaceutical care activities can be implemented in daily practice at national level. More than 270 participants from 35 countries took part in the event, representing NCAs, healthcare professionals and academia.

Another way to promote the implementation of pharmaceutical care is to develop further technical guidance. Progress was made throughout 2020 on the drafting of guidelines

Pharmaceuticals and pharmaceutical care in 2020

- adoption of **Resolution CM/Res(2020)3** on the implementation of pharmaceutical care for the benefit of patients and health services, in March 2020
- ongoing work on the drafting of a guidance document to harmonise the medication review process and on the revision of **Resolution ResAP(2007)2** on good practices for distributing medicines via mail order
- annual recommendations on the classification of medicines and their supply conditions
- regular updates of the **Melclass database**

34. EDQM, "New Council of Europe resolution to promote pharmaceutical care in Europe", https://go.edqm.eu/News0222020.

to harmonise the medication review process across Europe in different care settings and for various target patient groups. The guidelines will optimise the use of medicines, improve patient safety and patient health outcomes.

Significant progress was also made on the revision of **Resolution ResAP(2007)2** on good practices for distributing medicines via mail order which protect patient safety and the quality of the delivered medicine.[35] The revised resolution will provide member states with state-of-the-art recommendations related to the remote dispensation of medicines.

The CD-P-PH/PHO issued its annual recommendations on the classification of medicines and their supply conditions (prescription and non-prescription status). This work is of relevance to health authorities and all stakeholders involved in the medication supply chain in Europe, as it aims to ensure patient safety and accessibility of medicines. These annual recommendations are included in the Melclass database.

The CD-P-PH/PHO also published the outcomes of the survey "New trends as regards the supply modes of medicines", which was conducted in 2019 among the experts participating in the committee's work. The aim of the survey was to gather information about the sale of medicines (with a valid marketing authorisation) in establishments other than community pharmacies and in internet pharmacies, and the impact that this may have on medicine classification practices.

35. See https://go.edqm.eu/QSSres.

PUBLICATIONS, DATABASES AND WEBSITE

Reviews of the classification of medicines

The following reviews of the classification of medicines were published on the EDQM website in the course of 2020:

- corticosteroids for topical use (Anatomical Therapeutic Chemical, ATC, group: D07A);
- other analgesics and antipyretics (ATC group: N02B);
- nasal preparations (ATC group: R01).

Melclass database

The Melclass database (https://melclass.edqm.eu/) contains national information about the classification status and supply conditions of medicines. Throughout 2020, this tool 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.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

Interactions took place in 2020 with international organisations such as the South-Eastern Europe Health Network (SEEHN) and professional bodies active in the field of public health and pharmacy practice, such as the International Pharmaceutical Federation (FIP) and the European Association of Hospital Pharmacists (EAHP). The objective was to align efforts aimed at ensuring safe and appropriate use of medicines in Europe, and in particular to foster implementation of pharmaceutical care in health systems.

European Paediatric Formulary in 2020

- compilation of information on products and extemporaneous preparation of paediatric formulations that may be useful in the treatment of COVID-19 for 4 active substances
- practical evaluation of 2 monographs
- 2 new monographs published for public consultation
- 6 monographs added to the work programme

EUROPEAN PAEDIATRIC FORMULARY

Helping health professionals deliver medicines appropriate for children

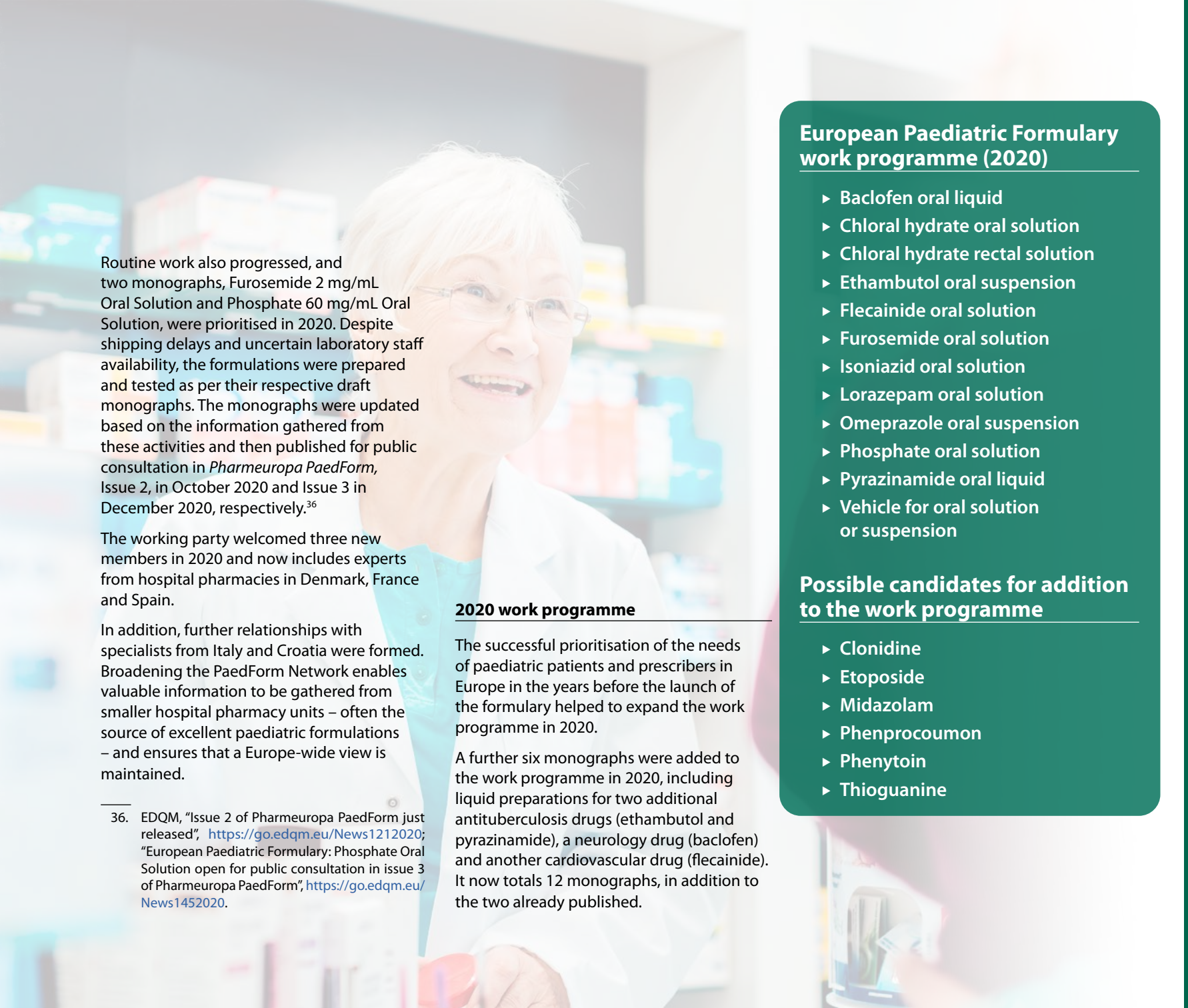
The European Paediatric Formulary (PaedForm) is a freely available, pan-European collection of formulations for extemporaneous preparations that are currently described in national formularies or are already well-established in European countries. Its aim is to give clinicians, pharmacists and healthcare providers access to formulations of appropriate quality, allowing the preparation of medicinal products when no licensed alternative is available on the market.

Key facts and figures

Broad participation

Following its launch in 2019, work on the European Paediatric Formulary continued to progress in 2020 thanks to the dedication of its working party members. Over a third of these members are hospital pharmacists who found themselves overwhelmed by the COVID-19 pandemic.

This first-hand experience prompted the working party to rapidly collate information on products and extemporaneous preparation of paediatric formulations that may be useful in the treatment of COVID-19 for the benefit of individual hospital pharmacists. Initially, information on chloroquine and hydroxychloroquine, drugs that were used in the early phases of the pandemic as experimental treatment, was published in table form. As the pandemic spread and guidance on appropriate treatment options changed, the working party provided updated information. Information on dexamethasone and lopinavir with ritonavir was added and is still being kept up to date, while updating of the information on chloroquine and hydroxychloroquine was stopped (see “EDQM initiatives in the context of COVID-19”, page 12).



Routine work also progressed, and two monographs, Furosemide 2 mg/mL Oral Solution and Phosphate 60 mg/mL Oral Solution, were prioritised in 2020. Despite shipping delays and uncertain laboratory staff availability, the formulations were prepared and tested as per their respective draft monographs. The monographs were updated based on the information gathered from these activities and then published for public consultation in *Pharmeuropa PaedForm,* Issue 2, in October 2020 and Issue 3 in December 2020, respectively.[36]

The working party welcomed three new members in 2020 and now includes experts from hospital pharmacies in Denmark, France and Spain.

In addition, further relationships with specialists from Italy and Croatia were formed. Broadening the PaedForm Network enables valuable information to be gathered from smaller hospital pharmacy units – often the source of excellent paediatric formulations – and ensures that a Europe-wide view is maintained.

36. EDQM, "Issue 2 of Pharmeuropa PaedForm just released", https://go.edqm.eu/News1212020; "European Paediatric Formulary: Phosphate Oral Solution open for public consultation in issue 3 of Pharmeuropa PaedForm", https://go.edqm.eu/News1452020.

2020 work programme

The successful prioritisation of the needs of paediatric patients and prescribers in Europe in the years before the launch of the formulary helped to expand the work programme in 2020.

