

# European Regulations for Medicines

## Place and Role of the EDQM and the European Pharmacopoeia

Dr Susanne Keitel  
Director, EDQM



## Structure

- Council of Europe, European Union and EDQM
- The EU regulatory framework in pharmaceuticals and its key players
- EDQM and the European Pharmacopoeia
- Pharmacopoeial Harmonisation



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# The Council of Europe

Founded in 1949

Development of European common and democratic principles

47 member countries

Headquarters in Strasbourg

Core values:

- protection of human rights
- pluralist democracy and the rule of law



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# The Council of Europe is not the European Union!



- **European Union (EU):** a unique economic and political partnership between currently **28 European countries** ⇒ more than 500 million citizens.
- **European Council:** the EU's main decision-making body. It defines the general political direction and priorities of the European Union.

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# European Directorate for the Quality of Medicines & HealthCare

- A Council of Europe Directorate, based on the Convention on the Elaboration of a European Pharmacopoeia (PA, 1964)
- Mission: to contribute to a basic human right: access to good quality medicines and healthcare

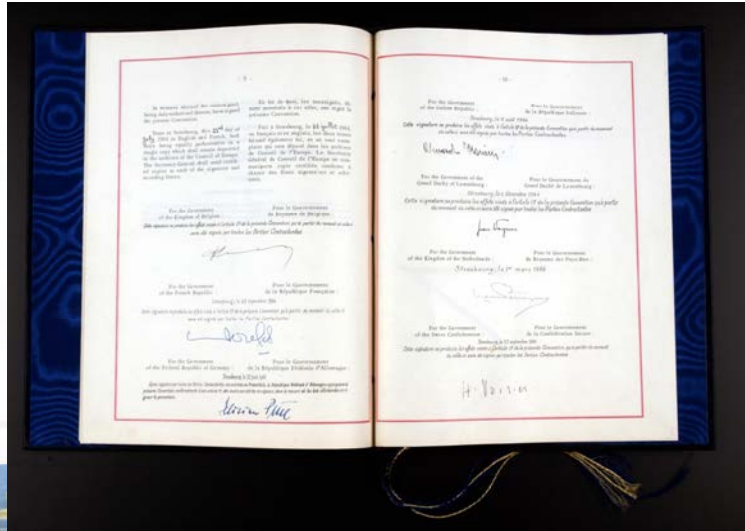


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# European Pharmacopoeia Convention



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# European Pharmacopoeia Convention

## Article 1:

The Contracting Parties undertake

- a) Progressively to elaborate a Pharmacopoeia which shall be common to the countries concerned and which shall be entitled "European Pharmacopoeia";
- b) To take the necessary measures to ensure that the monographs which will be adopted... and which will constitute the European Pharmacopoeia shall become the official standards applicable within their respective countries.

Strasbourg, 22. July 1964

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# Why still national Pharmacopoeias?

- For texts of interest to one Member State only; for texts out of the scope of the Ph. Eur. (e.g. national formularies)
- Three main approaches (country specific):
  - Discontinuation of the national pharmacopoeia (e.g. Sweden, Finland, the Netherlands), Ph. Eur. as the only pharmacopoeia, potentially translated into national language
  - Maintenance of a national pharmacopoeia to complement the Ph. Eur.:
    - Inclusion of the Ph. Eur. in the national pharmacopoeia (e.g. BP, Royal Spanish Pharmacopoeia).
    - Publication of a National pharmacopoeia in addition to the Ph. Eur. (e.g. France, Germany, Switzerland, Austria)

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# Ph. Eur. / National Pharmacopoeia / 3<sup>rd</sup> country Pharmacopoeia in the EU

Ph. Eur.

With respect to the quality part (chemical, pharmaceutical and biological) of the dossier, all monographs including general monographs and general chapters of the European Pharmacopoeia are applicable.

Nat. Ph.

The monographs of the European Pharmacopoeia shall be applicable to all substances, preparations and pharmaceutical forms appearing in it. In respect of other substances, each Member State may require observance of its own national pharmacopoeia.

