European Regulations for Medicines – Place and Role of the EDQM and the European Pharmacopoeia

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Structure

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

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

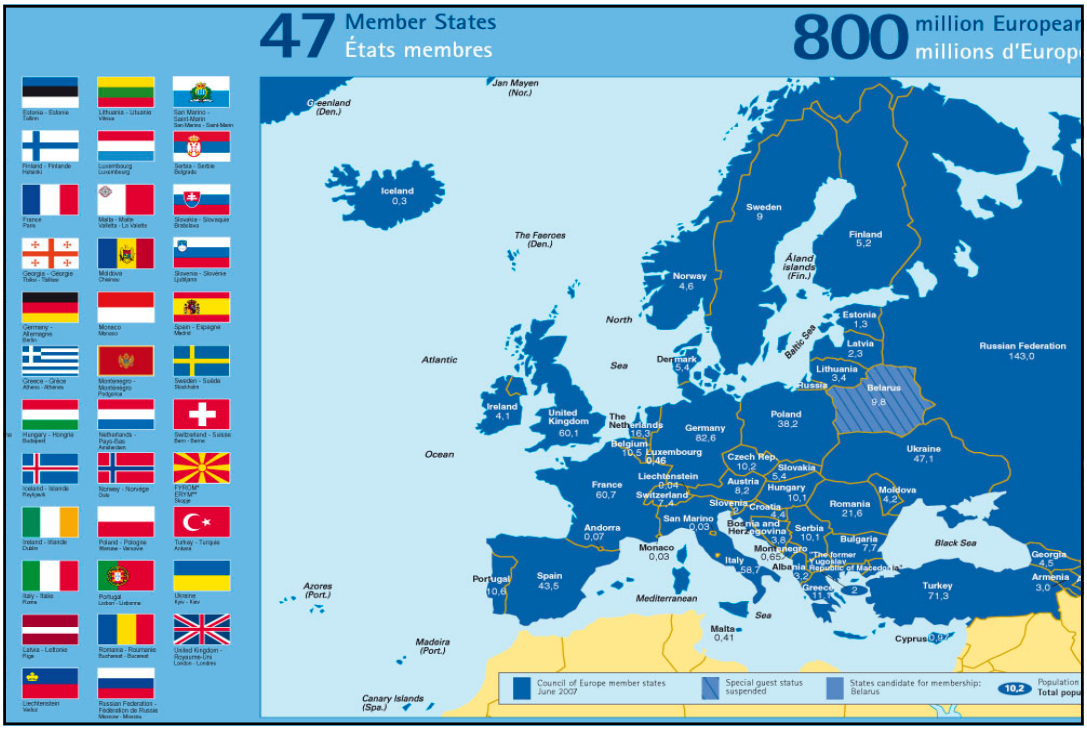
Human Rights... Democracy... Rule of Law

Objectives

- to protect human rights, pluralist democracy and the rule of law;
- to promote awareness and encourage the development of Europe's cultural identity and diversity;
- to find common solutions to the challenges facing European society;
- to consolidate democratic stability in Europe by backing political, legislative and constitutional reform.

The Council of Europe is not the European Union!

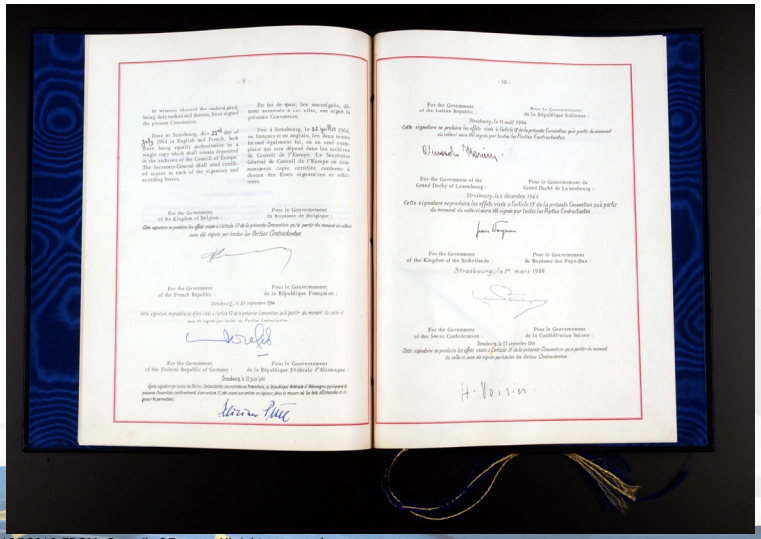
- **European Union (EU):** a unique economic and political partnership between currently 28 European countries ⇒ more than 500 million citizens.
- **European Council:** The EU's main decision-making body. It defines the general political direction and priorities of the European Union.