A further six monographs were added to the work programme in 2020, including liquid preparations for two additional antituberculosis drugs (ethambutol and pyrazinamide), a neurology drug (baclofen) and another cardiovascular drug (flecainide). It now totals 12 monographs, in addition to the two already published.

European Paediatric Formulary work programme (2020)

- Baclofen oral liquid
- Chloral hydrate oral solution
- Chloral hydrate rectal solution
- Ethambutol oral suspension
- Flecainide oral solution
- Furosemide oral solution
- Isoniazid oral solution
- Lorazepam oral solution
- Omeprazole oral suspension
- Phosphate oral solution
- Pyrazinamide oral liquid
- Vehicle for oral solution or suspension

Possible candidates for addition to the work programme

- Clonidine
- Etoposide
- Midazolam
- Phenprocoumon
- Phenytoin
- Thioguanine

PUBLICATIONS, DATABASES AND WEBSITE

The year 2020 started with the registration of over 100 new users of the PaedForm online platform in January, following its launch at the end of 2019.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

The EDQM maintained its link with the Paediatric Committee (PDCO) of the EMA. This link is vital in shaping the work programme because it makes it possible to prioritise monographs for products for which there is a current and/or foreseen unmet need. This ensures that the European Paediatric Formulary complements licensed medicines for use in the paediatric population.

The EDQM continues its efforts to maintain and develop existing partnerships with national formularies, hospital pharmacies and universities, and to make new connections with other stakeholders.

QUALITY AND SAFETY OF SUBSTANCES OF HUMAN ORIGIN

Throughout 2020, the EDQM 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.

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. They 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 steering committee for blood transfusion activities at the EDQM; it elaborates guidelines and recommendations, supports their implementation and oversees the tasks of its subordinate working groups.

Blood transfusion activities in 2020

- Publication of the **20th edition** of the *Guide to the preparation, use and quality assurance of blood components*
- **B-PTS programme continued:** 6 studies performed
- **Conference** entitled "Keeping up with Reality and Quality: A Challenge for European Blood Establishments"

Key facts and figures

The year 2020 saw the publication of the 20th edition of the *Guide to the preparation, use and quality assurance of blood components* (Blood Guide). In this edition, the pre-existing "Principles" and "Standards" sections were merged, an evolution favoured by users that will facilitate its use as standards are now better identified.

The EDQM continued to run the Blood Proficiency Testing Scheme (B-PTS) and the Blood Quality Management (B-QM) programmes to support blood establishments (BEs) in implementing EU blood legislation, as well as the principles laid out in the Blood Guide and the Good Practice Guidelines (GPGs). Both programmes have been co-funded by the European Commission and the EDQM since 2010.

Blood Proficiency Testing Scheme

The **B-PTS Programme** is a form of external quality assessment. Participation in the scheme provides BE laboratories with an objective means of assessing and demonstrating the reliability of their testing procedures.

Six studies were organised in 2020 with an average of 51 laboratories participating in each. Despite the impact of the COVID-19 pandemic on transportation, shipments necessary for B-PTS studies were prioritised, enabling BEs to continue releasing blood that meets quality and safety requirements.

Nucleic Amplification Technique (NAT)

B-PTS050 HBV, HCV, HIV

Serology

B-PTS051 anti-HCV
B-PTS052 anti-HIV/p24
B-PTS053 anti-Treponema
B-PTS054 HBsAg/Anti-HBc

Immuno-haematology

B-PTS055 ABO, Rhesus, Kell, extended phenotyping and irregular antibodies

▶ *B-PTS studies conducted in 2020*

Blood Quality Management Programme

The **B-QM Programme** is an education and assistance programme aimed at supporting European BEs in developing, implementing and improving their QMS, taking into account the specificities of the blood transfusion field.

The B-QM Programme delivers:

- on-site training/assessment schemes, including Blood Training Visits (B-TVs);
- Blood Mutual Joint Visits (B-MJVs);
- and Blood Mutual Joint Audits (B-MJAs);
- learning tools, including training courses, conferences and practical guidance.

Only one on-site B-MJV was conducted in 2020 as a result of the COVID-19 pandemic.

Blood Supply Contingency and Emergency Plan

With a view to strengthening national and EU level plans to ensure the continuity of blood supply in emergency situations – a topic most relevant given the challenges faced in 2020 – the EDQM initiated the **Blood Supply Contingency and Emergency Plan (B-SCEP)** project, holding the first meeting of the B-SCEP working group in September. Recommendations, including strategies that can be expanded into concrete plans, and guidance will be issued in 2021.

Romanian Blood System reorganisation project

A new Delegation Agreement was signed between the EDQM and European Commission/DG REFORM in 2020, entrusting the EDQM with co-ordinating the reorganisation of the Romanian Blood System, including both the Romanian blood transfusion service and its regulatory oversight. The project started on 1 October and is scheduled to last 26 months maximum.

The project objective is to enable the country to ensure access to safe and high-quality blood components and to meet national needs for blood components by building a well-designed, fit-for-purpose and implementable model for a restructured national blood system which meets EU blood legislation requirements and Council of Europe/EDQM standards.

General matters and policies

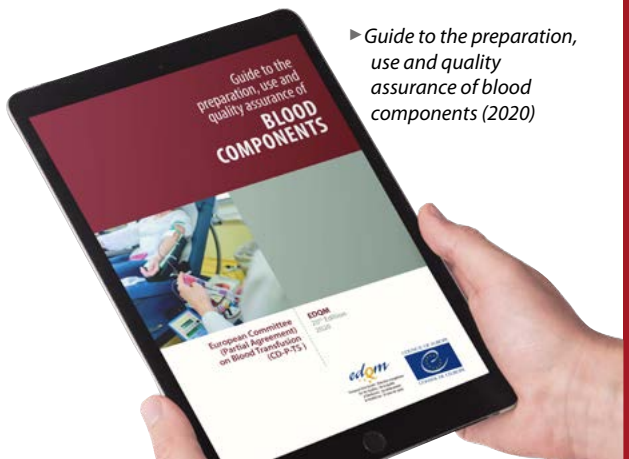
Risk behaviours with an impact on blood donor management and transfusion safety

As required by Resolution CM/Res(2013)3,[37] a dedicated working group is responsible for the continuous collection of data on the incidence and prevalence of sexually transmitted infections that might impact the safety of transfusions. This working group has compiled and published a compendium of deferral policies applied by member states to donors displaying behaviour that creates risks for the safety of transfusion.

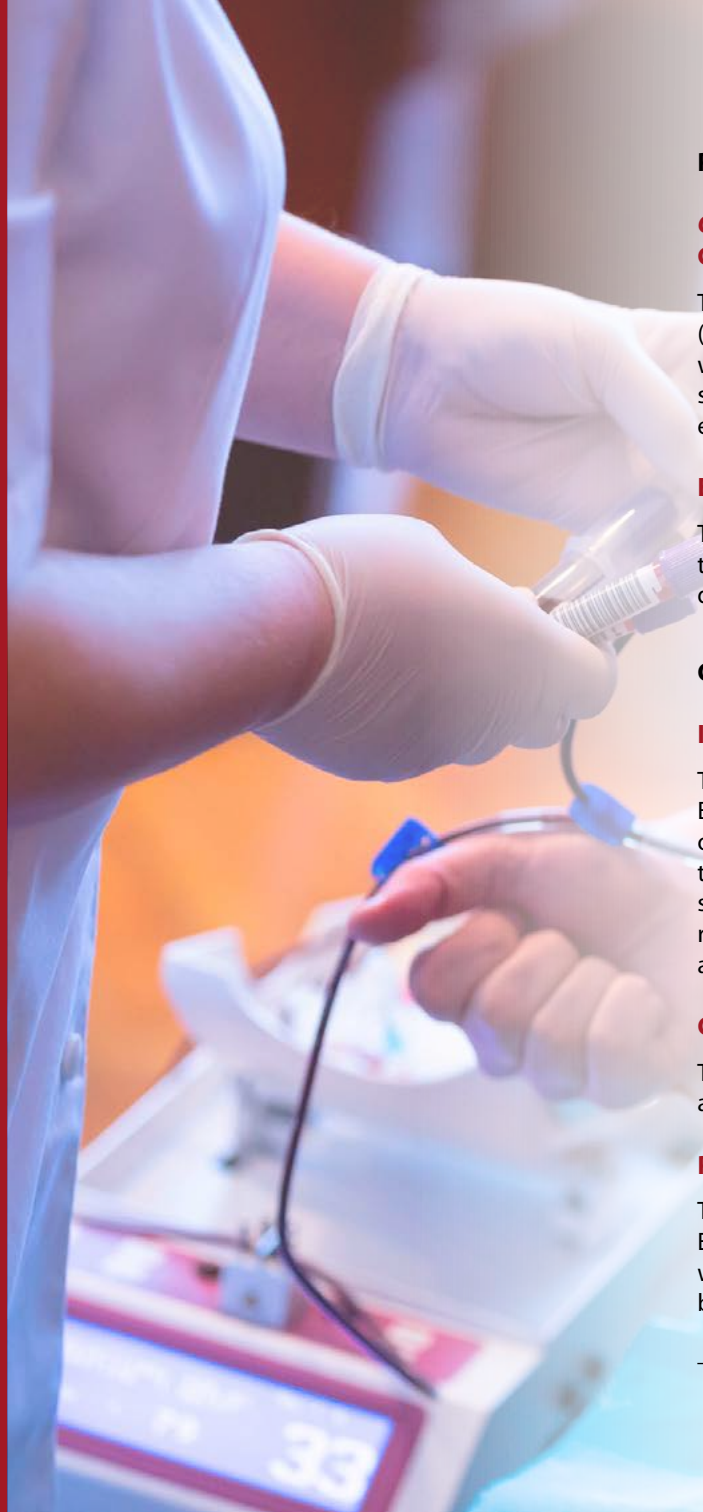
Eligibility criteria for convalescent plasma donors

In the light of the COVID-19 pandemic, the CD-P-TS decided to create a new working party to elaborate eligibility criteria for convalescent plasma donors.