3<sup>rd</sup> country Ph.

In case where starting and raw materials, active substance(s) or excipient(s) are described neither in the European Pharmacopoeia nor in the pharmacopoeia of a Member State, compliance with the monograph of a third country pharmacopoeia can be accepted. In such cases, the applicant shall submit a copy of the monograph accompanied by the validation of the analytical procedures contained in the monograph and by a translation where appropriate.

Directive 2003/63/EC, 3. MODULE 3: CHEMICAL, PHARMACEUTICAL AND BIOLOGICAL INFORMATION FOR MEDICINAL PRODUCTS CONTAINING CHEMICAL AND/OR BIOLOGICAL ACTIVE SUBSTANCES, 3.2 Content and Basic Principles

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## The EU Commission – the “Policy and Law Makers” -

- Development of the regulatory framework
- Marketing authorisation procedures, GMP, GCP, Clinical Trials...
- New/special topics in pharmaceutical politics (e.g. Falsified Medicines Directive)
- International relations and co-operation (ICH, WHO)
- Publication of the relevant legislation and guidance documents in the EU concerning pharmaceuticals (EudraLex, Notice to Applicants ...)

# The European Union Legal System

## Aim and Definitions

**Core objective:** European unification based on a harmonised legal system

**Community law:** independent legal system

**Precedence over national legal provision**

**Three different independent types of legislation**

- primary legislation
- secondary legislation
- case law

# The EU Pharmaceutical Legislation

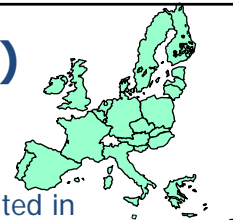
	to whom?	effect?
<b>Regulation</b>	all "persons" in the EU	directly binding, super-sedes national law
<b>Directive</b>	EU-Member States	to be transposed into national law
<b>Decision</b>	single "person(s)" (MAH, EU-MS, .. )	directly binding, case by case, super-sedes national law
<b>Guidelines</b>	interested "parties" (MAH, ...)	to give guidance ("soft-law")

## Quality « Players » in the EU

- EMA and national competent authorities (NCA)
- CHMP/CVMP/HMPC Working parties:
  - Quality Working Party (+ CVMP + HMPC)
  - Biologicals Working Party
  - GMP/GDP Inspectors Working Group ....
- EDQM:
  - European Pharmacopoeia
  - OMCL network
  - Certification of Suitability
  - .....

## European Medicines Agency (EMA)

- A European Union body responsible for the evaluation, supervision and pharmacovigilance of medicinal products.
- Set up in 1995 (EC Regulation No. 2309/93), currently located in London, UK.
- EMA not the FDA for Europe!
- Coordinates the existing scientific resources of Member States.
- Works through a network of about 4500 European experts. It draws on the resources of the approx. 44 National Competent Authorities (NCAs) in 31 EU and EEA countries.
- A single evaluation is carried out through the Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP) for the centralised procedure.
- Works closely with the EDQM (Ph. Eur., Certification, OMCL-Network...).



