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

INTERNATIONAL REGULATORY FORUM OF HUMAN CELL THERAPY AND GENE THERAPY PRODUCTS

16 MARCH 2016, OSAKA, JAPAN

Dr Stephen J. Wicks

Scientific Regulatory Policy and Intelligence

The Council of Europe

Founded in 1949: the oldest pan-European organisation

47 member countries, >820 million Europeans

Headquarters in Strasbourg (France)

Protects human rights
Promotes democracy
Protects the rule of law

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

From the European Pharmacopoeia…

Activities based on the Convention on the Elaboration of a European Pharmacopoeia (1964)

edqm 50 years/ans
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

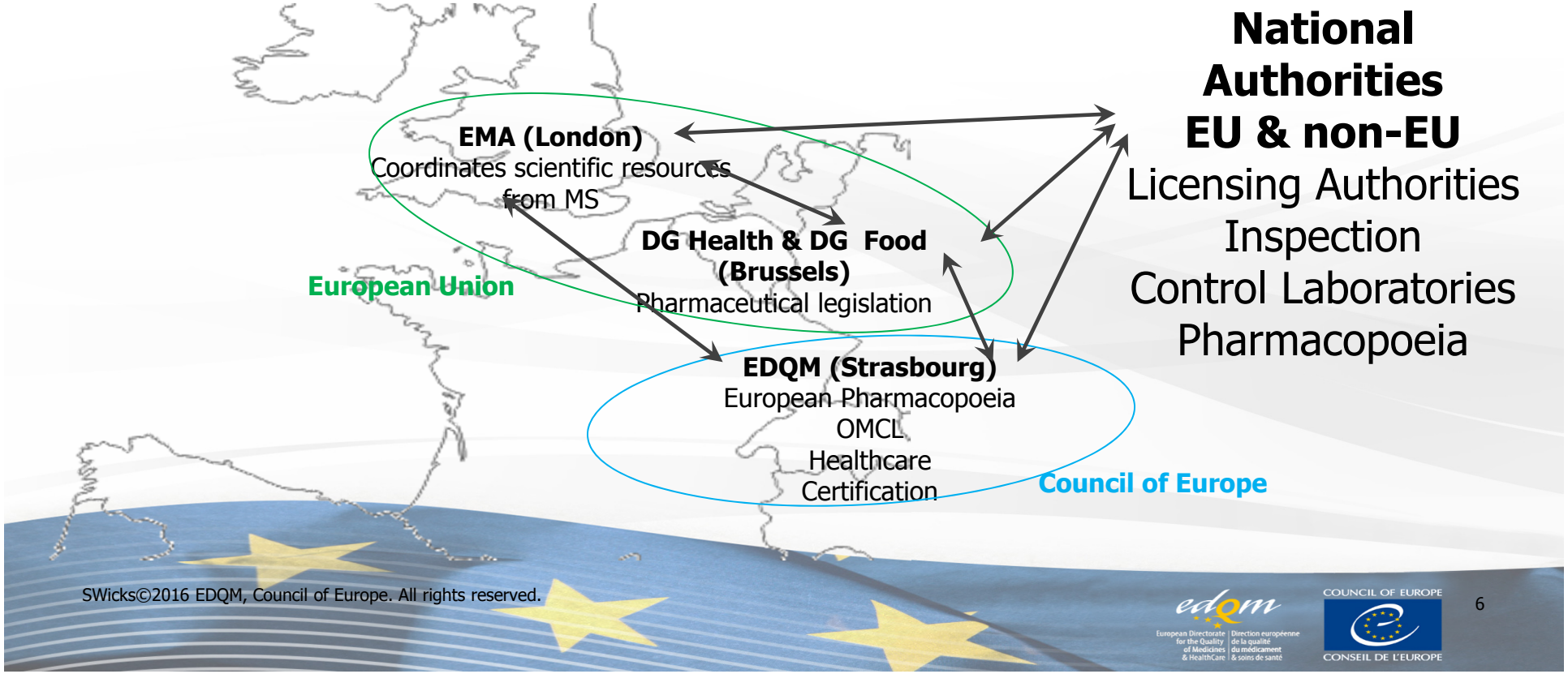
Leader in protecting public health by enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use

Mission: contribute to the **basic human right of access to good quality medicines and healthcare** and to promote and protect human and animal health

