Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

Update from each Pharmacopoeia

Moderator: Petra Doerr, EDQM, Council of Europe

EDQM 60 1964 - 2024

COUNCIL OF EUROPE 75 1949 - 2024 CONSEIL DE L'EUROPE

Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

European Pharmacopoeia
Cathie VIELLE

EDQM 60 1964 - 2024
COUNCIL OF EUROPE 75 1949 - 2024 CONSEIL DE L'EUROPE

Our Medium-Term Strategy

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

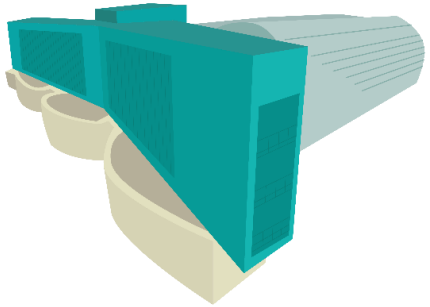
COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

The European Pharmacopoeia celebrated its 60th anniversary

Contents

The EDQM, who we are

The **European Directorate for the Quality of Medicines and HealthCare (EDQM)** is a structural part of the Council of Europe, an international and intergovernmental organisation.



- Founded in **1964**
- Ensuring **access and availability to good quality medicines and healthcare in Europe**

4 major policy areas

Medicines

Pharmaceutical Care

Substances of Human Origin (SoHO) (blood, tissues and cells and organs)

Consumer Health (cosmetics, tattoos, and food contact materials)

- **39** Members & the **EU, 33** Observers
- A network of more than **2000 experts**

Our strategic objectives

(available on EDQM website*)

1. Responsiveness	We will respond to and/or address current and emerging public health challenges and priorities for the benefit of patients and consumers.
2. Global outreach	We will enhance the global outreach and impact of the EDQM.
3. Stakeholder engagement	We will actively engage with our stakeholders to increase trust and credibility, improve decision-making, and ensure the sustainability of the organisation.
4. Sustainability	We will ensure a sustainable EDQM by future-proofing our operations and activities.
5. Modernisation	We will modernise our working methods to increase the quality and efficiency of our contribution to public health.
6. People development	We will develop our people, our teams, and our organisational culture to achieve our goals.
7. Culture of service	We will establish and enhance a culture of service.

(*) https://www.edqm.eu/documents/52006/0/EDQM_Medium-Tern_Strategy_Document_EN.pdf/98c714a7-8aae-7a01-5e48-c93c70ea25ff?t=1716378183686

The Way Forward

For each strategic objective, we have set ourselves sub-objectives. These outline our priorities and form our implementation plan.

Strategic Objective 2

example

We will enhance the global outreach and impact of the EDQM.

To achieve this objective, we will:

- Develop and implement a strategy outlining the role of the EDQM in global convergence/harmonisation and its positioning as a key public health organisation.
- Increase global reliance on EDQM standards and activities to improve access to medicines.
- Strive towards elaboration of globally harmonised standards and promote reliance on them.

And launch the following initiatives:

Our Initiatives:

- Elaborate a strategy and roadmap on enhancing EDQM global outreach and impact,
- Foster acceptance of CEPs globally, and,
- Develop a strategy on training and knowledge sharing towards our stakeholders.

Strategic Objective 3

example

We will actively engage with our stakeholders to increase trust and credibility, improve decision- making and ensure the sustainability of the organisation.

We will consider stakeholder engagement as a critical component for the successful completion of our activities and for the overall sustainability of the organisation.

To achieve this objective, we will:

- Increase the transparency and clarity of our processes and communication.
- Share knowledge through a collaborative environment that fosters dialogue.
- Identify emerging issues and opportunities, and work together to find common solutions.
- Cultivate our networks to enhance our scientific competence and maximise the positive impact of the EDQM on public health.

And launch the following initiative:

Our Initiative:

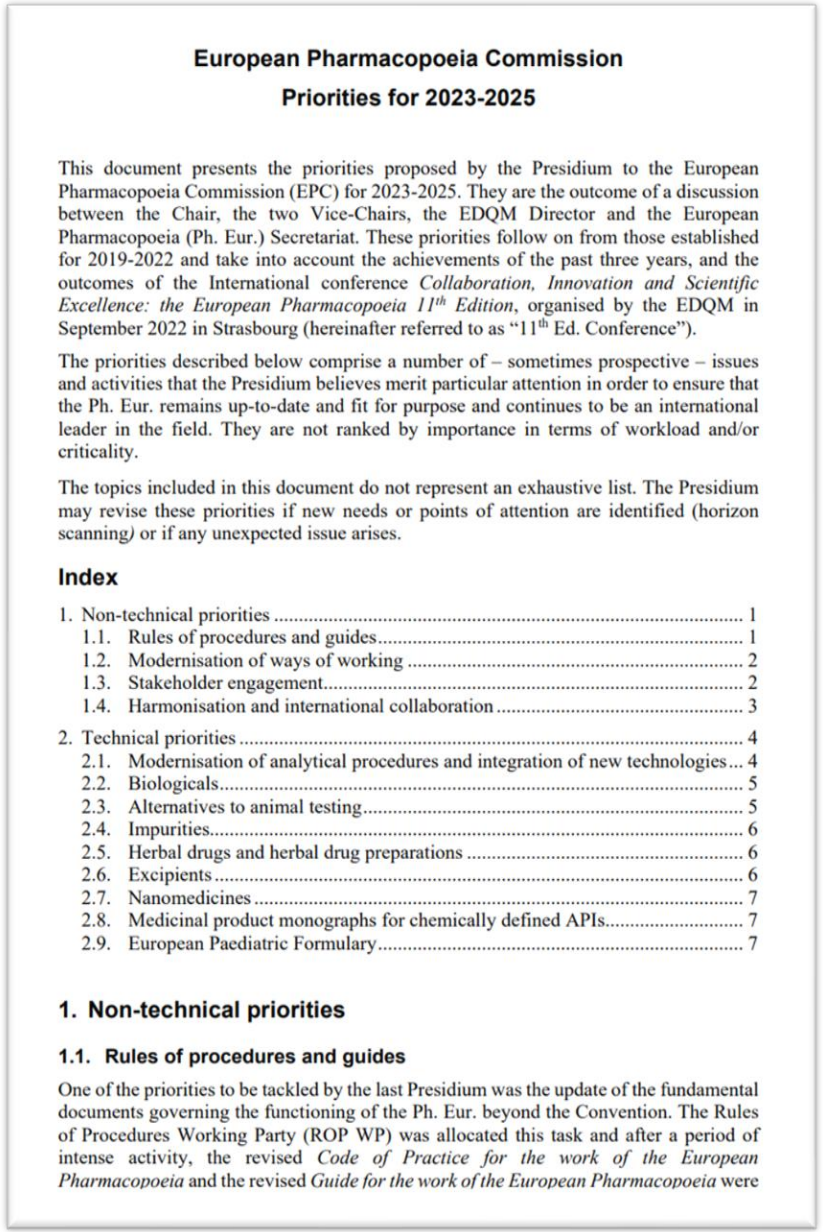
- Develop and implement a stakeholder engagement strategy.