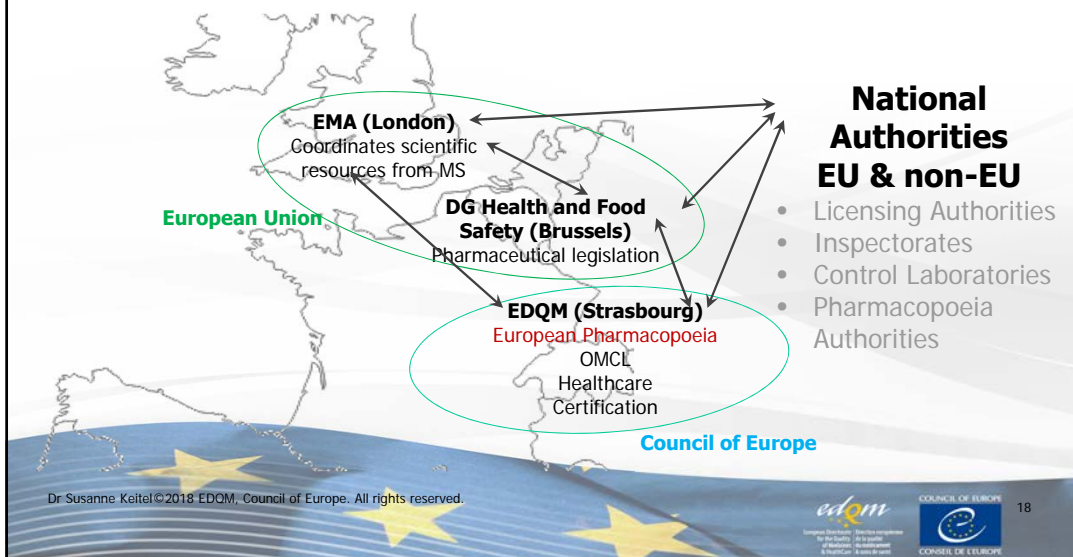


# National Authorities

Act as “full provider” for the applicants – responsible for the different marketing authorisation procedures and different kinds of medicinal products.

- Nominate experts for the evaluation of the application for the centralised marketing authorisation process.
- Act as rapporteur or co-rapporteur in the assessment of centralised applications via their CXMP members.
- Participate in working parties, *ad hoc* groups, promote pharmaceutical politics development.
- Responsible for pharmacovigilance.
- Contribute to the activities of the EDQM.

# Key players for the quality of medicines



# Structure

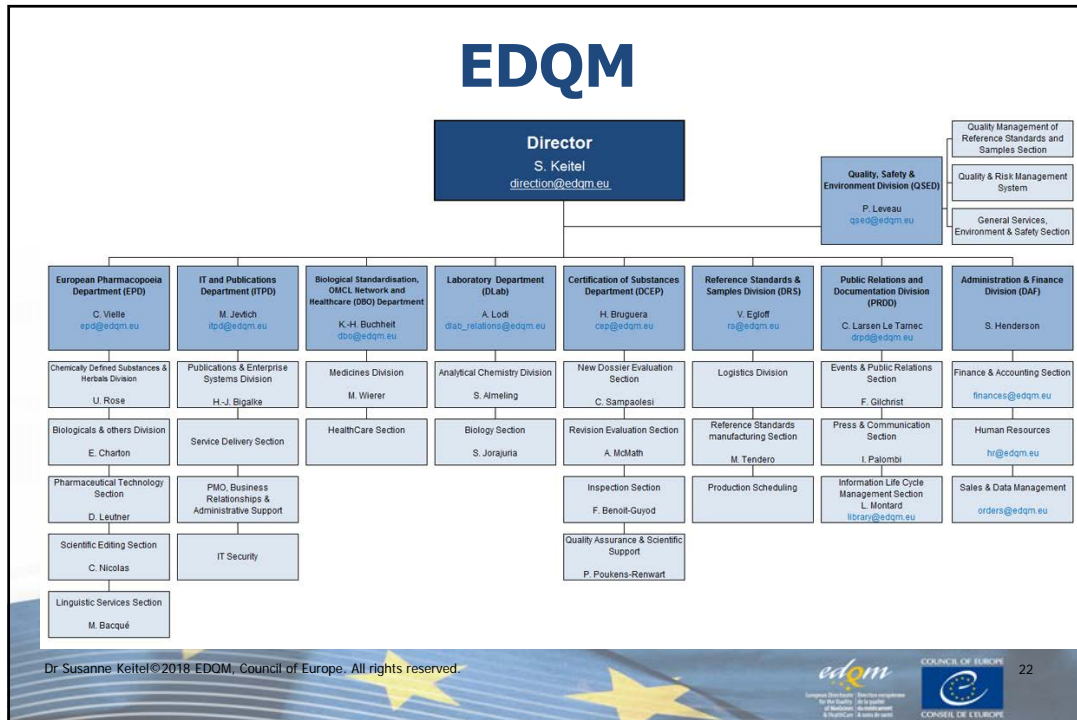
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# From the European Pharmacopoeia....