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

European Pharmacopoeia Convention



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

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)

Ph. Eur. / National Pharmacopoeia / 3rd 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.

3rd 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

Structure

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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)
- Publishing 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 Pharmaceutical Legislation

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

Quality « Players » in the EU in the field

EMA and national competent authorities (**NCA**)

CHMP/CVMP/**HMPC** Working parties:

- Quality Working Party (+ CVMP + HMPC)
- GMP/GDP Inspectors Working Group ….

HMA and its working groups esp.: Homeopathic Medicinal Products Working Group (**HMPWG**)

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 / EC Regulation No. 726/2004). Its office is 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.).

National Competent 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

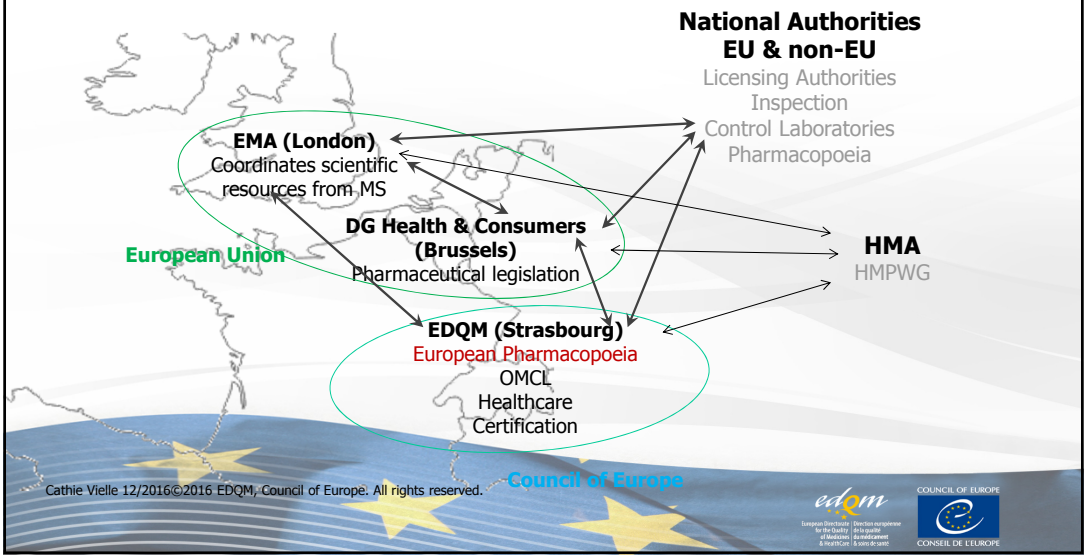
Heads of Medicines Agencies (HMA)

- **network** of the Heads of the EU/EEA NCAs
- Vision: Protecting and promoting public health in Europe is the main principle which inspires the HMA action.
- Mission: to foster an effective and efficient European medicines regulatory system.

Homeopathic Medicinal Products Working Group (HMPWG)

- One of the HMA working groups, dedicated to homeopathic medicinal products for human and veterinary use
- To provide guidance, advice and expertise in the fields
- To address regulatory and scientific issues concerning homeopathic medicinal products on request by the European Commission, the Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human (CMD(h)) and Co-ordination Group for Mutual Recognition and Decentralised Procedures - Veterinary (CMD(v)), the Heads of Medicines Agencies and the EDQM;

Key players for the quality of medicines



Structure

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- **The European Pharmacopoeia and EDQM**

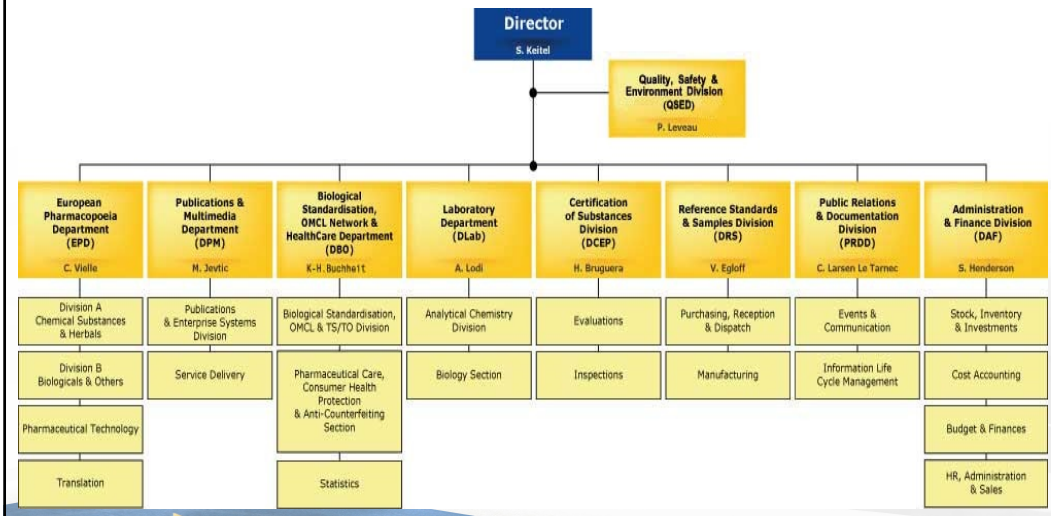
From the European Pharmacopoeia....