...to the EDQM

- **1994**: EU signs the Ph. Eur. Convention; Creation of the procedure of Certification for active substances & creation of the European Network for OMCLs
- 2007: transfer of activities on blood transfusion and organ transplantation
- 2008: transfer of activities for healthcare activities and combating counterfeits
- 2009: transfer of activities on cosmetics and food-packaging

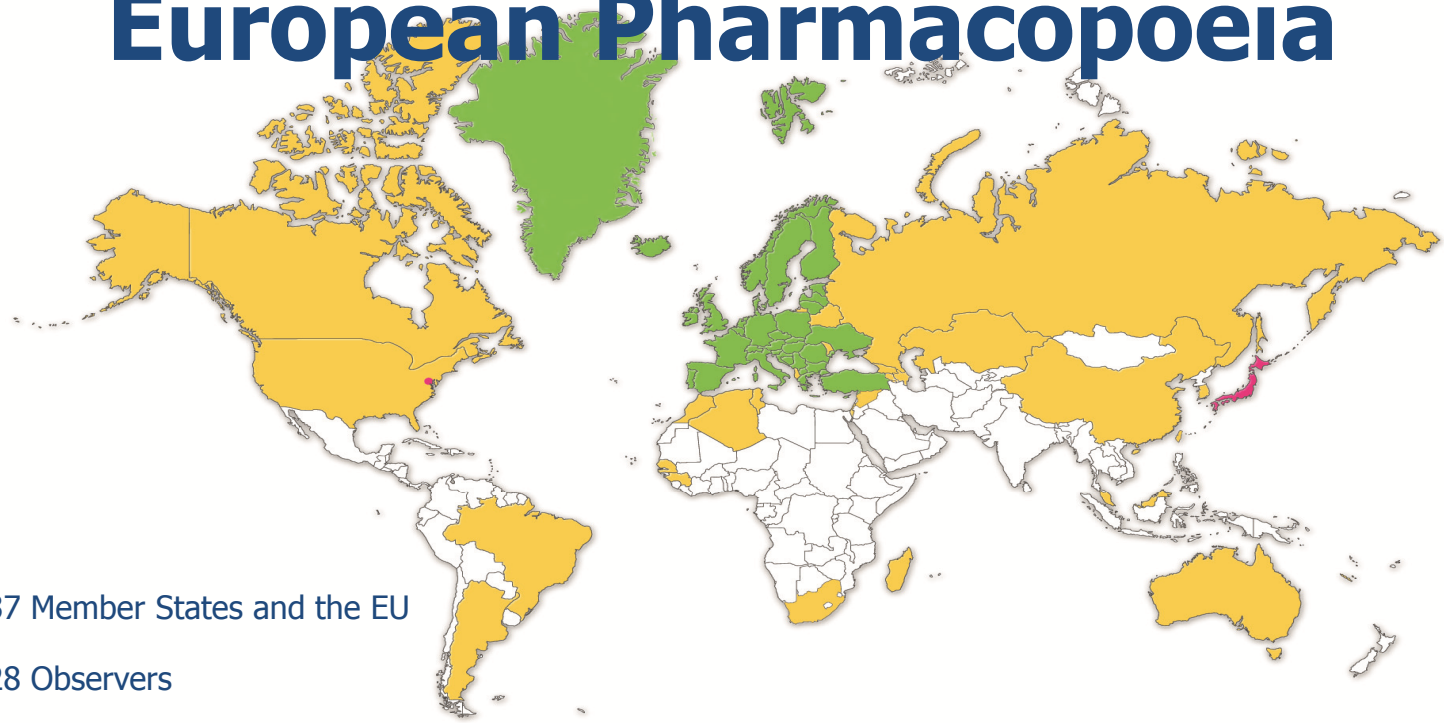
European interaction



European Pharmacopoeia

- Protecting public health - one common compulsory standard
- Mandatory status in EU/EEA by European pharmaceutical legislation
- 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 the EU, i.e. raw material, preparations, dosage forms, containers must comply with the Ph. Eur. requirements when they exist.