37. Resolution CM/Res(2013)3 on sexual behaviours of blood donors that have an impact on transfusion safety, available at https://go.edqm.eu/BTrec.



▶ *Guide to the preparation, use and quality assurance of blood components (2020)*



PUBLICATIONS, DATABASES AND WEBSITE

Guide to the preparation, use and quality assurance of blood components, and Good Practice Guidelines

The 20th edition of the *Guide to the preparation, use and quality assurance of blood components*[38] (commonly referred to as the "Blood Guide") was published in May 2020. A dedicated working group is entrusted with updating the Blood Guide and keeping it in line with scientific developments and regulatory changes in the periods between consecutive editions of the guide.

European database of frozen blood units of rare blood groups

The European database of frozen blood units of rare blood groups is fully operational and continued to support BEs looking for blood with rare phenotypes for patients in need of a transfusion. To date, six BEs have voluntarily contributed their lists of frozen units of rare blood groups.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

International blood conference

The conference "Keeping up with Reality and Quality: A Challenge for European Blood Establishments", held as a series of webinars from 27 to 29 October, celebrated 10 years of co-operation between the EDQM and the European Commission in the field of blood transfusion and provided a forum to assess current challenges in securing sustainable blood supplies and a resilient blood transfusion sector in Europe. The proceedings, including recommendations and conclusions, will be issued in 2021 (see "2020 – A year rich in events and meetings", page 70).

Co-operation with the European Commission

The EDQM continued to participate as an observer in the 2020 meetings of the EU competent authorities for blood, which are organised by the European Commission.

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

The EDQM was invited to join the group responsible for revising the "PIC/S GMP Guide for Blood Establishments". As an outcome of this collaboration, the revised document published by PIC/S was harmonised with the text of the Good Practices Guidelines of the Blood Guide, published by the EDQM/Council of Europe, a hallmark for international harmonisation.

38. See https://freepub.edqm.eu/publications/AUTOPUB_48/detail.

ORGAN TRANSPLANTATION AND TISSUES AND CELLS FOR HUMAN APPLICATION

Promoting strict quality and safety standards

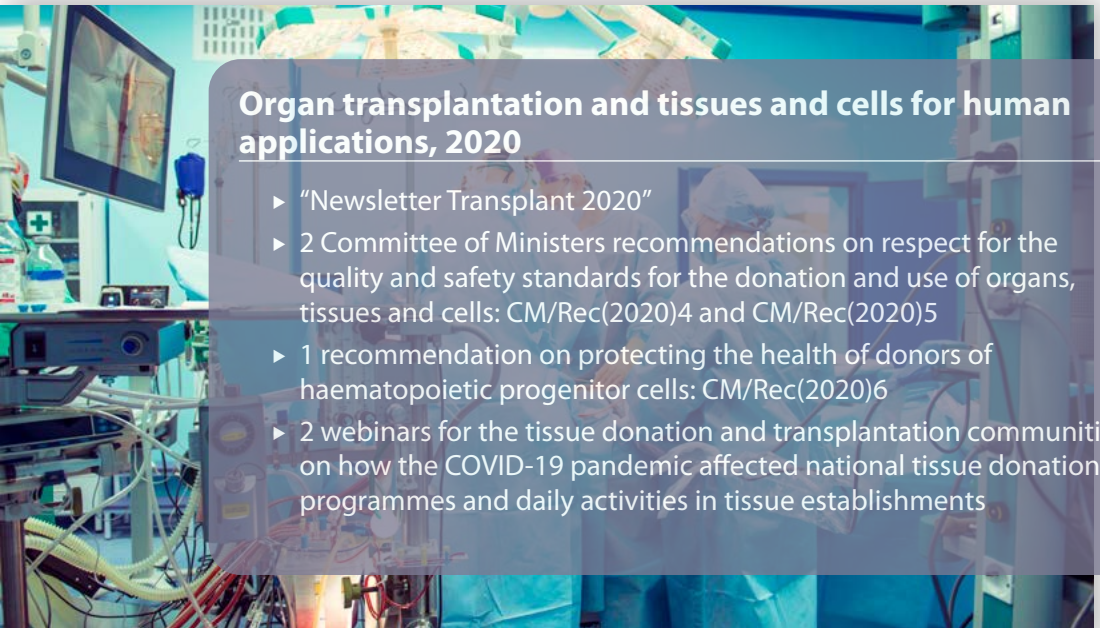
The European Committee on Organ Transplantation (CD-P-TO) is the steering committee responsible for transplantation activities at the EDQM. Its mandate includes drafting guidelines and recommendations aimed at improving access to transplants, establishing strict safety, quality and ethical standards for organ transplantation, collecting international data, monitoring practices in Europe and contributing to the fight against organ trafficking.

Key facts and figures

In 2020, the **Committee of Ministers of the Council of Europe** adopted several recommendations that had been drafted by the CD-P-TO. Recommendations CM/Rec(2020)4[39] and CM/Rec(2020)5[40] called on member states to ensure that **quality and safety standards for the donation and use of organs, tissues and cells** are respected in accordance with the technical guides published by the EDQM.[41] With these guides, the EDQM supports health professionals and health authorities with the latest scientific information and contributes to making Europe both a world leader in transplantation and a model for international co-operation in the sector. The adoption of these recommendations represents an acknowledgment of the important work carried out by the EDQM in this area and provides the CD-P-TO and relevant ad hoc working groups with the legal basis to continue drafting and updating these guides.

In addition, the Committee of Ministers also adopted a recommendation[42] calling on member states to take measures to protect the health of donors of **haematopoietic progenitor cells**. This text provides guidance for the screening and evaluation of potential donors, short- and long-term post-donation follow-up, and highlights the need to collect data to enable professionals to learn from experience and maximise the safety of future donors.

39. Recommendation CM/Rec(2020)4 on the quality and safety of organs for transplantation, available at https://go.edqm.eu/CMRec20204.
40. Recommendation CM/Rec(2020)5 on the quality and safety of tissues and cells for human application, available at https://go.edqm.eu/CMRec20205.
41. "Guide to the quality and safety of tissues and cells for human application"; "Guide to the quality and safety of organs for transplantation". More information available at https://go.edqm.eu/OTg.
42. Recommendation CM/Rec(2020)6 on establishing harmonised measures for the protection of haematopoietic progenitor cell donors, available at https://go.edqm.eu/CMRec20206.



Organ transplantation and tissues and cells for human applications, 2020

- "Newsletter Transplant 2020"
- 2 Committee of Ministers recommendations on respect for the quality and safety standards for the donation and use of organs, tissues and cells: CM/Rec(2020)4 and CM/Rec(2020)5
- 1 recommendation on protecting the health of donors of haematopoietic progenitor cells: CM/Rec(2020)6
- 2 webinars for the tissue donation and transplantation communities on how the COVID-19 pandemic affected national tissue donation programmes and daily activities in tissue establishments

The CD-P-TO and its relevant subordinate bodies continued to develop and promote programmes and projects aimed at disseminating best practices in the fight against transplant-related crimes in 2020. In the context of Council of Europe Resolutions CM/Res(2013)55[43] and CM/Res(2017)2,[44] 34 member states have designated National Focal Points (NFPs) in charge of regularly collecting data on patients who travelled abroad for transplantation. This information is essential to gain better knowledge of this phenomenon and to ensure that the same principles of transparency, traceability and continuity of care provided to patients having received an organ transplant in their country apply to those transplanted abroad. Data exchange at international level is shedding light on unethical transplantation practices, their long-term outcomes and their potential risks for both individuals and public health. It is also enabling possible transplant tourism hotspots to be identified. Ultimately, this exercise lays the factual basis needed to provide comprehensive information on these matters, supports the drafting of recommendations at national and international level and fosters interagency co-operation to address transplant-related crimes. The Network of NFPs met virtually in November 2020. At this meeting, the data submitted to the EDQM International Database on Travel for Transplantation was discussed. It emerged that some member states seemed to be destinations for potentially unethical transplant procedures, requiring careful investigation by both the patients' countries of origin and their countries of destination.

An important milestone for the Council of Europe Convention against Trafficking in Human Organs[45] was reached in 2020. The ratifications of Switzerland and Spain (the 10th and 11th, respectively) signify that the Committee of the Parties for this convention will have to be convened within one year. This committee will be responsible for monitoring the implementation of the convention using a multisector and multidisciplinary approach and will facilitate the collection, analysis and exchange of information, experience and good practice between states to improve their capacity to prevent and combat trafficking in human organs.

Maintaining a safe, sufficient and accessible supply of critical and essential tissues for human application during the COVID-19 pandemic and working towards a gradual return to the "new normal" is of vital importance to public health systems that support donation and transplantation. With this in mind, the EDQM held a series of webinars[46] for the tissue donation and transplantation communities to discuss how the COVID-19 pandemic was affecting national tissue donation programmes and daily activities in tissue establishments. They offered opportunities to exchange ideas on the latest recommendations on testing practices and to support forward-looking decisions, in particular through the application of comprehensive QMSs and a thorough assessment of new risks during all critical steps and procedures in tissue establishments.