- 1964: Activities based on an International Convention of the Council of Europe to promote free movement of medicines in Europe
- 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 for 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

EDQM



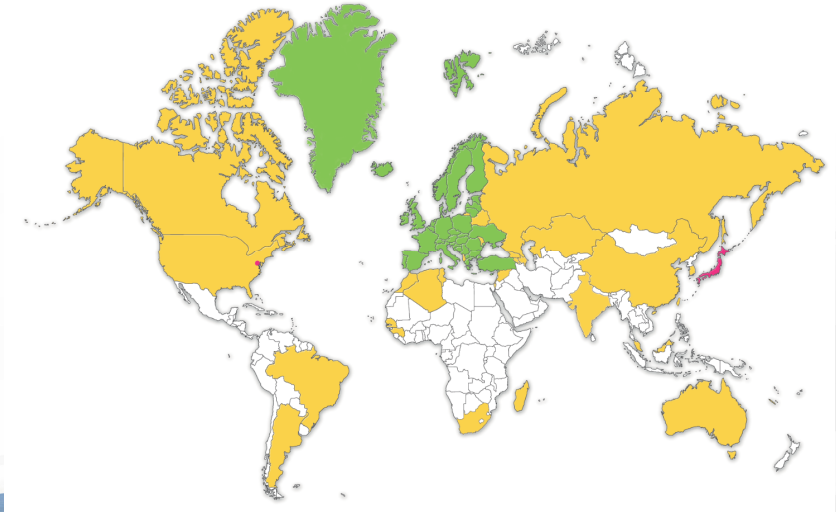
European Pharmacopoeia (Ph. Eur.)

- 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 37 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.

Ph. Eur. Commission

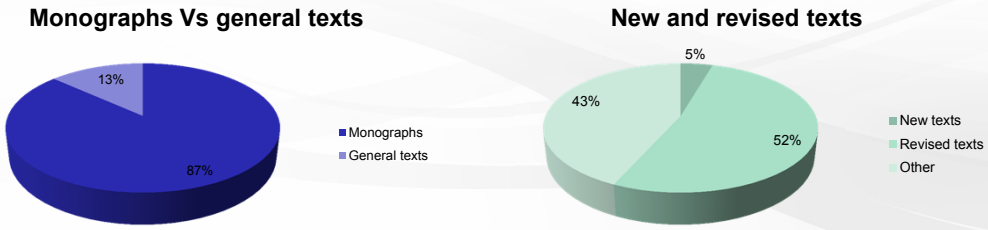
- One delegation per member state or observer
- 37 Member States plus a delegation from the EU (a representative from DG Health & Consumer and the EMA); 27 Observer countries (*India since November 2016*), Taiwan Food and Drug Administration (TFDA) and World Health Organization (WHO).
- Delegates come from health ministries, health authorities, pharmacopoeias, universities, or industry and are appointed by the national authorities on the basis of their expertise.
- Three sessions a year; texts are adopted by unanimous vote.
- Currently 20 permanent Groups of Experts & 51 ad hoc Working Parties (including 37 active ones including "HOM" and "HMM")
- EDQM/EPD provides the secretariat