Convention on the Elaboration of a European Pharmacopoeia

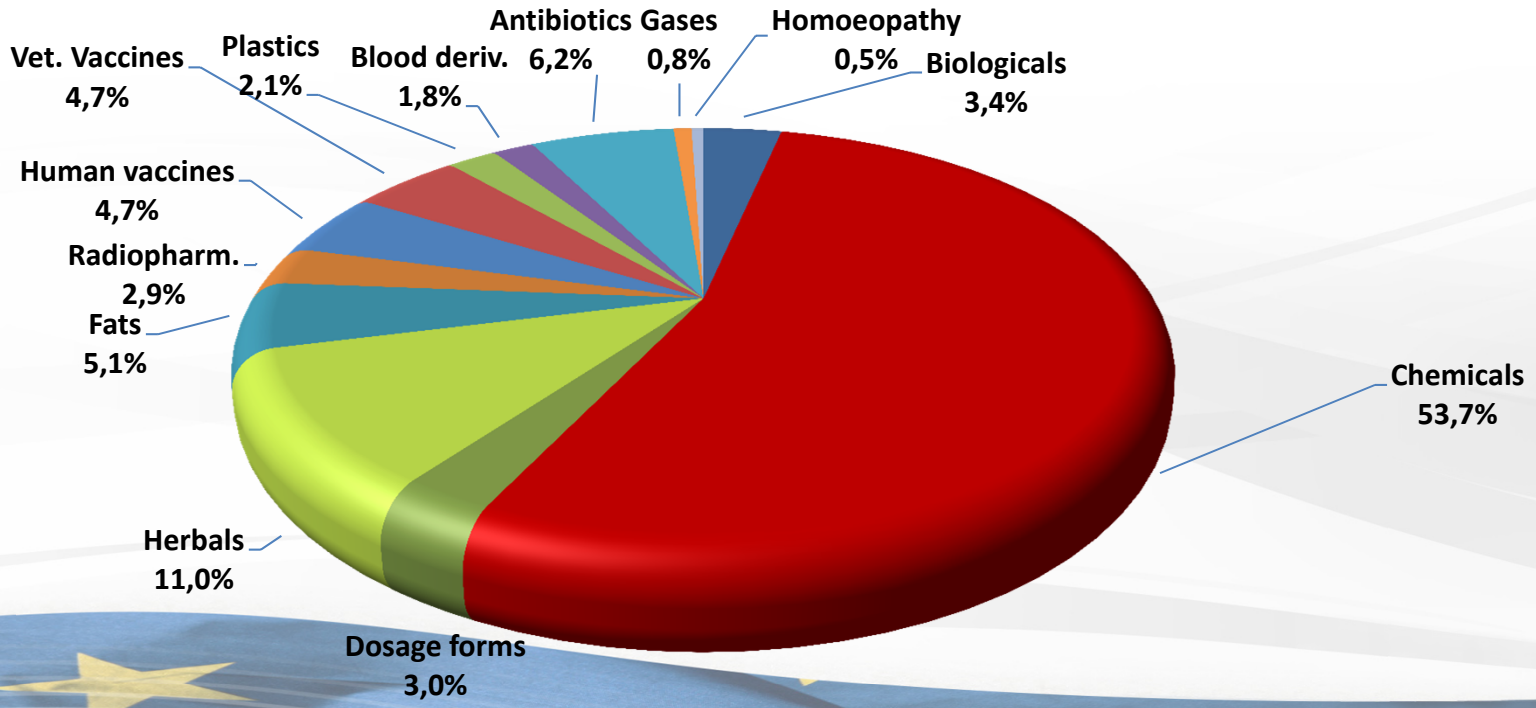


37 Member States and the EU

28 Observers

Contents of the European Pharmacopoeia:

Nearly 2400 Monographs and more than 330 General chapters



Cell and Gene Therapy in the Ph. Eur.

5.14. Gene transfer medicinal products for human use

2.6.27. Microbiological control of cellular products **[REVISION]**

5.2.12. Raw materials of biological origin for the production of cell-based and gene therapy medicinal products **[NEW]**

Cell and Gene Therapy in the Ph. Eur.

2323 Human haematopoietic stem cells

5.2.3. Cell substrates for the production of vaccines for human use

5.2.4. Cell cultures for the production of veterinary vaccines

2031 Monoclonal antibodies for human use

0784 Recombinant DNA technology, products of

1468 Products of fermentation [indirect gene products]

2.2.59. Glycan analysis of glycoproteins

2262 Bovine Serum

Chapter 2.6.27: Microbiological control of cellular products

Originally developed for use with the monograph on Human haematopoietic stem cells (2323) in place of the test for sterility (2.6.1) which is often not the method of choice for these products.