► *Newsletter Transplant*

43. Resolution CM/Res(2013)55 on establishing procedures for the collection and dissemination of data on transplantation activities outside a domestic transplantation system, available at https://go.edqm.eu/CMRes201355.
44. Resolution CM/Res(2017)2 on establishing procedures for the management of patients having received an organ transplant abroad upon return to their home country to receive follow-up care, available at https://go.edqm.eu/CMRes20172.
45. CETS No. 216, available at www.coe.int/en/web/conventions/full-list/-/conventions/treaty/216.
46. See https://go.edqm.eu/TOTCtraining.

PUBLICATIONS, DATABASES AND WEBSITE

The "Newsletter Transplant 2020" was published in co-operation with the Spanish National Transplant Organisation (ONT).[47] This publication continues to function as a unique source of official information, allowing the monitoring and benchmarking of practices in member states. It summarises comprehensive information and data from 71 countries worldwide on donation and transplantation activities, management of waiting lists, organ donation refusals and authorised centres for transplantation activities. This publication has become an international reference in the field, supporting policy makers, health professionals and national health authorities.

The International Database on Travel for Transplantation has continued to grow as more countries submit information about patients who travel abroad to receive an organ transplant. New countries not in the Council of Europe have joined the network and new areas of study have been included in the database to better assess the phenomenon of travel for transplantation. This data is analysed on a regular basis by the Network of NFPs on Travel for Transplantation.

47. EDQM, "Newsletter Transplant 2020 now available", https://go.edqm.eu/News1012020.

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

As part of a co-operation agreement between the European Commission and the EDQM, several meetings were organised to achieve key milestones in various projects. These included creating quality and safety standards for tissue establishments, benchmarking post-mortem blood testing practices, training professionals on biovigilance and quality management, harmonising activity data collection in the fields of tissues and cells, and the elaboration of the EU 2019 annual report on serious adverse reactions and events (SARE) in the fields of tissues and cells and blood.

As a way of enhancing co-operation between the two institutions and avoiding duplication of efforts, EDQM representatives attended meetings of EU competent authorities in the fields of organs and of tissues and cells, relevant meetings of expert subgroups and key meetings of relevant EU-funded projects.

Key professional associations in the field of organs, tissues and cells continued to participate in the work of the EDQM, in particular through the drafting of technical guidance and the dissemination of the texts throughout the professional community.

In addition, in the context of the fight against organ trafficking, the Secretariat of the CD-P-TO participated in the drafting of the World Medical Association (WMA) statement on measures for the prevention and fight against transplant-related crimes,[48] which was adopted during the 71st WMA General Assembly on 31 October 2020. This document explicitly calls on governments to accede to the Council of Europe Convention against Trafficking in Human Organs.

48. See https://go.edqm.eu/WMA20201031.

CONSUMER HEALTH

Work related to the co-ordination of market studies and proficiency testing schemes in the area of quality control of cosmetics continued in 2020, relying for this purpose on the European Network of Official Cosmetics Control Laboratories. Efforts to enhance and develop standards in the field of food contact materials continued.

COSMETICS

Monitoring the quality and safety of cosmetic products

The European Committee on Cosmetics and Consumer Health (CD-P-COS) is tasked with responding to emerging health risks 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.[49] Activities on the work programme focus on fostering collaboration between member states and with observers.

The European Network of Official Cosmetics Control Laboratories (OCCLs) contributes to consumer health protection by strengthening market surveillance and the enforcement of European and national regulations by competent authorities. Participation in the activities of the network 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 50 OCCLs follow the network activities, including laboratories from 21 EU member states, 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 co-ordination of the OCCL Network.

49. Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up, https://rm.coe.int/16805d3dc4.

Cosmetics in 2020

- **30 laboratories** participated in the two meetings of the **OCCL Network**.
- **One PTS study on allergenic substances in lotion and shampoo** was carried out and **three more PTSs launched**: phthalates in nail polish and perfume, 1,4-dioxane in bath cosmetic products, isothiazolinones and colorants in bath cosmetic products.
- **One method** was published online for the **determination of polar nitrosamines in cosmetics**. An inter-laboratory study was started for the determination of non-polar *N*-nitrosamines in cosmetics.
- **One MSS on allergens in cosmetic products** was finalised and the MSS on cosmetics for children was continued with the launch of a third round of data collection.

European Committee on Cosmetics and Consumer Health

The CD-P-COS held one videoconference with all its members and observers and took part, along with the European OCCL Network and representatives from the European Commission, in two further videoconferences to anticipate new regulations in Europe for product compliance and market surveillance, and the recently adopted measures restricting the use of chemical substances in tattoo inks.

Protection of healthy volunteers in cosmetics testing

Based on a survey of its members completed in 2019, the CD-P-COS exchanged views on how to improve the protection of healthy volunteers in studies related to the use, quality and effects of cosmetics. Following on from the nine recommendations presented in the survey report, a comprehensive guidance document was drafted for the attention of health authorities, while also taking into account guidelines and regulations already in place at national or European level.

Safe cosmetics for young children

The committee collected proposals for amended safety requirements and recommendations for the risk assessment of cosmetic products for young children. The first edition of this guidance document was released in 2012,[50] and national experts in three member states co-ordinated the preparation of a fully updated, new edition in 2020.

OCCL Network

Asbestos and heavy metals in cosmetics

EU regulations prohibit the use of asbestos and heavy metals such as arsenic, nickel or barium in the production of cosmetic products. Traces of prohibited substances may in some cases be (technically) unavoidable.

Since 2019, the OCCL Network members have been collecting information on the different threshold levels to be applied in quality control of cosmetic products. Manufacturers and other business operators are required to address the presence of substance traces in safety reports and closely monitor their concentration.

Quality control of cosmetics: market surveillance studies

Information on perfume content in cosmetics (such as a "perfume-free" label) is important for consumers, as many fragrances can cause allergic reactions. The OCCL Network completed a Europe-wide market surveillance study to check if perfume-free cosmetic products are as safe as they claim to be. Results showed that 7.7% of samples tested were non-compliant with legislative requirements due to a missing or false declaration of allergenic fragrance compounds and that 3.1% of products marketed as "perfume-free" contained fragrance compounds.[51]

N-nitrosamines in cosmetics

As a way of enabling cosmetics control laboratories to test cosmetic products for the presence of toxic *N*-nitrosamines, a group of four laboratories jointly ran a common test protocol to assess the feasibility and reproducibility of an analytical procedure. Following the positive outcome, the analytical procedure for the determination of polar nitrosamines in cosmetics was published.[52]

Sunscreens

The efficacy of sunscreens is essential to ensure consumer protection in the short and long term. A survey was circulated to investigate strategies for the market surveillance of sunscreens in different countries with the objective of sharing good practices within the OCCL Network and possibly of discussing the need for alternative methods for sun protection factor determination.

Proficiency Testing Scheme studies

Proficiency testing is an essential part of quality management in cosmetics control laboratories and helps to ensure that they produce reliable data and that test results are comparable across Europe.

In 2020, 17 control laboratories participated in a study aimed at assessing their ability to determine the concentration of allergenic substances. Participants had the opportunity to use different analytical techniques, most of them involving GC-MS.

The EDQM joined control laboratories in Austria, Germany and Switzerland to collect and evaluate their proficiency in the determination of hydrogen peroxide in hair dyes and other hair products.

50. See www.edqm.eu/en/list-publications-cosmetic-products-and-tattoo-inks.

51. EDQM, "EDQM reports presence of allergenic fragrances in cosmetics sold as 'perfume-free'", https://go.edqm.eu/News1282020.

52. EDQM, "New method for determination of polar *N*-nitrosamines in cosmetic products", https://go.edqm.eu/News1532020.

PUBLICATIONS, DATABASES AND WEBSITE

The analytical procedure for the determination of polar *N*-nitrosamines in cosmetic products validated within the OCCL Network was published and can be downloaded from the EDQM website for free (see "*N*-nitrosamines in cosmetics", page 59). The method uses liquid chromatography coupled to mass spectrometry.

The EDQM webpages dedicated to the OCCL Network and activities on cosmetics were reviewed to improve visibility and add profiles of several OCCLs.

A summary report on the MSS on allergens in cosmetic products sold as "perfume-free" was published on the EDQM website in December 2020 and the figures on the observed non-compliance rates raised media attention (see "Quality control of cosmetics: market surveillance studies", page 59).

COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

The EDQM regularly exchanged information on market surveillance activities with the working groups of the Platform of European Market Surveillance Authorities for Cosmetics of the European Union (EU PEMSAC).

Representatives of the European Commission attended the sessions of the CD-P-COS and of the OCCL Network.