Priorities of the EPC

"Collaboration (…) is crucial for the continuous improvement of the Ph. Eur. Any action enhancing this collaboration will be supported"

"International collaboration is in the DNA of the Ph. Eur."

→ Full commitment and support of the EPC



European Pharmacopoeia Commission

Priorities for 2023-2025

This document presents the priorities proposed by the Presidium to the European Pharmacopoeia Commission (EPC) for 2023-2025. They are the outcome of a discussion between the Chair, the two Vice-Chairs, the EDQM Director and the European Pharmacopoeia (Ph. Eur.) Secretariat. These priorities follow on from those established for 2019-2022 and take into account the achievements of the past three years, and the outcomes of the International conference *Collaboration, Innovation and Scientific Excellence: the European Pharmacopoeia 11th Edition*, organised by the EDQM in September 2022 in Strasbourg (hereinafter referred to as "11th Ed. Conference").

The priorities described below comprise a number of – sometimes prospective – issues and activities that the Presidium believes merit particular attention in order to ensure that the Ph. Eur. remains up-to-date and fit for purpose and continues to be an international leader in the field. They are not ranked by importance in terms of workload and/or criticality.

The topics included in this document do not represent an exhaustive list. The Presidium may revise these priorities if new needs or points of attention are identified (horizon scanning) or if any unexpected issue arises.

Index

1. Non-technical priorities

1.1. Rules of procedures and guides

One of the priorities to be tackled by the last Presidium was the update of the fundamental documents governing the functioning of the Ph. Eur. beyond the Convention. The Rules of Procedures Working Party (ROP WP) was allocated this task and after a period of intense activity, the revised *Code of Practice for the work of the European Pharmacopoeia* and the revised *Guide for the work of the European Pharmacopoeia* were

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Follow the EDQM on:

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Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

Indian Pharmacopoeia
Gaurav Pratap SINGH JADAUN

Indian Pharmacopoeia Standards for Ensuring Quality of Medicines in India

PDG Stakeholders' Forum

October 3, 2024

INDIAN PHARMACOPOEIA (IP)

Official Book of Drug Standards in India

IP REFERENCE STANDARDS (IPRS) & IMPURITIES

Official Physical Standards for Assessing the Quality of Drugs

NATIONAL FORMULARY OF INDIA (NFI)

Reference Book to Promote Rational Use of Generic Medicines

PHARMACOVIGILANCE PROGRAMMES OF INDIA (PvPI)

WHO Collaborating Centre for Pharmacovigilance in Public Health Programmes and Regulatory Services

Indian Pharmaceutical Industry

Ranks 3rd for pharma production by volume and 14th by value

World leader in production and supply of vaccines (~60% of total vaccines and 70% of WHO Vaccines)

62% generic exports are to highly regulated markets. Supplies 40% generic demand in USA & 25% in UK

Supplies high-quality medicines at affordable cost and known as ‘Pharmacy of the world’

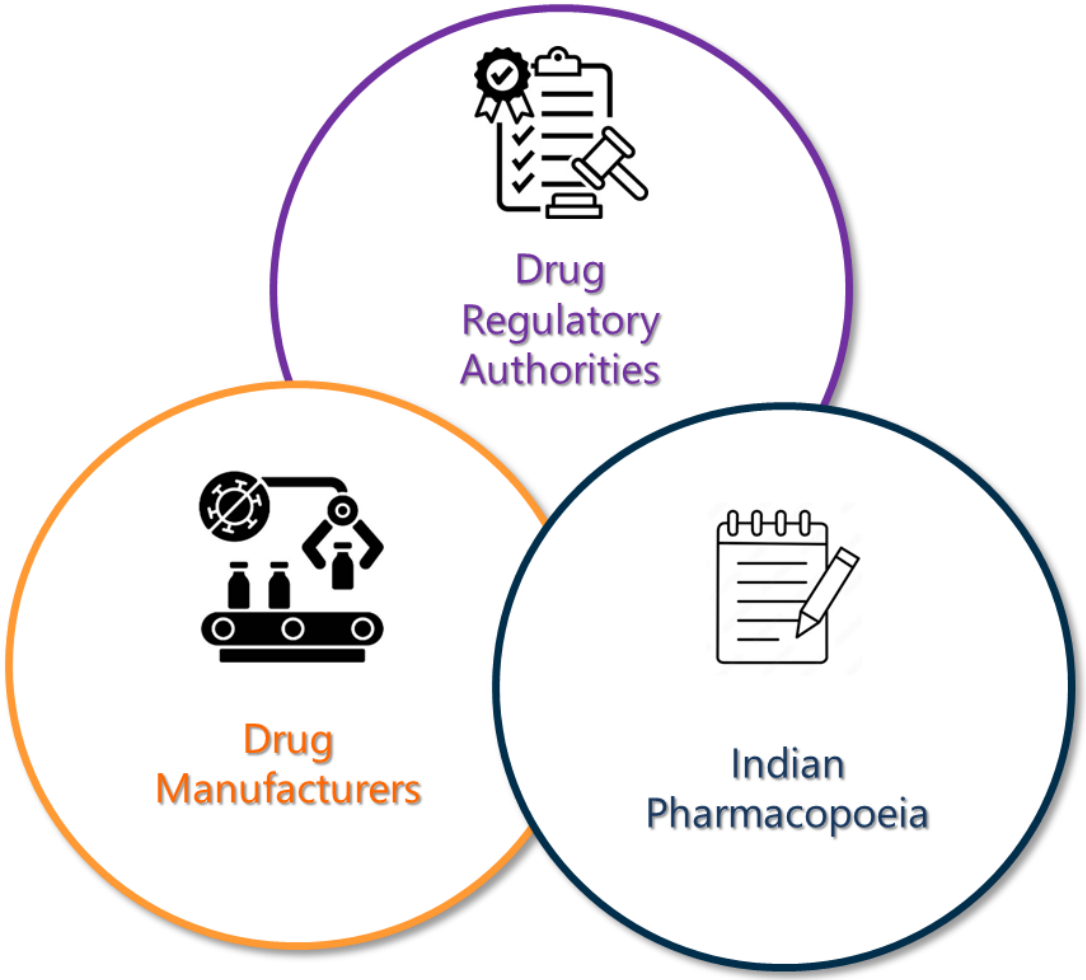
Drug Regulatory Framework

Drugs regulation in India is governed by the provisions of the Drugs & Cosmetics Act, 1940

Both Central and State drug regulatory authorities perform the functions as per their mandate

CDSCO is the Central Drug Regulatory Authority in India

IPC coordinates with regulatory authorities and drug manufacturers for developing standards