- better sensitivity
- broader range
- more rapid

Referred to in chapter *5.14 Gene transfer medicinal products for human use* and *2323 Human haematopoietic stem cells*

Revision of 2.6.27

Expanded to take in to account the **characteristics of cell based preparations** and the limitations of microbiological control

- Shelf life before patient administration
- Amounts available for testing (limited volume)
- Sampling related issues
- Production process makes them more susceptible to environmental contamination

Revision of 2.6.27

Published twice for public comment

- Pharmeuropa 25.4: Many comments - redrafted specifically to address the scope
- Pharmeuropa 27.3 (republished):

Revision of 2.6.27

- Now has greater flexibility for incubation temperatures
- Change to the micro-organism used - addresses common contaminants
- Flexibility to modify the list of micro-organisms
- Introduces reference to *2.6.1 Sterility test* and *5.1.6 Alternative methods for control of microbiological quality*
- Volume handling [1-10 mL] [10-1000 mL]

Revision of 2.6.27

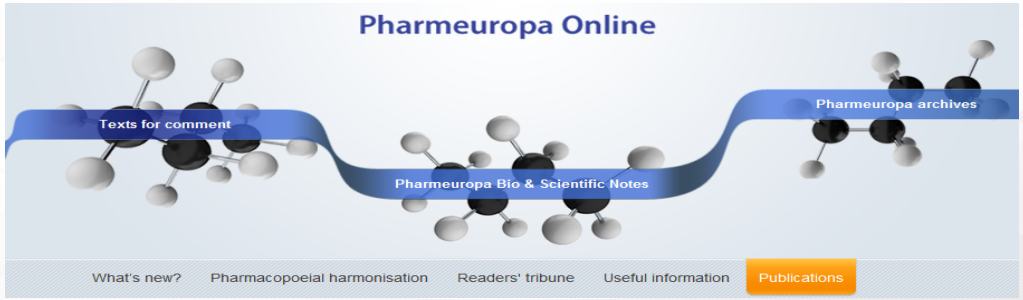
Discuss further comments in the Cell Therapy Working Party.

Provisional dates

- Adoption by Commission 155 (June 2016)
- Published in Ph. Eur. 9.1 (January 2017)
- Implementation (July 2017)

Draft chapter 2.6.27

Consultation now closed but can be reviewed in Pharmeuropa pharmeuropa.edqm.eu



Free access (after registration)

Chapter 5.2.12 Raw materials

RCG Working Party

- 14 Members + 2 observers
- European Medicines Agency and EDQM working together
  - Chair (current and former) of EMA BWP
  - Chair of EMA CAT
  - Members of EMA BWP
  - EMA observer
- Manufacturers
- Chair: Dr Jaana Vesterinen