FOOD CONTACT MATERIALS AND ARTICLES

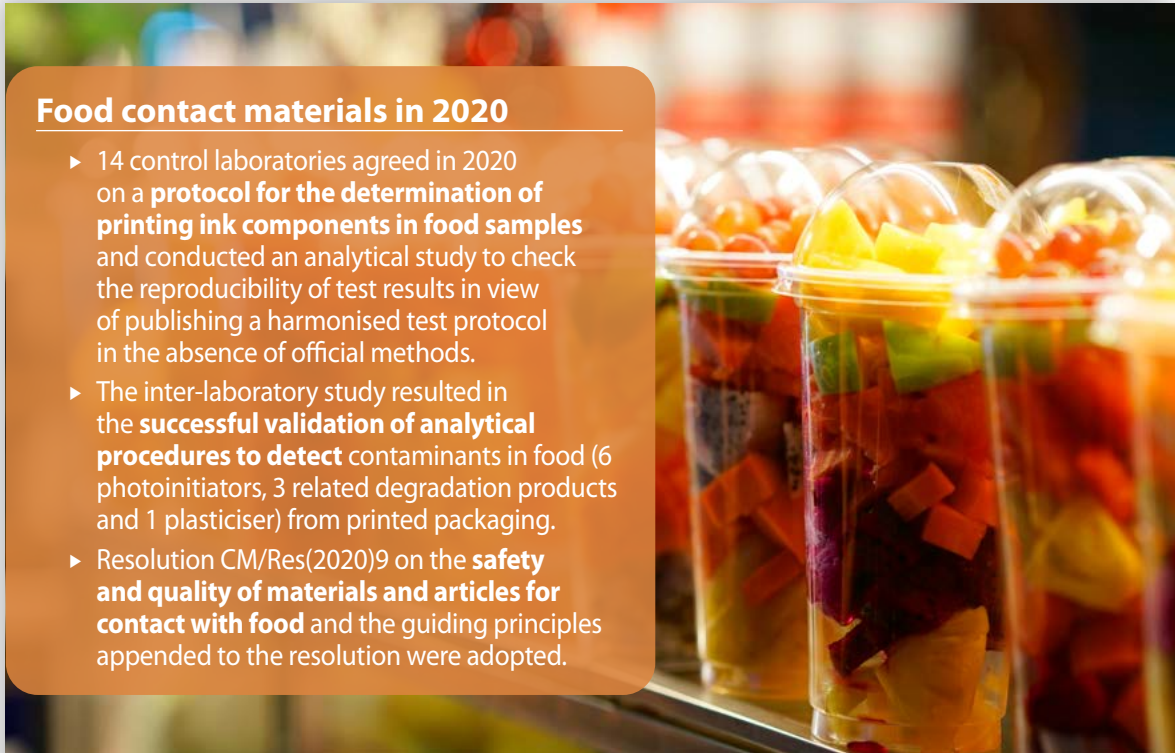
The European Committee for Food Contact Materials and Articles (CD-P-MCA) is tasked with the elaboration of harmonised measures that supplement EU and national legislation to ensure the safety of packaging, containers, utensils and other food contact materials and articles.

Three subordinate working groups support the CD-P-MCA's work: one focuses on food contact materials made from paper and board and the other two on printed food contact materials and on guidance for the preparation of compliance documentation. Nine working group meetings on compliance documentation, enamels, paper and board, and on printing inks were held with the participation of experts from the public and private sectors.

The work programme is aimed at protecting human health across Europe through common quality and safety requirements, as well as through the development and updating of testing methods.

The published technical guides are used as reference documents by manufacturers, safety evaluators and control laboratories.[53]

53. Free EDQM publications are available at https://register.edqm.eu/freepub.



Food contact materials in 2020

- 14 control laboratories agreed in 2020 on a **protocol for the determination of printing ink components in food samples** and conducted an analytical study to check the reproducibility of test results in view of publishing a harmonised test protocol in the absence of official methods.
- The inter-laboratory study resulted in the **successful validation of analytical procedures to detect** contaminants in food (6 photoinitiators, 3 related degradation products and 1 plasticiser) from printed packaging.
- Resolution CM/Res(2020)9 on the **safety and quality of materials and articles for contact with food** and the guiding principles appended to the resolution were adopted.

Key facts and figures

The Council of Europe resolution on food contact materials[54] was adopted in October 2020. The annex to this resolution includes guiding principles for the implementation of suitable policies regarding the safety and quality of materials and articles for contact with food. This resolution will serve as a framework for all technical guidance published by the EDQM on specific food contact materials.

The CD-P-MCA initiated additional work to help business operators ensure compliance with the guiding principles for the quality and safety of food contact materials and applicable regulations.

Technical guidance on paper and board materials and articles was adopted following a stakeholder consultation.

A practical guide for manufacturers and regulators on food contact materials made from metals and alloys was first published in 2013.[55] In view of new scientific evidence and the experience gathered following the first edition of the guide, the CD-P-MCA agreed on amendments proposed by experts from competent authorities, official and private control laboratories and industry for the second edition of the guide, which is currently in preparation.

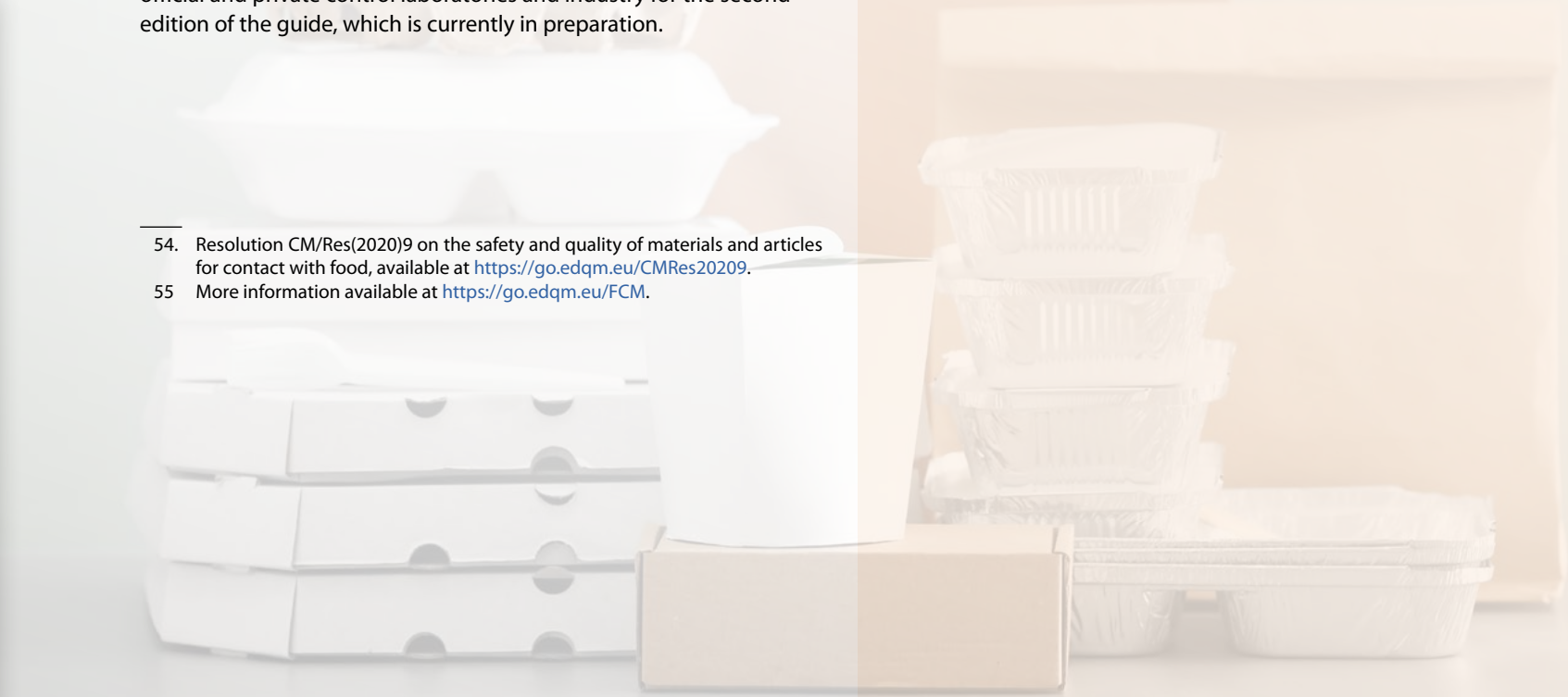
COMMUNICATION WITH PARTNERS AND STAKEHOLDERS

National competent authorities contribute to the elaboration of guidelines, provide expertise and carry out experimental testing.

Throughout 2020, the national experts continued to review resolutions and technical documents elaborated in the past.

The EDQM and national experts joined forces to prepare common rules for selecting the test conditions to be applied in the control of metals and alloys and further materials for food contact. This work is co-ordinated by the Joint Research Centre (JRC) of the European Commission.

The EDQM exchanged views with industry associations, organised stakeholder consultations and held expert meetings on technical provisions and guidance for manufacturers, control laboratories and authorities.



54. Resolution CM/Res(2020)9 on the safety and quality of materials and articles for contact with food, available at https://go.edqm.eu/CMRes20209.
55 More information available at https://go.edqm.eu/FCM.

QUALITY MANAGEMENT SYSTEM

The EDQM continued to invest in its QMS as a matter of priority in 2020, with a specific focus on Ph. Eur. RSs. Following the audits of official certification and accreditation bodies, the EDQM saw the confirmation of its ISO 9001:2015 certificate and was granted accreditation according to ISO 17025:2017. The EDQM is therefore certified for six processes and the EDQM Laboratory is ISO 17025 accredited for 21 tests, including nuclear magnetic resonance spectroscopy (NMR) and quantitative nuclear magnetic resonance spectroscopy (qNMR). The EDQM's customers and interested parties can therefore rest assured of the consistent quality of the goods and services provided by the EDQM, as well as its commitment to not only maintain, but also continuously improve quality standards for all its activities.