- 1964: Activities based on an International Convention of the Council of Europe to develop harmonised and common standards for medicines
- Mandatory status for all EU/EEA Member States since 1975 via EU pharmaceutical legislation
- 1994: EU signs the Ph. Eur. Convention
- 1994: creation of the European Network of Official Medicines Control Laboratories (OMCL)

# ..... to the EDQM

- 1994: creation of the procedure of certification of suitability to the monographs of the Ph. Eur.
- 2007: transfer of activities on blood transfusion and organ transplantation
- 2008: transfer of activities on combating counterfeits and healthcare activities
- 2009: transfer of activities on cosmetics and food-packaging



# European Pharmacopoeia (Ph. Eur.)

- Protecting public health - one common compulsory standard.
- The Ph. Eur. is the official pharmacopoeia in Europe – complemented by national pharmacopoeias for texts of interest to only one Member State.
- Mandatory at the same date in 38 Member States (CoE) and the EU (decision of Ph. Eur. Commission).
- Legally binding quality standards for ALL medicinal products in its member states, i.e. raw material, preparations, dosage forms, containers must comply with the Ph. Eur. requirements when they exist.

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## Ph. Eur. Commission

- One delegation per member state or observer
- 38 Member States plus a delegation from the EU (a representative from DG Health & Food Safety); 28 Observer countries, Taiwan Food and Drug Administration (TFDA) and World Health Organization (WHO).
- Delegates mainly come from health ministries, health authorities, pharmacopoeias and universities and are appointed by the national authorities on the basis of their expertise.
- Three sessions a year;
- Draft texts are published for public consultation and adopted by unanimous vote.
- EDQM/EPD provides the secretariat



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## Ph. Eur. network



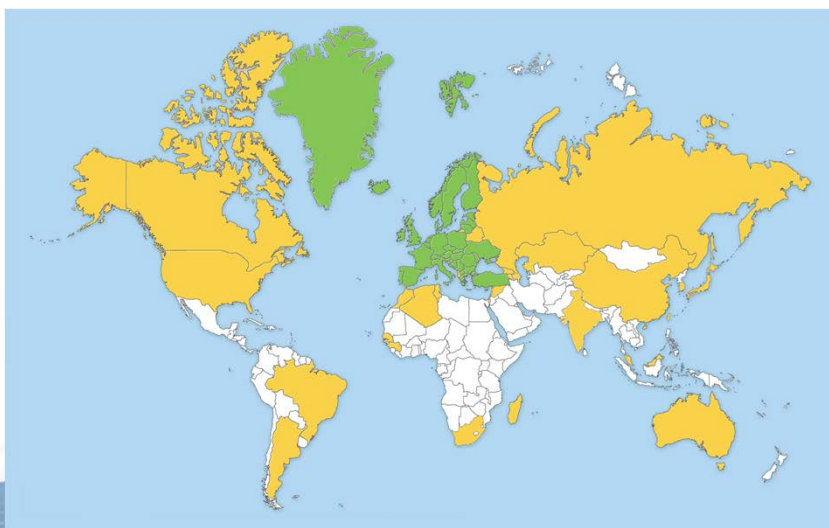
- 59 active Groups of experts and working parties (+ 13 “dormant”) elaborating and revising texts, meeting up to 3 times a year
- More than 800 experts (mainly from the Competent Authorities (**NPAs, Assessors, OMCL, Inspectors**), Industry, University)
- Mainly from Ph. Eur. member states, but since 2016 also from abroad (US FDA, Australia, China, India, Korea, Madagascar....)

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## Members and Observers



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## The Pharmacopoeia in the EU Legislation

“The monographs of the European Pharmacopoeia shall be applicable to all substances, preparations and pharmaceutical forms appearing in it. In respect of other substances, each Member State may require observance of its own national pharmacopoeia.....”