Indian Pharmacopoeia Commission (IPC)

An autonomous Institute under the Ministry of Health & Family Welfare, Government of India

Three-tier structure comprising of General Body, Governing Body, and Scientific Body

Expert Working Groups (EWGs) with subject experts to guide on standards' setting process

Expert Working Groups (EWGs) with subject experts to guide on standards' setting process

Indian Pharmacopoeia (IP)

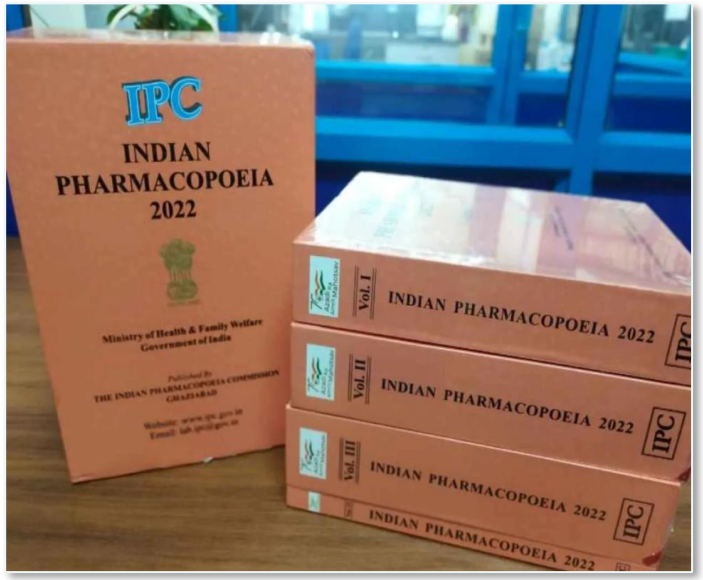
Official book of drug standards in India as per the Drugs & Cosmetics Act 1940

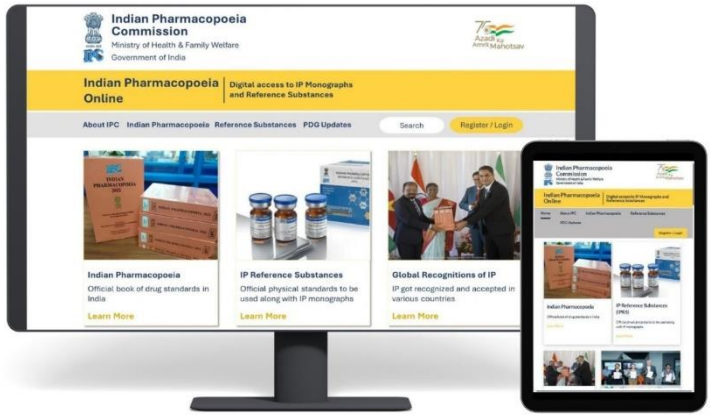
Contains monographs on APIs, formulations, excipients, veterinary medicines etc.

Monograph development by public comments and expert consultations

IP standards are authoritative and legally enforceable

Helps ensuring the quality of medicines being manufactured and marketed in India

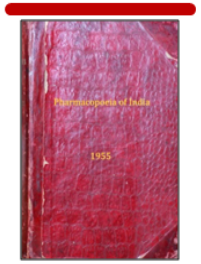




Publication History of IP Editions

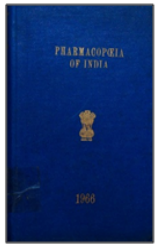
1955 — First Edition

1 Volume
986 Monographs
Title of monographs in Latin
Supplement in 1960



1966 — Second Edition

1 Volume
890 Monographs
Title of monographs changed from Latin to English
Supplement in 1975



1985 — Third Edition

1 Volume
886 Monographs
Anti-cancer Monographs Incorporated
Addenda in 1989 & 1991

1996 — Fourth Edition

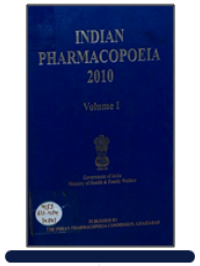
2 Volumes
1149 Monographs
Addenda in 2000, 2002, and 2005
Veterinary Supplement in 2000