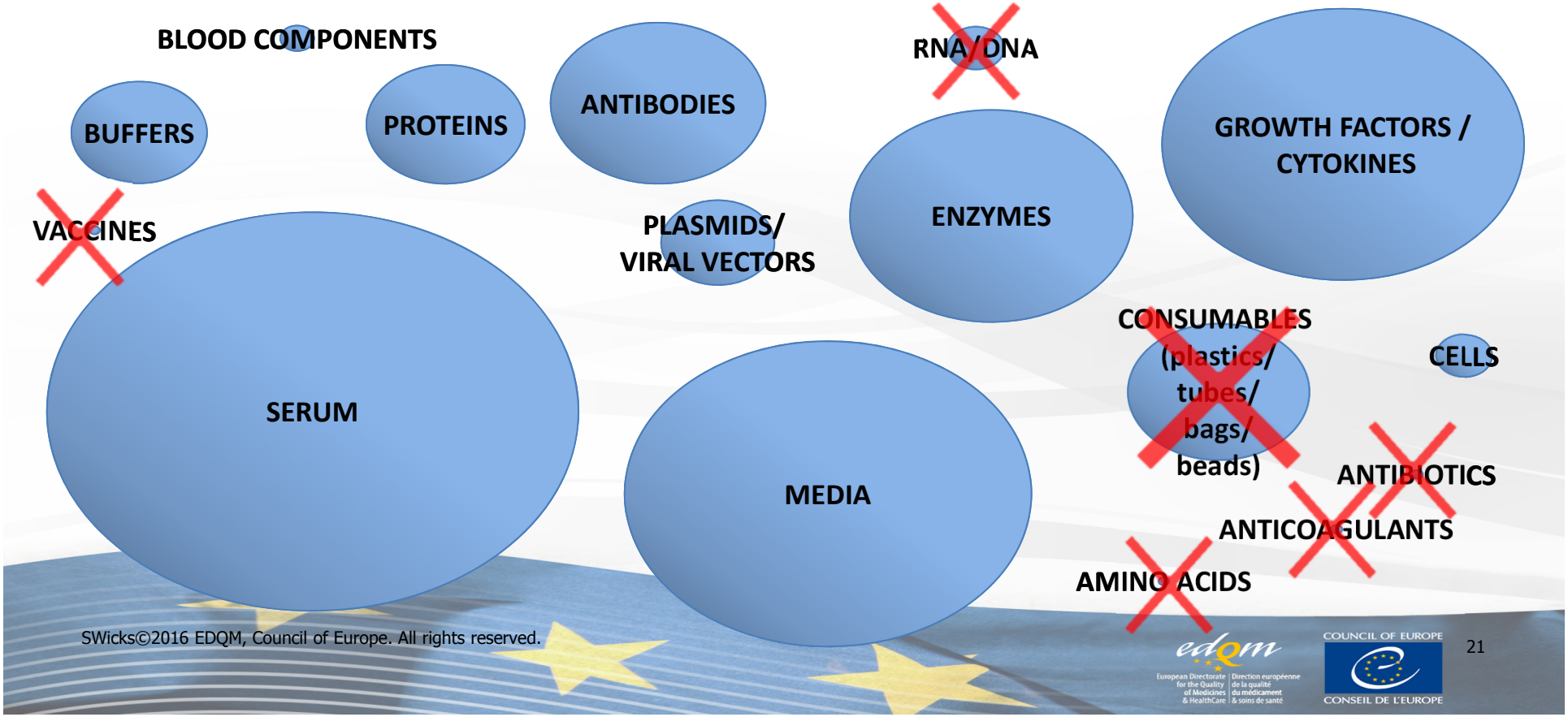
Background

- The Ph. Eur. Commission decided to establish the RCG WP (Raw Materials for the Production of Cellular and Gene Transfer Products WP) in June 2012
- RCG WP started its drafting work in 2012
- EDQM & EMA organised an International symposium (April 2013) to gather input from stakeholders
- [http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/11/WC500153798.pdf]

RCG Symposium outcomes

- EDQM and the EMA gathered views of stakeholders on the proposed Ph. Eur. text
- Challenges for all stakeholders
  - lack of harmonisation in the quality standards for raw materials
  - variability in approaches (grades / quality / stage of use)
- Types of raw materials / quality attributes that would need to be included in a Ph. Eur. text.

April 2013 EDQM/EMA Workshop: Raw materials most critical from a quality perspective



Chapter aims

5.2.12 is a general chapter - covers the quality requirements of raw materials used for the production of cell-based and gene therapy products.

- the text is non-mandatory
- harmonises current variable practices
- helps users to identify the critical quality attributes of raw materials
- helps users to manage batch-to-batch variation and change control for raw materials
- encourages raw material manufacturers to record and share information on the origin and quality of the raw material

Pharmeuropa Comments

- definitions (raw material / starting material)
- responsabilities of raw material manufacturers and users
- risk assessment
- GMP aspects / quality systems
- raw material quality grades
- references to existing Ph. Eur. texts and monographs
- origin / traceability
- testing for viruses

Chapter 5.2.12

1. Scope
2. Risk Assessment
3. General requirements
   - 3-1. Origin
   - 3-2. Production
   - 3-3. General quality requirements
     (ID / Tests / Ref. mat/batch)
   - 3-4. Storage
   - 3-5. Labelling
4. Sera and serum replacements
   - *4.1 Definition*
   - *4.2 Production*
   - *4.3 Identification*
   - *4.4 Tests*
   - *4.5 Assay*
5. Proteins produced by recombinant DNA technology
6. Proteins extracted from biological material
7. Vectors

5.2.12 Progress

- Adopted at the 153rd Commission session (November 2015)
- Publication in the Ph. Eur. 9th edition (July 2016)
- Effective date 01 January 2017

Summary

- 5.2.12 to be published in Ph. Eur. 9
- Revised chapter 2.6.27 to be published in Ph. Eur. 9.1
- Evolution in the Ph. Eur. approach to cell and gene therapy
- As the field develops – continually revise the chapters and monographs of the Ph. Eur.

Join the Ph. Eur.

No change

Experts from Ph. Eur. member states (re)nominated in Nov. 2016 via NPAs

Nominations open to experts from non Ph. Eur. member states or observers:

NEW!

- Candidatures (nomination form, CV, Declaration of interest form) to be sent to the Secretariat via the Helpdesk system
- Ph. Eur. Commission decision
- More information to be published soon on EDQM's website

Thankyou for your attention

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