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## The Pharmacopoeia in the EU Legislation

However, where a material in the European Pharmacopoeia or in the pharmacopoeia of a Member State has been prepared by a method liable to leave impurities not controlled in the pharmacopoeia monograph, these impurities and their maximum tolerance limits must be declared and a suitable test procedure must be described.

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## The Pharmacopoeia in the EU Legislation

In cases where a **specification** contained in a monograph of the European Pharmacopoeia or in the national pharmacopoeia of a Member State might be **insufficient** to ensure the quality of the substance, the competent authorities may **request more appropriate specifications** from the marketing authorisation holder. ...

## The Pharmacopoeia in the EU Legislation

....The **competent authorities shall inform** the authorities responsible for the pharmacopoeia in question. The **marketing authorisation holder shall provide** the authorities of that pharmacopoeia with the **details** of the alleged insufficiency and the additional specifications applied.

Directive 2001/83/EC, Annex 1, 3. MODULE 3: CHEMICAL, PHARMACEUTICAL AND BIOLOGICAL INFORMATION FOR MEDICINAL PRODUCTS CONTAINING CHEMICAL AND/OR BIOLOGICAL ACTIVE SUBSTANCES, 3.2 Content and Basic Principles

# The Pharmacopoeia in the EU Legislation

## To summarise:

The Ph. Eur. is legally binding, but the legislation foresees a mechanism to provide the pharmacopoeia authority with information on the quality of products on the market; an excellent tool to ensure that monographs are not cast in stone but routinely updated to reflect the state-of-the-art.

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## The European Pharmacopoeia

- An (if not *the*) example of a successful regional pharmacopoeial cooperation and harmonisation
- Technical decisions taken by consensus
- Some key success factors: strong political will, common legal basis, convergent/ harmonised regulatory environment

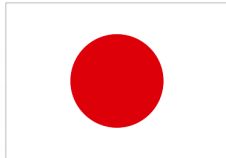
→ *Feasibility at an international level?*

## International harmonisation initiatives

- Pharmacopoeial Discussion Group
- Bilateral harmonisation initiatives, e.g. prospective harmonisation of API monographs between USP & Ph. Eur.
- International Meetings of World Pharmacopoeias

# Pharmacopoeial Harmonisation

## The three "ICH Pharmacopoeias"



Japanese  
Pharmacopoeia  
Governmental



Ph. Eur.  
EDQM,  
Council of Europe  
Inter-governmental



US Pharmacopoeia  
Private  
organisation

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# The PDG & Harmonisation

- Pharmacopoeial Discussion Group (PDG) set up in 1990.
- Drives international harmonisation of pharmacopoeial requirements among the world's three major pharmacopoeias, the Ph. Eur., JP and USP - a single set of global specifications.

## Aims:

- Avoid redundant testing by suppliers and pharmaceutical industry to meet different standards
- Reduce the overall cost of pharmaceutical research world-wide by avoiding duplication of work (preparation of dossiers and studies)
- Reduce the time required for medicines to be made available to patients

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## PDG Harmonisation

- Monographs and general methods of analysis proposed by national associations of manufacturers of pharmaceutical products
- To ensure rapid publication of signed-off texts, the PDG procedure has been woven into the Ph. Eur. procedure
- Texts are published in Pharmeuropa and approved by the Ph. Eur. Commission
- Harmonisation in parallel and in coordination with ICH activities
- Priority of pharmacopoeias according to EU legislation  
Ph. Eur. > national pharmacopoeia > third country pharmacopoeias, e.g. USP, JP

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## International Meetings of World Pharmacopoeias

- New initiative for harmonisation/convergence at a global scale following a meeting of world pharmacopoeias.
- Outcome to date: "Good Pharmacopoeial Practices", a document describing policies and approaches to monograph development, publicly available on WHO website.
- Intended to serve as basis for exchanges and networking between different pharmacopoeias to identify opportunities for collaboration and, where relevant, work sharing and recognition.
- WHO as a "neutral platform".
- 9<sup>th</sup> meeting in Da Nang, Vietnam, in April 2018 identified concrete further steps forward for, e.g., exchange of information.

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# Thank you!