2007 — Fifth Edition

3 Volumes
Published by CIPL
1623 Monographs
Addenda in 2008

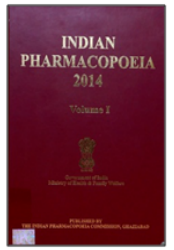
2010 — Sixth Edition

3 Volumes
Published by IPC
1968 Monographs
Biotech Monographs Incorporated
Addendum in 2012



2014 — Seventh Edition

4 Volumes
Separate Veterinary Volume
2586 Monographs
Radiopharmaceutical Monographs Incorporated
Addenda in 2015 & 2016



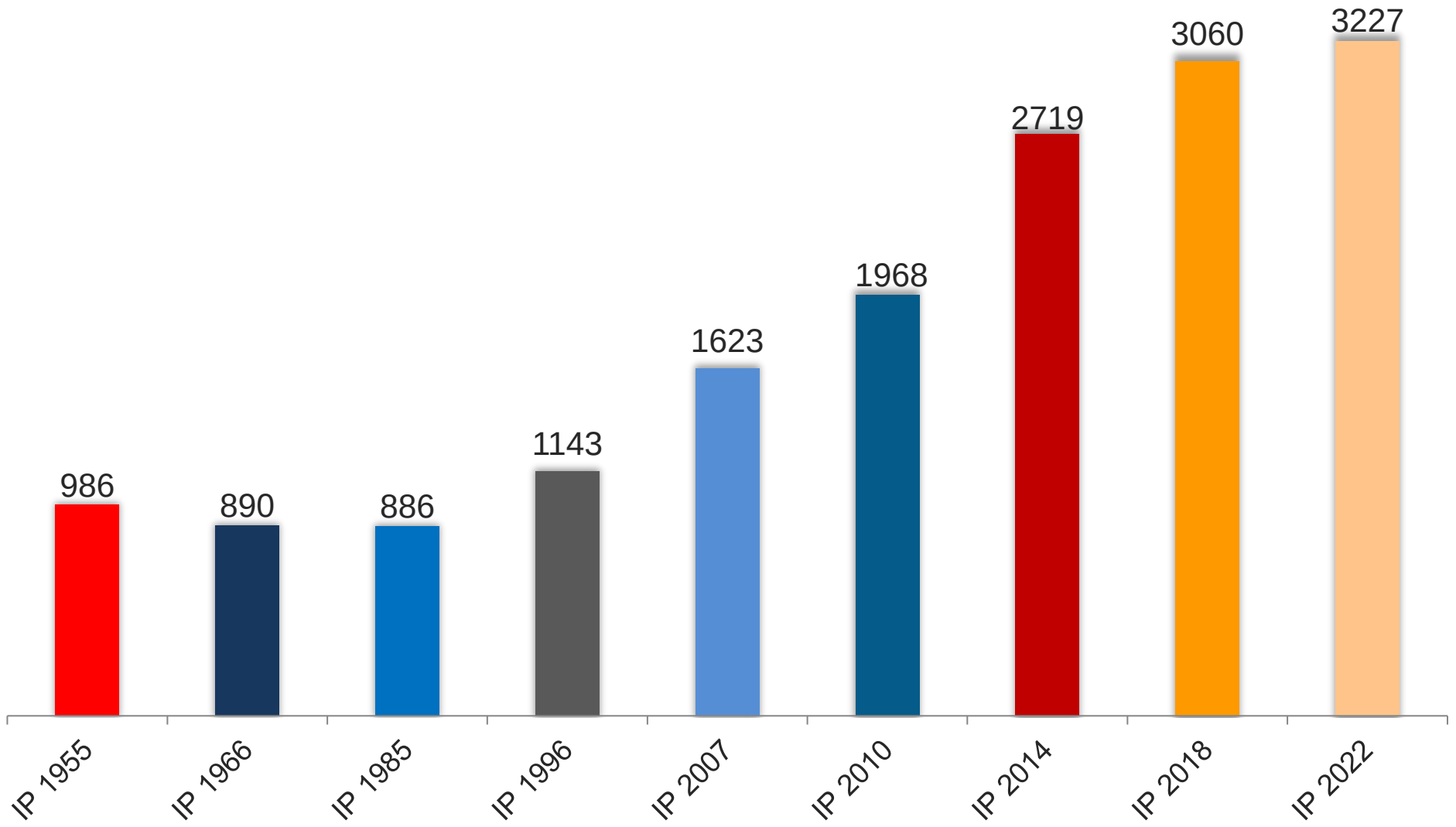
2018 — Eighth Edition

4 Volumes
3060 Monographs
Allergen Monograph Incorporated
Addenda in 2019 & 2021

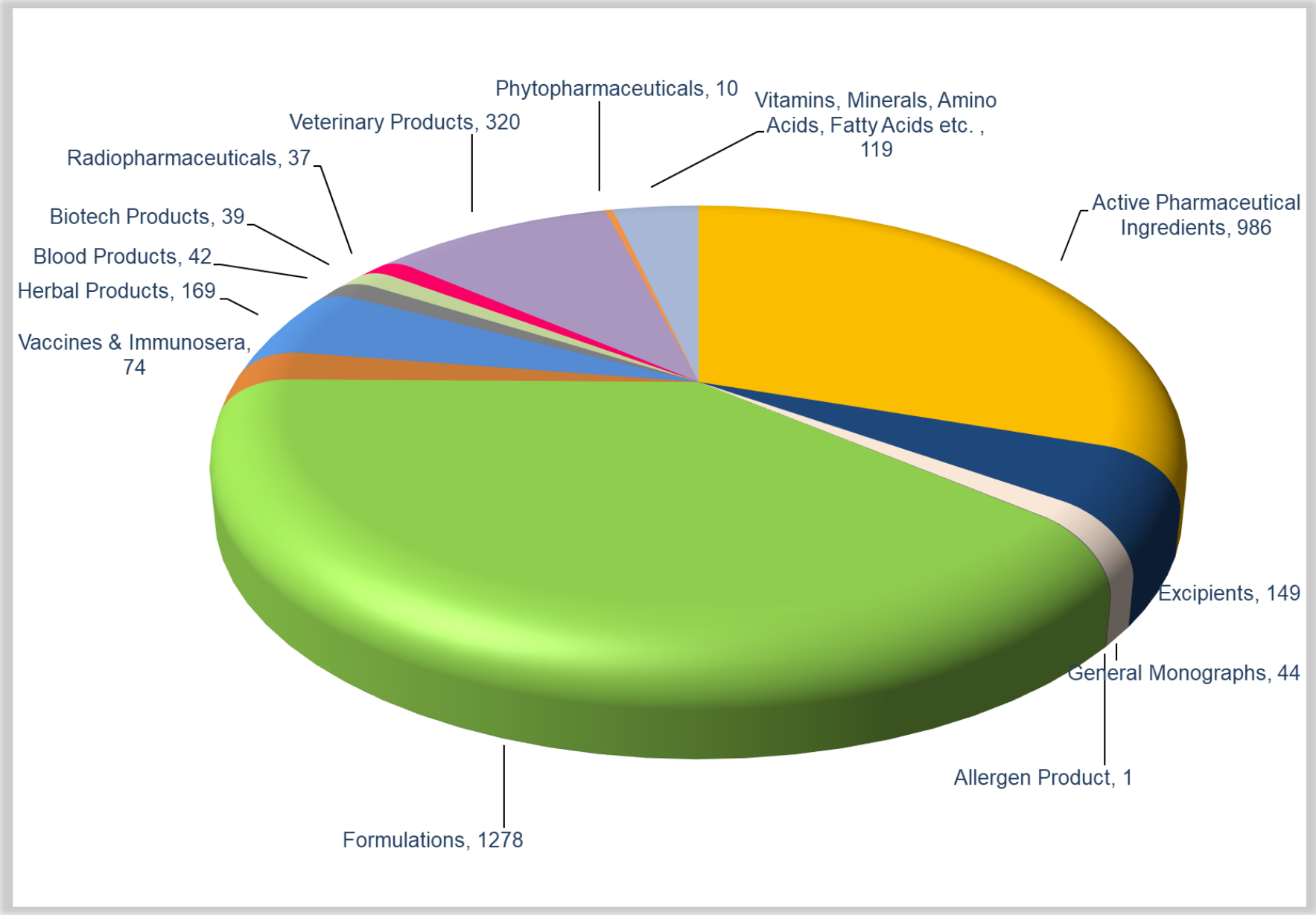
2022 — Ninth Edition

4 Volumes
3152 Monographs
Phytopharmaceuticals Monographs Incorporated
General Chapters on Elemental Impurities & Nitrosamines

Monograph Numbers in IP Editions



IP 2022: Monograph Status



Response to COVID-19

Pharmacopoeia Monographs

- Developed monographs on COVID-19 drugs (Remdesivir, Favipiravir,Ivermectin)
- IP became first Phamacopoeia to have monographs on Remdesivir and Favipiravir

Guidance to Industry

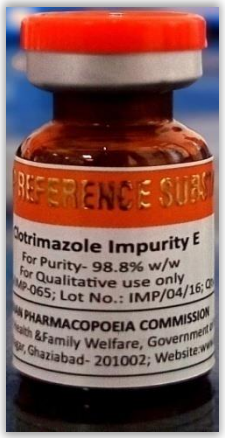
- Developed guidance on ‘Rapid Microbiological Methods’ for early batch release of COVID-19 related drugs during pandemic