CO-OPERATION WITH INTERNATIONAL PARTNERS

The EDQM places high value on its co-operation with a range of international partners for all of its activities. They would be impossible without the support of NPAs, NCAs, OMCLs, inspectorates and more than 2 000 experts in pharmaceutical sciences, as well as specialists in healthcare issues such as blood transfusion and organ transplantation, from around the globe. Similarly, as an integral part of the European regulatory network, the EDQM meets and collaborates regularly with national regulatory authorities and the European Commission, as well as its technical agencies, such as the EMA.

Co-operation with national authorities

Representatives of NCAs are members of the Ph. Eur. Commission and its currently 61 expert groups and working parties. National authorities also take part in the work of the Ph. Eur. by submitting requests for revisions and reviewing draft texts published in *Pharmeuropa online*.

Communication with NPAs was strengthened in 2020 to support authorities in the context of the COVID-19 pandemic, initially by organising weekly meetings, and monthly meetings since after the summer break.

The 2020 annual meeting of the NPAs of Ph. Eur. member states, initially foreseen to take place in Helsinki, was replaced by a virtual meeting (see "The European Pharmacopoeia", page 23).

The GEON Annual General Meeting, originally planned as a face-to-face meeting in Oslo, Norway, was held as a web conference from 12 to 15 May 2020 with a reduced programme (six topic sessions instead of nine). The online format enabled a greater audience to participate with, in all, about 470 participants joining the different sessions during the conference week (see also "The European Network of Medicines Control Laboratories", page 33).

The EDQM also has observer status to the Heads of Medicines Agencies (HMA), the network of the heads of the NCAs whose organisations are responsible for the regulation of medicinal products for human and veterinary use in the European Economic Area, and to its Working Group of Enforcement Officers (WGEO), and is a member of its Working Group of Quality Managers (WGQM).

Involvement in international harmonisation

Globalisation and expansion in international trade have created a growing need to develop global quality standards for medicines. The EDQM has a long-established collaboration with sister pharmacopoeias to harmonise pharmacopoeial monographs. The most prominent example in this area is the Pharmacopoeial Discussion Group (PDG), jointly run with the United States Pharmacopeia (USP) and the Japanese Pharmacopoeia (JP), with WHO and its International Pharmacopoeia as observers.

In addition, the EDQM has played a crucial role in the drafting of a Good Pharmacopoeial Practices guide and its annexes, under the auspices of the WHO International Meeting of World Pharmacopoeias (IMWP) platform since its inception in 2012.

The EDQM represents the Ph. Eur. within these initiatives. All the relevant groups of experts and working parties of the Ph. Eur. are involved (see also "The European Pharmacopoeia", page 22).

The EDQM also participates in the Innovative Medicines Initiative's (IMI) VAC2VAC project by contributing to its Scientific and Ethics Advisory board. The overall objective of the "Vaccine batch to vaccine batch comparison by consistency testing" project is to provide proof of concept of the consistency approach for batch release testing of established vaccines with the target of replacing some of the *in vivo* methods still used to test human and veterinary vaccines. The *in vitro* methods developed and qualified/validated within the initiative may be further evaluated through their inclusion in the Biological Standardisation Programme (BSP) and ultimately included in the Ph. Eur. depending on the outcome of the BSP studies.

In addition, the EDQM continues to play an active role in international harmonisation and collaboration activities and has observer status to the ICH Assembly.

EDQM scientists actively participate in the development and revision of ICH guidelines that are important for the quality of medicines, including ICH guidelines Q3C, Q3D, Q3E, Q2/Q14, Q5A, Q9 and Q13, and play an important role in ICH discussion forums such as the Quality Discussion Group (QDG) and the Generics Discussion Group (GDG).

Participating in the QDG is of particular strategic relevance for the EDQM as this group is a think-tank for matters related to the quality of medicines and respective harmonised guidance for the ICH Management Committee and Assembly.

The same holds true for the EDQM's engagement in the International Pharmaceutical Regulators Program (IPRP), where the EDQM is an observer to the Management Committee and co-chairs the Quality Working Group.

The EDQM is also involved in the veterinary counterpart to the ICH, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for

Veterinary Use (VICH), and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) (see also "Certification of suitability to the Ph. Eur. monographs", page 28, and "Blood transfusion", page 50).

These are an important and valuable part of the EDQM's activities owing to their positive impact on the availability of good quality medicines and healthcare worldwide.

Co-operation with the EU and the EMA

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

It is also a member of the European Union Network Data Board (EUNDB), created at the end of 2014 and co-chaired by the EMA and an NCA, and of the International Standards on Identification of Medicinal Products in the EU (EU ISO IDMP) Task Force (created in 2015), including the corresponding subordinate groups.

The EDQM works closely with the EMA and national authorities to ensure continued consistency with the approaches of licensing authorities, for example regarding the Ph. Eur. and certification activities. It has observer status with a number of EMA bodies, including the Committee for Advanced Therapies (CAT), the Herbal Medicinal Products Committee (HMPC), the joint CHMP/CVMP Quality Working Party (QWP), the Good Manufacturing and Distribution Practice Inspectors Working Group (GMDP IWG), the Biologics Working Party (BWP) and the Immunologicals Working Party (IWP). Members of EMA working groups (for which the EMA provides the secretariat) or of the EMA Secretariat itself are observers to some of the Ph. Eur. Commission's groups of experts and working parties, for example 6B (human blood and blood products), 15 and 15V (vaccines and sera for human use and veterinary use), and the BSP Steering Committee.

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

The EDQM and the EMA continue to collaborate on operating a long-established CAP Sampling and Testing Programme for products for human and veterinary use (see also "The European Network of Medicines Control Laboratories", page 35).

Co-operation on inspections

In 2020, the EDQM's Certification Department continued to be involved in the International API Inspection Programme (co-ordinated by the EMA) and the PIC/S.

The EDQM also participated in the PIC/S Expert Circle on Human Blood, Tissues and Cells in the context of the revision of the "PIC/S GMP Guide for Blood Establishments" and ensured that the revised document published by PIC/S is harmonised with the text of the Good Practices Guidelines of the EDQM *Guide to the preparation, use and quality assurance of blood components* (see also "Blood transfusion", page 50).

Co-operation with WHO

The EDQM co-operates extensively with WHO. In 2020, the EDQM continued to host WHO as an observer to the Ph. Eur. Commission and to collaborate with WHO in a number of joint meetings and consultations, including:

- as an observer to the WHO Programme on International Nonproprietary Names (INNs), because INNs are used in Ph. Eur. monographs;
- participation in the WHO Expert Committee on Biological Standardization (ECBS), with WHO participating as an observer in the meetings of the EDQM BSP Steering Committee, thus guaranteeing a smooth exchange of information;
- participation in the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) (see also "Reference Standards", page 25); and
- the sharing of data and joint inspections relating to the certification process for APIs.

The 11th IMWP took place in February 2020 at the EDQM premises in Strasbourg (France). Over 50 national and regional pharmacopoeial authorities, including the 39 countries represented by the Ph. Eur., renewed their commitment to strengthening their co-operation. Following up on discussions which had taken place at the 10th IMWP, the new framework for exchanging information between the PDG and the IMWP was presented by the PDG. The IMWP participants welcomed the proposal and agreed to run a one-year pilot phase to test this new framework (see above). A white paper on the value of pharmacopoeial standards and the role of pharmacopoeias for health systems was finalised at the meeting with a view to its publication by the WHO Secretariat on behalf of the world pharmacopoeias. The IMWP invited stakeholders to provide feedback on the usefulness of this white paper (see also "The European Pharmacopoeia", page 22).

The EDQM is responsible for the establishment, monitoring and distribution of WHO ISA and ICRS (for more details, see "Reference Standards", page 25).

The EDQM also contributes to the activities of the COVAX Regulatory Advisory Group (RAG),[56] in particular by providing expertise on the testing of COVID-19 vaccines, linked to its activities in the field of batch release (OCABR) and quality assurance in vaccine manufacturing and testing. The Coalition for Epidemic Preparedness Innovations (CEPI), Gavi and WHO co-lead COVAX, with UNICEF as a key delivery partner, to ensure equitable access to COVID-19 vaccines and end the acute phase of the pandemic by the end of 2021.

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

56. See https://epi.tghn.org/covax-overview/regulatory-advisory-group/.

Co-operation with manufacturers and industry associations

The EDQM continues to hold annual bilateral meetings with industry associations to promote exchanges on all aspects related to the work of the EDQM and to collect feedback on its activities. In the context of the health crisis, the EDQM also organised monthly meetings with all European industry organisations to keep them informed about the EDQM's business continuity plan and operating framework, and to discuss how the EDQM could help the pharmaceutical industry ensure a continued supply of quality medicines and support developers of COVID-19-related vaccines and medicines. Since September, these meetings have been organised on a quarterly basis.

2020: A YEAR RICH IN EVENTS AND MEETINGS

With in-person events and meetings ruled out, the EDQM adapted swiftly, using the online technology at hand to transform its scheduled events into virtual ones. This transition had a significant impact on its international outreach and global network. It provided its users and partners worldwide with a new way to interact, learn and get access to the latest information in real time.

EDQM transitions to online events and training due to COVID-19

The year 2020 was exceptionally eventful in the field of public health and the EDQM had a significant role to play.

In total, **45 live webinars** were held, attracting approximately **15 300 participant**s from more than 100 countries.