Members and Observers



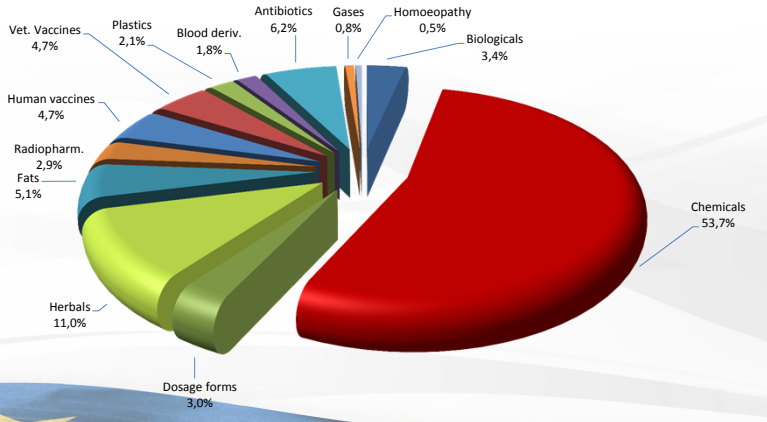
The 9th Edition (9.0):

- 2687 texts [2329 monographs + 358 general texts]

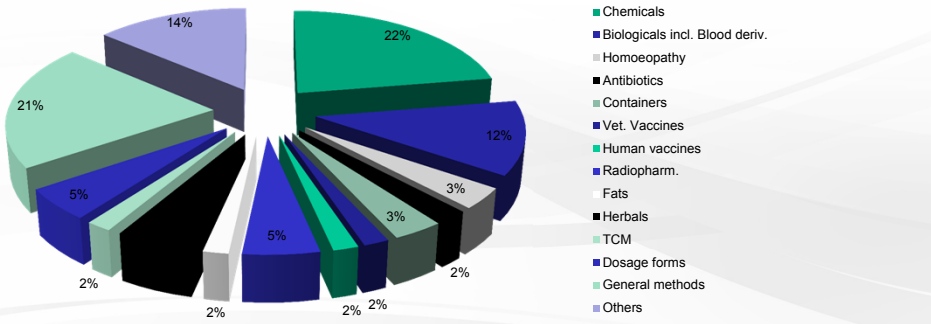


- around 2600 descriptions of reagents

The Ph. Eur. is active in a lot of areas …

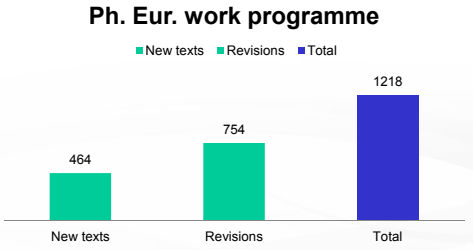


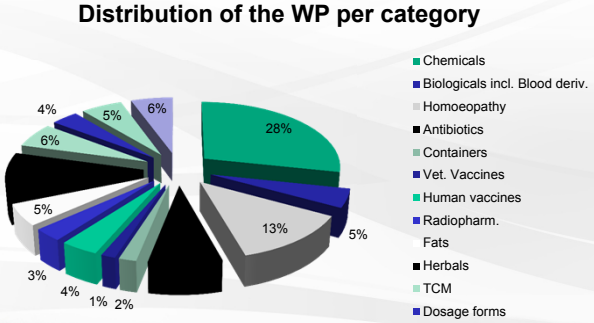
57 *active* Groups of experts and working parties



71 groups of experts and working parties, including 14 "dormant" ones

1218 items on the work programme (June 2016)





THE PH EUR IN THE EU DIRECTIVES

Homeopathic medicinal product:

Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.

(24) The rules relating to the manufacture, control and inspection of homeopathic medicinal products must be harmonized to permit the circulation throughout the Community of medicinal products which are safe and of good quality.

DIRECTIVE 2001/83/EC as amended OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the Community code relating to medicinal products for human use

PART 2: *PHARMACEUTICAL (PHYSICO-CHEMICAL, BIOLOGICAL OR MICROBIOLOGICAL INFORMATION (QUALITY))*

Basic principles and requirements

All monographs, including general monographs and general chapters of the *European Pharmacopoeia*, or failing that, of a Member State are applicable.

Where relevant, chemical and biological reference material of the *European Pharmacopoeia* shall be used. If other reference preparations and standards are used, they shall be identified and described in detail.

In case dilutions are involved, these dilution steps shall be done in accordance with the homeopathic manufacturing methods laid down in the relevant monograph of the *European Pharmacopoeia* or, in absence thereof, in an official pharmacopoeia of a Member State.

(a) *Terminology*

The Latin name of the homeopathic stock described in the marketing authorisation application dossier shall be in accordance with the Latin title of the *European Pharmacopoeia* or, in absence thereof, of an official pharmacopoeia of a Member State. Where relevant the traditional name(s) used in each Member State shall be provided.

COMMISSION DIRECTIVE 2009/9/EC of 10 February 2009
amending Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to medicinal products for veterinary use

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.....

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.

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 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

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.

Thanks!