Reference Standards

- Developed IPRS on COVID-19 related drug and made available to stakeholders (Remdesivir, Favipiravir, Ivermectin, Azithromycin, Hydroxychloroquine sulphate, Doxycycline hydrochloride, Dexamethasone)

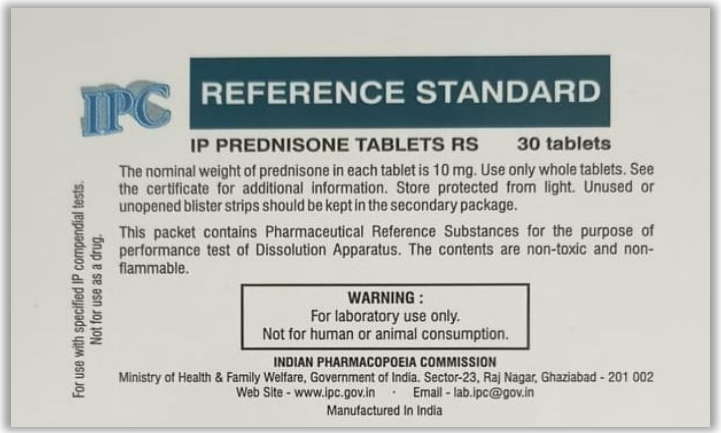
Types of Reference Standards

IP Reference Substances



Impurity Reference Substances

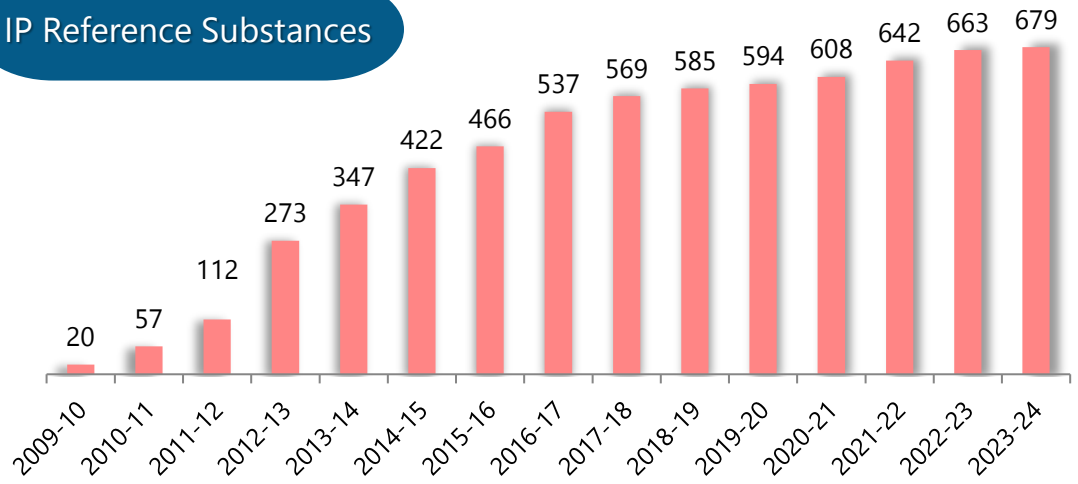
Phytochemical Reference Substances



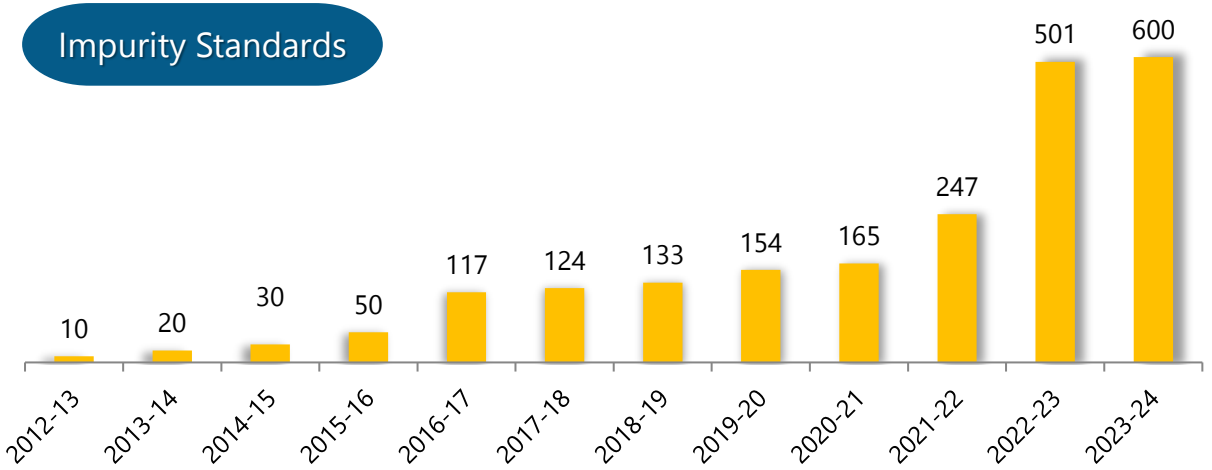
Prednisone Dissolution Calibrator Tablet

Development of IP Reference Substances

IP Reference Substances



Impurity Standards



Pharmacopoeial Collaborations

IPC signs MoU with United States Pharmacopoeia (USP)

MoUs also signed on pharmacopoeial cooperation with:

- British Pharmacopoeia, and
- Russian Pharmacopoeia (SCEEMP)

Strategic Actions and Challenges

Adoption of Impurity limits as per ICH guidelines

Introduction of Elemental Impurities in line with ICH Q3D

Inclusion of dissolution specifications in prolonged-release formulations with flexible monograph approach

Harmonization of pharmacopoeial text with the PDG

Addition of general chapter on Nitrosamines

Thank You

Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

Japanese Pharmacopoeia

Yoshiro SAITO

Update from each Pharmacopoeia

Implementation of the ICH Q3D Guideline in JP

Yoshiro Saito, Ph.D.

Deputy Director General
National Institute of Health Sciences (NIHS)

独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

The Japanese Pharmacopoeia (JP)

- JP 1st edition was published on June 25, 1886 and implemented on July 1, 1887.

  ⇒ ***JP has the history of over 135 years***

- JP is published by the Japanese Government as a Ministerial Notification by the Ministry of Health, Labour and Welfare (MHLW).
  - Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices Article 41
    - In order to ensure the proper properties and quality of pharmaceuticals, the MHLW must set forth and make public notice of the JP after gaining opinions from the Pharmaceutical Affairs and Food Sanitation Council (PAFSC).
    - The MHLW must consult with the PAFSC on any revisions to be made through discussions on all aspects of the JP made by the PAFSC at least every 10 years.

      ⇒ From 1991, new editions are published in every 5 years and their 2 supplements in between. Partial revision have been made as necessary.