International conferences

Virtual blood conference: "Keeping up with Reality and Quality: A Challenge for European Blood Establishments" (27-29 October 2020)

This conference, celebrating 10 years of co-operation between the EDQM and the European Commission in the field of blood transfusion, was held as a series of webinars in October. It addressed challenges faced by European BEs, such as the impact of the COVID-19 pandemic, the globalisation of the supplier market place for materials and equipment, the medical device and *in vitro* diagnostics regulations, and the changing scope of practice among healthcare professionals. It provided a forum to assess how best to secure sustainable blood supplies and maintain a resilient and efficient blood transfusion sector in Europe. The conference concluded with an overview of initiatives and projects at EU and EDQM level that contribute to supporting BEs in strengthening their systems.

Each webinar was attended by 250 participants, on average, representing BEs, national authorities, suppliers of medical devices and equipment, blood professional associations and international organisations, from 70 different countries. The proceedings, including recommendations and conclusions, will be issued in 2021 and will serve as a basis for any future revision of EU blood, tissue and cell legislation. Recordings of the webinars are publically available and an e-brochure was created to mark this success story. It highlighted the key milestones on the road to achieving a harmonised and common European set of standards, together with the benefits and added value of the different programmes available to BEs and provided a summary of the outcomes of an evaluation of EU legislation on safety and quality standards for SoHO.[57]

Symposia & workshops – Focused topic meetings

Management of extraneous agents in IVMPs (1 April 2020)

The approach to extraneous agent testing in IVMPs changed in 2020 with the introduction of a new and more flexible approach. In the revised text, which came into force on 1 July 2020, methods are no longer described in detail; instead users can tailor tests to

57. Webinar recordings: https://go.edqm.eu/BloodTraining. E-brochure "10 Years of Co-operation – Working together for a Safe and Sustainable blood supply", illustrating the conference background and initiatives: https://go.edqm.eu/BloodConfBrochure.

individual product needs. This new approach to extraneous agent testing is expected to increase the development of more robust *in vitro* methods and reduce the use of *in vivo* testing.

Intended primarily to help users prepare for implementation of the new approach, the workshop gave details on what had changed in the requirements and why, with a particular focus on risk management. The programme covered the regulatory landscape, the latest information on EMA guidelines and the validation of new techniques. Representatives from industry were also invited to share their views. The workshop attracted nearly 200 participants from 42 countries and the recording is available online.[58]

Elemental impurities: an update (10 September 2020)

This refresher webinar was divided into two parts. The first part focused on the implementation of Q3D in the texts of the Ph. Eur., highlighting what had changed in general and individual monographs, as well as in the use of risk-management principles for the control of elemental impurities. The second talk centred on Q3D implementation in the CEP procedure, covering the approaches available to CEP applicants as outlined in the CEP policy on elemental impurities. Over 1200 participants from 71 countries joined the webinar and the recording is available online.[59]

58. See https://go.edqm.eu/pheurtraining.
59. Ibid.

Training sessions

The EDQM organised three training sessions on the Ph. Eur. in 2020. The first focused on biological products and enabled participants to further their knowledge of the work and procedures of the Ph. Eur. on the subject. Each session focused on relevant Ph. Eur. texts and the use of RSs for biologics, such as plasma-derived products and synthetic peptides, biotherapeutics, vaccines for human use and advanced therapy medicinal products (ATMP).

In May, all the Ph. Eur. Commission chairs, experts, NPAs, delegates and observers were invited to a specific information session on the work of the Commission. Many of the 200 participants were newly appointed and the objective was to provide them with additional knowledge and skills for use in their new role. Numerous topics of interest regarding the Ph. Eur. were discussed and other EDQM activities such as the establishment of reference standards, the work of the OMCL Network and the CEP procedure were covered.

Four webinar training sessions were held in July. Each focused on a specific area of the Ph. Eur., allowing participants to join the sessions of their choice. The participants were able to chat with the speakers, respond to live polls and submit their questions for answers in real time. Each session attracted more than 1000 participants from over 75 countries.

Information on past Ph. Eur. training sessions is available online.[60]

60. Ibid.

► *Training session*

► *Training session*

International fairs and congresses – Expanding global presence

36th International Congress of the International Society of Blood Transfusion ISBT (12-16 December)

Many tradeshows went virtual in 2020 and the ISBT congress was no exception. A virtual booth was set up, enabling the hundreds of connected delegates to interact in real time with the EDQM. Information, in the form of e-brochures, presentations, videos, as well as links to on-demand training resources, was accessible to visitors at the click of a mouse. To ensure maximum engagement, visitors were able to chat live and to schedule one-to-one virtual meetings if they needed more in-depth answers to questions. This first-ever virtual exhibitor experience provided a global platform to highlight the EDQM's activities in this area.

Public awareness campaigns

Organ, tissue and cell transplantation

The 21st European Day for Organ Donation and Transplantation (EODD) was initially planned in co-operation with the Polish Transplant Co-ordinating Centre Poltransplant and the Polish National Centre for Tissue and Cell Banking to take place on 10 October in Warsaw (Poland).

The event, which has been organised by the EDQM/Council of Europe in a different country every year since 1996, is intended to increase public awareness of the need for organs, tissues and cells and to promote the principle of voluntary and non-remunerated donation.

Due to the pandemic situation, the decision was made in March 2020 to celebrate this awareness day online.

The 2020 message was "Take a minute to think about organ, tissue and cell donation" and the campaign, which ran from 2 to 10 October, was well received in European member states. National authorities and patients' associations also showed their support online.

Campaign materials, such as social media graphics, posters and e-mail signature banners, were made available for download on the EDQM's website and helped national contacts to spread the message about the importance of organ, tissue and cell donation.

Blood transfusion

The annual World Blood Donor Day (WBDD) is celebrated on 14 June. The EDQM showed its support for this worldwide campaign on its website and social media channels; a series of posts were shared on Twitter and Facebook, highlighting the campaign and the action taken by organisations around the globe. It was also the occasion to raise awareness on blood donation among Council of Europe staff based in Strasbourg and in its field offices.

APPENDICES

LIST OF COMMITTEES AND BODIES CO-ORDINATED BY THE EDQM

EUROPEAN PHARMACOPOEIA COMMISSION

The European Pharmacopoeia (Ph. Eur.) Commission was set up in 1964 in accordance with the Convention on the Elaboration of a European Pharmacopoeia. As of 31 December 2020, the Commission had 40 members, all contracting parties to the convention (39 member states and the EU). In addition, 30 observers from all over the world confirm the importance of the work of the Ph. Eur. Commission at international level. The Commission sets out the work programme and adopts the quality standards for medicines and their components to be applied in the territories of its member states. A total of 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 developing, manufacturing or controlling medicines and their components, and has become the gold standard reference in the sector.

BIOLOGICAL STANDARDISATION PROGRAMME STEERING COMMITTEE

The Biological Standardisation Programme (BSP) focuses on the standardisation of the methods and tools for the quality control of biologicals by establishing RSs and validating new methods with particular focus on replacing, reducing and refining the use of animals (3R 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 EU Commission, the EMA, the BWP, the IWP and WHO, and the EDQM Director.

NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES ADVISORY GROUPS

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

- general activities involving all of the member states of the Ph. Eur. Convention and the observer states. These activities cover work in the area of QMSs, such as audits and proficiency testing studies, as well as market surveillance studies, and contribute to combating falsified and illegal medicines. General activities are prepared and followed by the General OMCL Advisory Group;
- activities restricted to the EU and the EEA, and concerning products approved via the centralised procedure and the Mutual Recognition or Decentralised Procedure 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 OCABR activities, advisory groups ensure continuity of operations in the interval between the annual meetings of each specific network.

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

A network of about 100 assessors and 30 national inspectors participates in the work required for the evaluation of quality dossiers for pharmaceutical substances and the inspection of API manufacturing sites. The activities associated with the procedure for Certification of suitability to the Ph. Eur. monographs are guided by a steering committee and three technical advisory boards (TABs). The steering committee is composed of representatives of European working groups, and of licensing authorities and inspectorates. It takes decisions on general policy, examines and comments on matters brought to its attention by the TABs, 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 TABs and their chairs.

EUROPEAN COMMITTEE ON BLOOD TRANSFUSION

The European Committee on Blood Transfusion (CD-P-TS) addresses ethical, legal and organisational issues related to blood transfusion 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 currently composed of representatives from authorities working in the field of blood transfusion or at national BEs from 33 member states of the Council of Europe and observers such as the EC, WHO, the United States Food and Drug Administration (USFDA) and the Council of Europe's Committee on Bioethics (DH-BIO). It supervises the work of a number of individual projects and working groups, for example the working group in charge of the *Guide to the preparation, use and quality assurance of blood components,* the Plasma Supply Management Working Group and working groups responsible for quality management activities.

EUROPEAN COMMITTEE ON ORGAN TRANSPLANTATION

The European Committee on Organ Transplantation (CD-P-TO) focuses on expounding and promoting the principle of non-commercialisation of organ, tissue and cell donation, strengthening measures to avoid trafficking and elaborating ethical, quality and safety standards in the field of transplantation. It is currently composed of representatives from 36 member states of the Council of Europe, and observers including the European Commission, WHO, the Council of Europe's Committee on Bioethics (DH-BIO), Eurotransplant, Scandiatransplant, the European Society for Organ Transplantation (ESOT), The Transplantation Society (TTS), the European Association of Tissue and Cell Banks (EATCB), the European Eye Bank Association (EEBA), the European Society of Human Reproduction and Embryology (ESHRE) and the World Marrow Donor Association (WMDA). It supervises the activities of a number of individual projects and working groups, e.g. the ad hoc working groups that work on the elaboration of 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*. In addition, it oversees the work of the International Network of NFPs on Travel for Transplantation and that of multiple working groups and advisory groups that implement the activities in the field of tissues and cells included in the standing Grant Agreement with the European Commission.