JP 1st Edition

Establishment of JP

Free Access (Shared Knowledge of Society)

PDG

Pharmacopoeial Harmonization

Regulatory Perspective

Scientific Perspective

Commission

Request for review

Ministry of Health, Labour and Welfare (MHLW)

Report

Result

JP Expert Committees

Committee members
Experts from outside

Regulatory Harmonization

ICH Member

Comments

Comments

Public

Universities

Research Institutes

Pharmaceuticals Manufacturers' Associations

Contents of JP

1. **General Notices** - specification of general rules: 49 paragraphs in JP18-2
2. **General Rules for Crude Drugs** - specification of general rules for crude drugs: 10 paragraphs in JP18-2

3. **General Rules for Preparations** - general notices for preparations, general notices for packaging of preparations, monographs for preparation, monographs for preparations related to crude drugs : 75 paragraphs in JP18-2

4. **General Tests, Processes and Appratus :** 90 General tests in JP18-2 - Chemical methods, Physical Methods, Powder Property Determinations, Biological/Biochemical/Microbial tests, Tests for crude drugs, Tests for preparations, Tests for containers and packing materials, Reference standards/standard solutions, Reagents, Test solutions, Measuring Instruments, Appliances

5. **Official Monographs :** 2048 articles in JP18-2

6. **Reference Spectra** - Ultraviolet-visible, Infrared

Japanese Pharmacopoeia

Legally binding part

7. **General Information :** 71 chapters in JP18-2

   Basic Concepts on Pharmaceutical Quality, Physics and chemistry, Solid-state properties, Biotechnological/biological products, Microorganisms, Crude drugs, Drug formulation, Containers and package, Reference Standards, Pharmaceutical Excipients, Others

8. **Appendix**

Non-legally binding part

(As of July, 2024)

Basic Principles for Preparation of JP18 (dated October 19, 2016)
- Five Principles for JP Revision -

1. Including all drugs which are important from the viewpoint of health care and medical treatment
2. Making qualitative improvement by introducing the latest science and technology
3. Promoting further internationalization in response to globalization of drug market
4. Making prompt partial revision as necessary and facilitating smooth administrative operation
5. Ensuring transparency regarding the revision, and disseminating the JP throughout Japan and the rest of the world

Basic Principles for Preparation of JP18 (dated October 19, 2016)
- Principle for the control of impurities -

2. Making qualitative improvement by introducing the latest science and technology

2-6. Improvements in the control of impurities in response to international trends:

- In response to international trends, the control of impurities in consideration of risks and especially the control of elemental impurities in consideration of ICH Q3D "Guidelines for Elemental Impurities" shall be carried out based on the roadmap to be included in the JP.

Timeline of ICH Q3D related matters in Japan

Adoption of ICH Q3D Guideline in Japan (September 30, 2015)

Scope: New finished drug products (as defined in ICH Q6A and Q6B) and new drug products containing existing drug substances.

JP17-2
Published on June 28, 2019

- General Test 2.66 Elemental Impurities – Procedures
- General Information G1. "Control of elemental impurities in drug products" (corresponding to the ICH Q3D guideline)

JP18
Published on June 7, 2021

- General Notice 34
- General Test 2.66 Elemental Impurities

JP18-1
Published on December 12, 2022

- Removing heavy metals tests and/or individual metal impurity tests from 863 monographs

JP18-2
Published on June 28, 2024

- Removing arsenic tests from 21 monographs in JP18-2

Basic Principles for Preparation of JP18 (October 19, 2016)

- A roadmap for inclusion of ICH Q3D in JP

Expansion of the scope of the ICH Q3D (December 28, 2020)

- Handling of Elemental Impurities in Prescription Drugs (PSEHB/PED Notification No. 1228-7)
  English version: https://www.pmda.go.jp/files/000239969.pdf
- Question and Answer (Q&A) about Handling of Elemental Impurities in Prescription Drugs
  English version: https://www.pmda.go.jp/files/000239970.pdf

⇒ **Expand to existing products, generic drugs, JP products**

Main Prospective Challenges to Implement ICH Q3D in Japan

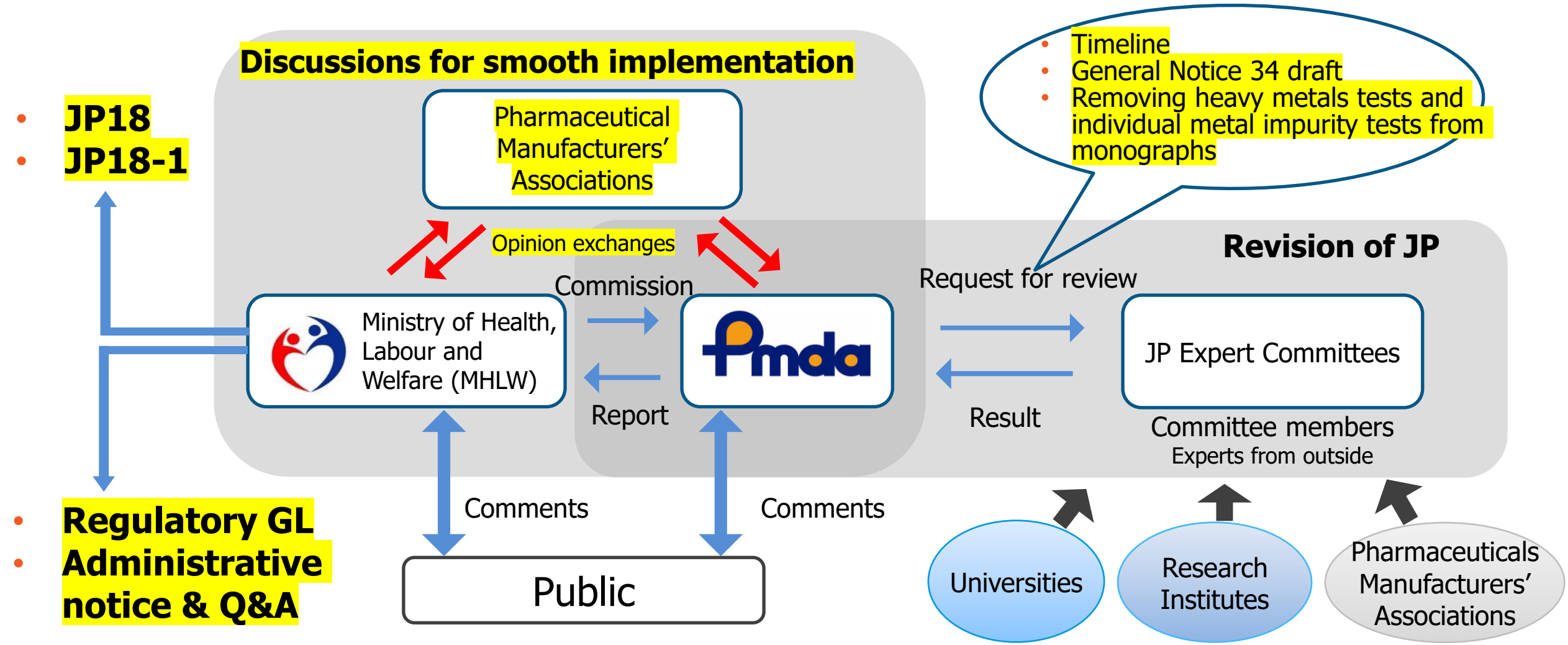
- Preparation period for implementation of ICH Q3D
  - Analytical instruments (e.g. ICP-OES, ICP-MS)
  - Risk assessments on a lot of drug products and their components
- Different timing of implementation of ICH Q3D
  - ICH Q3D stated application to existing products is not expected prior to 36 months after publication
  - Implementation in EP on December 1, 2017 and in the USP on January 1, 2018
  - Early implementation by global manufacturers, sufficient preparation period for domestic manufacturers
- Different expectations to implement ICH Q3D between drug marketing authorization holders (MAH) of and suppliers of drug substances, excipients, container/closure systems, etc. (Suppliers).
  - Several options for risk assessments (i.e. Options 1, 2a, 2b and 3)
- Clarification of regulatory expectations to implement ICH Q3D
  - Acceptable risk assessments
  - Regulatory dossier
  - Heavy metals tests and individual metal impurity tests in monographs

Exchange of Opinions among Pharmaceutical Manufacturers' Associations and Regulators (1)

- Several meetings were set up for pharmaceutical manufacturers' associations (e.g. innovators, generic drug manufacturers, API manufacturers, and packaging manufacturers) and MHLW/PMDA to address following challenges.

  - Feasible preparation period for implementation of ICH Q3D
  - How to conduct/justify risk assessments
  - How to indicate control of elemental impurities in regulatory dossiers
  - How to handle heavy metals tests and individual metal impurity tests in monographs

Exchange of Opinions among Pharmaceutical Manufacturers' Associations and Regulators (2)



Implementation of ICH Q3D in the JP

JP17-2
(published in 2019, legally binding)

<2.66> Elemental Impurities Procedures

Analytical procedure + validation

General Information
(Non-legally binding)

Control of Elemental Impurities in Drug Products (ICH Q3D)

Control

Integrated into <2.66> in the JP

JP18 (published in 2021)
(legally binding)

General Notice for Elemental Impurities (34)

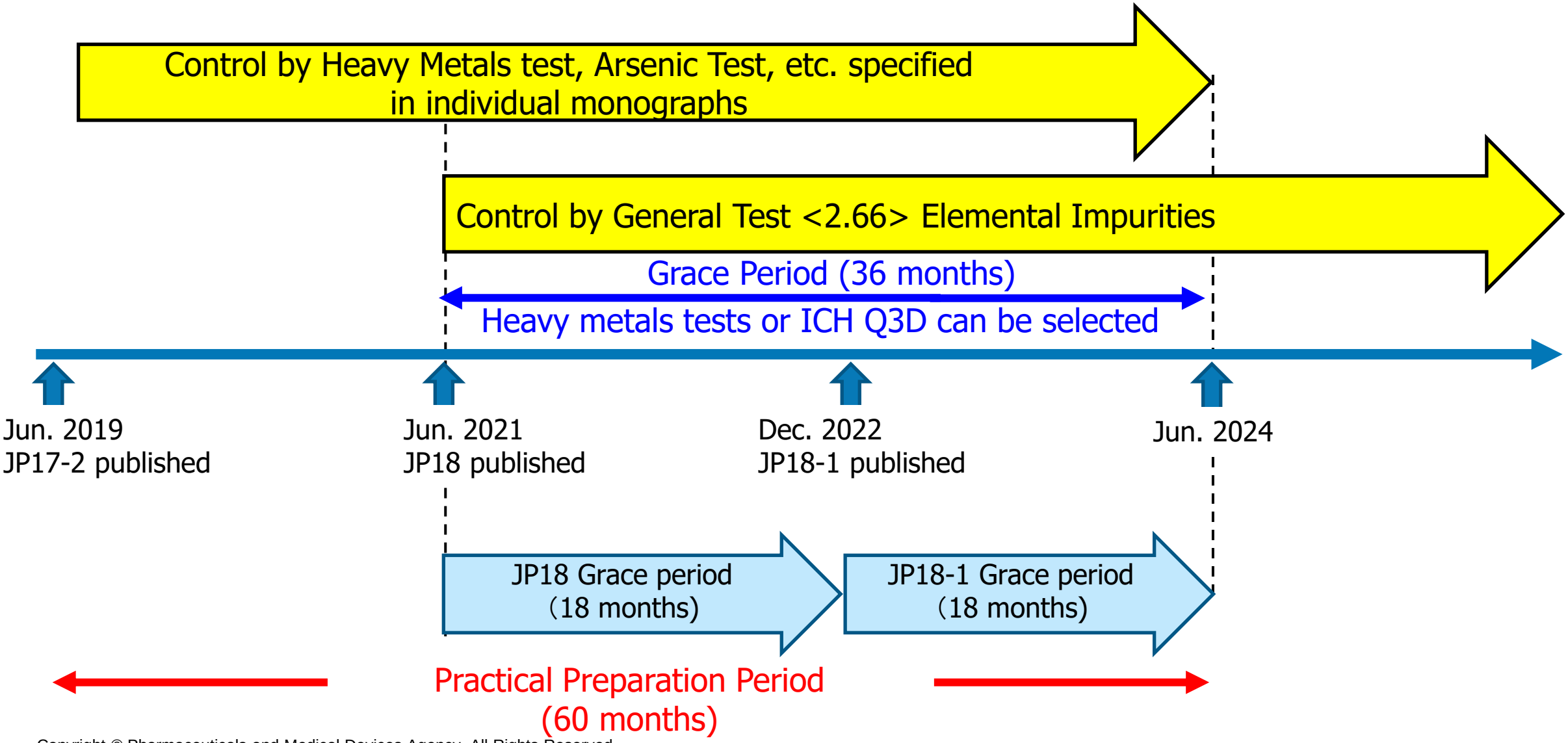
✚

<2.66> Elemental Impurities

Implementation of ICH Q3D in JP18

- ✓ Removing Heavy Metals Test and/or Individual Metal Impurity Test from 863 Monographs in JP18-1
- ✓ Removing Arsenic Tests from 21 Monographs in JP18-2

Preparation Period for Implementation of ICH Q3D



Common Expectations to Implement ICH Q3D among Stakeholders

- Handling of Elemental Impurities in Prescription Drugs (PSEHB/PED Notification No. 1228-7 dated December 28, 2020)
  ⇒ Clarify each responsibility of MAH and suppliers to implement ICH Q3D
  - MAH: are required to conduct appropriate control of elemental impurities in drug products.
  - Suppliers: are required to conduct appropriate control of elemental impurities on the basis of risk assessment and to provide relevant information as far as possible to contribute to the control of elemental impurities by the MAH.