EUROPEAN COMMITTEE ON PHARMACEUTICALS AND PHARMACEUTICAL CARE

The European Committee on Pharmaceuticals and Pharmaceutical Care (CD-P-PH) supports authorities in times of increasing social gaps and resource constraints to make the medication process safer and more responsible and accessible to all who need it. It is currently composed of representatives from 31 member states of the Council of Europe and four observers, including WHO.

Its work programme has three focus areas: classification of medicines as regards their supply, pharmaceutical care and practices, and combating the falsification of medical products and similar crimes. It is supported by its subordinate committees: the Committee of Experts on the Classification of Medicines as Regards their Supply (CD-P-PH/PHO), the Committee of Experts on Quality and Safety Standards for Pharmaceutical Practices and Pharmaceutical Care (CD-P-PH/PC) and the Committee of Experts on Minimising Public Health Risks Posed by Falsification of Medical Products and Similar Crimes (CD-P-PH/CMED).

EUROPEAN COMMITTEE FOR COSMETICS AND CONSUMER HEALTH

The European Committee for Cosmetics and Consumer Health (CD-P-COS) was formed in early 2018 to respond to emerging risks to human health arising from the use of cosmetics. It replaces part of the former Committee on Consumer Health Protection (CD-P-SC), which was adjourned by decision of the Committee of Ministers at the end of 2017, and is currently composed of representatives from national ministries with public health responsibilities from 32 member states of the Council of Europe, and three observers. Activities on the work programme focus on collaboration and knowledge sharing between participating countries. The CD-P-COS oversees the European Network of Official Cosmetics Control Laboratories (OCCLs), contributes to consumer health protection and supports market surveillance activities of the competent authorities.

EUROPEAN NETWORK OF OFFICIAL COSMETICS CONTROL LABORATORIES

The OCCL Network was set up on a voluntary basis to foster cross-border collaboration, share technical expertise and enhance quality management in accordance with international standards. More than 50 OCCLs participate in regular network activities, including laboratories from EU member states. Besides the EU, participation is open to other Council of Europe States Parties to the Convention on the Elaboration of a European Pharmacopoeia.

EUROPEAN COMMITTEE FOR FOOD CONTACT MATERIALS AND ARTICLES

The European Committee for Food Contact Materials and Articles (CD-P-MCA) was formed in early 2018. It replaces part of the former Committee on Consumer Health Protection (CD-P-SC), which was adjourned by decision of the Committee of Ministers at the end of 2017, and is currently composed of representatives from national ministries with public health responsibilities from 30 member states of the Council of Europe, and two observers. Activities on the work programme focus on the safety of food contact materials and articles and define harmonised measures that supplement EU and national legislation. It is supported by three subordinate working groups: one dealing with food contact materials made from paper and board, another working on printed food-contact materials and one handling matters of compliance documentation. The technical guides published by the CD-P-MCA are used as reference documents by manufacturers and other business operators, safety evaluators and control laboratories.

GLOSSARY

3R principles	replacement, reduction and refinement (animal testing)
API	active pharmaceutical ingredient
ATC	Anatomical Therapeutic Chemical
ATMP	advanced therapy medicinal product
BE	blood establishment
B-MJA	Blood Mutual Joint Audit
B-MJV	Blood Mutual Joint Visit
B-PTS	Blood Proficiency Testing Scheme
B-QM	Blood Quality Management
BRP	biological reference preparation
BRR	biological reference reagent
BSP	Biological Standardisation Programme
BVS	batch validity statement
BWP	Biologics Working Party
CAP	centrally authorised product
CAS number	Chemical Abstracts Service Registry number
CAT	Committee for Advanced Therapies
CD-P-COS	European Steering Committee for Cosmetics and Consumer Health (see "List of committees and bodies co-ordinated by the EDQM", page 76)
CD-P-MCA	European Steering Committee for Food Contact Materials and Articles (see "List of committees and bodies co-ordinated by the EDQM", page 76)
CD-P-PH	European Steering Committee on Pharmaceuticals and Pharmaceutical Care (see "List of committees co-ordinated and bodies by the EDQM", page 75)
CD-P-PH/CMED	Committee of Experts on Minimising the Public Health Risks Posed by Falsification of Medical Products and Similar Crimes
CD-P-PH/PC	Committee of Experts on Quality and Safety Standards in Pharmaceutical Practices and Pharmaceutical Care
CD-P-PH/PHO	Committee of Experts on the Classification of Medicines as Regards their Supply
CD-P-TO	European Steering Committee on Organ Transplantation (see "List of committees and bodies co-ordinated by the EDQM", page 75)
CD-P-TS	European Steering Committee on Blood Transfusion (see "List of committees and bodies co-ordinated by the EDQM", page 75)
CEP	Certificate of suitability to the monographs of the European Pharmacopoeia
CEPI	Coalition for Epidemic Preparedness Innovations
CHMP	EMA Committee for Medicinal Products for Human Use
CLEN	Customs Laboratories European Network
CLP	classification, labelling and packaging
CM	continuous manufacturing
COVAX	COVID-19 Vaccines Global Access
CRS	chemical reference substance
CuSum	cumulative sum control chart
DCP	decentralised procedure
DoE	design of experiments
EA	European Co-operation for Accreditation
EAHP	European Association of Hospital Pharmacists
EATCB	European Association of Tissue and Cell Banks

ECBS	Expert Committee on Biological Standardisation
ECSPP	Expert Committee on Specifications for Pharmaceutical Preparations
EDQM	European Directorate for the Quality of Medicines & HealthCare
EEA	European Economic Area
EEBA	European Eye Bank Association
ELISA	enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EMRN	European Medicines Regulatory Network
EODD	European Day for Organ Donation and Transplantation
EQAAS	External Quality Assurance Assessment Scheme
ESHRE	European Society of Human Reproduction and Embryology
ESOT	European Society for Organ Transplantation
EU	European Union
EUNDB	European Union Network Data Board
FIP	International Pharmaceutical Federation
GC	gas chromatography
GEON	General European Network of Official Medicines Control Laboratories (OMCLs)
GMDP-IWG	GMP/GDP Inspectors Working Group
GMP	Good Manufacturing Practice
GPG	Good Practice Guidelines
GPhP	Good Pharmacopoeial Practices
GTP	gene therapy product
HMA	Heads of Medicines Agencies
HMP	herbal medicinal product
HMPC	Herbal Medicinal Products Committee
HPTLC	high-performance thin-layer chromatography
HRS	herbal reference standard
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICRS	international chemical reference substance
ICU	intensive care unit
IGDG	ICH Generics Discussion Group
IMWP	International Meeting of World Pharmacopoeias
INN	international nonproprietary name
IPRP	International Pharmaceutical Regulators Program
ISA	International Standards for Antibiotics
ISBT	International Society of Blood Transfusion
IVMP	immunological veterinary medicinal product
IWP	Immunologicals Working Party
JP	Japanese Pharmacopoeia
JRC	Joint Research Centre
LC	laboratory committee
MAA	marketing authorisation application
MeNP	1-methyl-4-nitrosopiperazine
MJA	Mutual Joint Audit
MJV	Mutual Joint Visit
MRP	Mutual Recognition Procedure
MS	mass spectrometry
MSPC	multivariate statistical process control
MSS	market surveillance study
MSSIP	MSS on suspected illegal products
NCA	national competent authority
NDEA	*N*-nitrosodiethylamine

NDMA	*N*-nitrosodimethylamine
NFP	national focal point
NMBA	*N*-nitroso-*N*-methyl-4-aminobutyric acid
NMR	nuclear magnetic resonance
NPA	national pharmacopoeia authority
OBPR	Official Batch Protocol Review
OCABR	Official Control Authority Batch Release
OCCL	Official Cosmetics Control Laboratory
OMCL	Official Medicines Control Laboratory
OMCL GTWG	OMCL Network's Gene Therapy Working Group
ONT	National Transplant Organisation, Spain
PA	pyrrolizidine alkaloids
PaedF	Paediatric Formulary
PAT	process analytical technology
PDCO	EMA Paediatric Committee
PDG	Pharmacopoeial Discussion Group
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PTS	Proficiency Testing Scheme
QbD	quality by design
QDG	Quality Discussion Group
QM	quality management
QMS	quality management system
QWP	Quality Working Party
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
REMCO	ISO Committee on Reference Materials
RS	reference substance
RTEMIS	Real-Time Remote Inspections
RTRT	real-time release testing
SARE	serious adverse reactions and events
SDS	safety data sheet
SEEHN	South-Eastern Europe Health Network
SoHO	substances of human origin
SPOC	Single Point of Contact
SUP	suspicious unknown product
TAB	technical advisory board
TCM	traditional Chinese medicine
TFDA	Taiwan Food and Drug Administration
TGA	Therapeutic Goods Administration (Australia)
TSE	transmissible spongiform encephalopathy
TTS	The Transplantation Society
TV	training visit
UNICEF	United Nations Children's Fund
USFDA	United States Food and Drug Administration
USP	United States Pharmacopeia
VBRN	Veterinary Batch Release Network
VICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Veterinary Use (veterinary counterpart to the ICH)
WBDD	World Blood Donor Day
WGEO	Working Group of Enforcement Officers
WGQM	Working Group of Quality Managers
WHO	World Health Organization
WMA	World Medical Association
WMDA	World Marrow Donor Association

This publication presents the work carried out in 2020 by the European Directorate for the Quality of Medicines & HealthCare, Council of Europe, highlighting its particular achievements.

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

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