English version: https://www.pmda.go.jp/files/000239969.pdf

- Question and Answer (Q&A) about Handling of Elemental Impurities in Prescription Drugs
  ⇒ Clarify regulatory expectations on implementation of ICH Q3D
  - 31 QAs (e.g. regulatory dossier, change control) are provided.

English version: https://www.pmda.go.jp/files/000239970.pdf

Common Expectations to Implement ICH Q3D among Stakeholders

2024 New notifications

- Question and Answer (Q&A) about Handling of Elemental Impurities (Administrative Notice dated June 25, 2024)
  - ✓ 35 QAs regarding the following topics are provided.
    - Scope etc.
    - Application for Approval
    - Risk Assessment
    - Others

Revision of the Administrative Notice dated December 28, 2020.

- Q&A about Application for Approval of Drug Product Associated with the Enactment of the First Supplement to the 18th edition of the Japanese Pharmacopoeia (Administrative Notice dated June 25, 2024)
  - ✓ 9 QAs (e.g. Scope, application for approval, risk assessment etc.) are provided regarding elemental impurities.

Conclusions

- ICH Q3D was adopted in JP.

- The regulatory guideline to expand the scope from new drugs to existing products was issued on December 28, 2020.
- JP General Notice 34 on elemental impurities and JP General Test <2.66> Elemental Impurities were included in JP18 on June 7, 2021.

⇒ The requirements on elemental impurities became legally binding to existing drug products within the scope of ICH Q3D.

- Individual JP monographs within the scope of ICH Q3D were reviewed in accordance with the publicized approach.
  - Heavy metals tests and/or individual impurity tests were removed from 863 JP monographs in JP18-1.
  - Arsenic tests were removed from 21 JP monographs in JP18-2.

- QAs about implementation of ICH Q3D was published to clarify regulatory expectations.

- **Opinions were exchanged through several meetings to have same expectations among industries and regulators to implement ICH Q3D in Japan.**

Thank you for your attention !!

Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

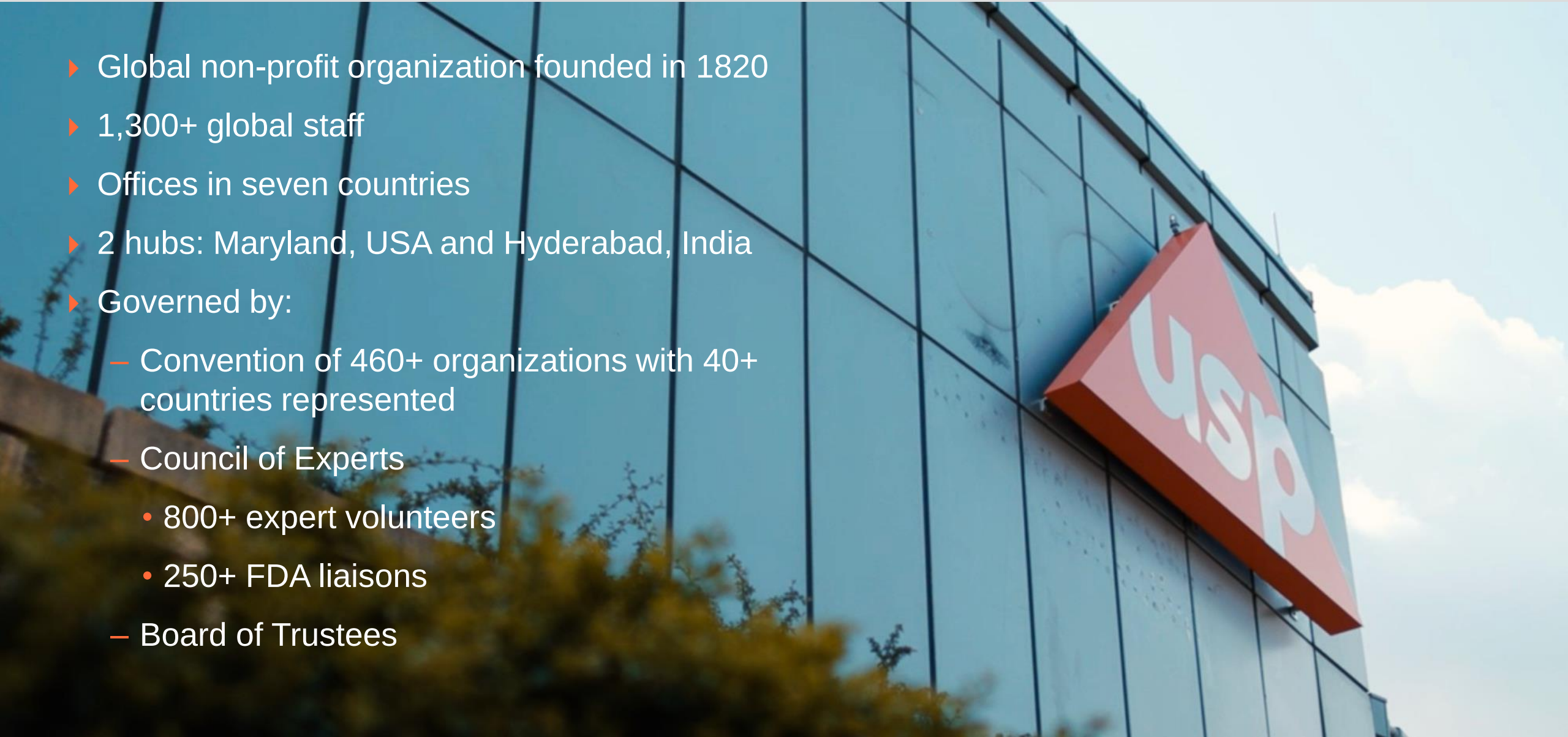
US Pharmacopoeia
Jaap VENEMA

USP Overview and Impact

Jaap Venema, Ph.D.
Chief Science Officer & Chair, Council of Experts

PDG Stakeholder Event
October 3, 2024

USP Today



- Global non-profit organization founded in 1820
- 1,300+ global staff
- Offices in seven countries
- 2 hubs: Maryland, USA and Hyderabad, India
- Governed by:
  - Convention of 460+ organizations with 40+ countries represented
  - Council of Experts
    - 800+ expert volunteers
    - 250+ FDA liaisons
  - Board of Trustees

USP impact

USP standards used in 150+ COUNTRIES around the world

Every year, BILLIONS of people rely on medicines based on USP standards

Our scientists and volunteers dedicate 70,000+ HOURS of time each year to our mission

REGIONAL CHAPTER: AFRICA | ASIA-PACIFIC | CHINA | EUROPE | LATIN AMERICA | MIDDLE EAST | SOUTH ASIA

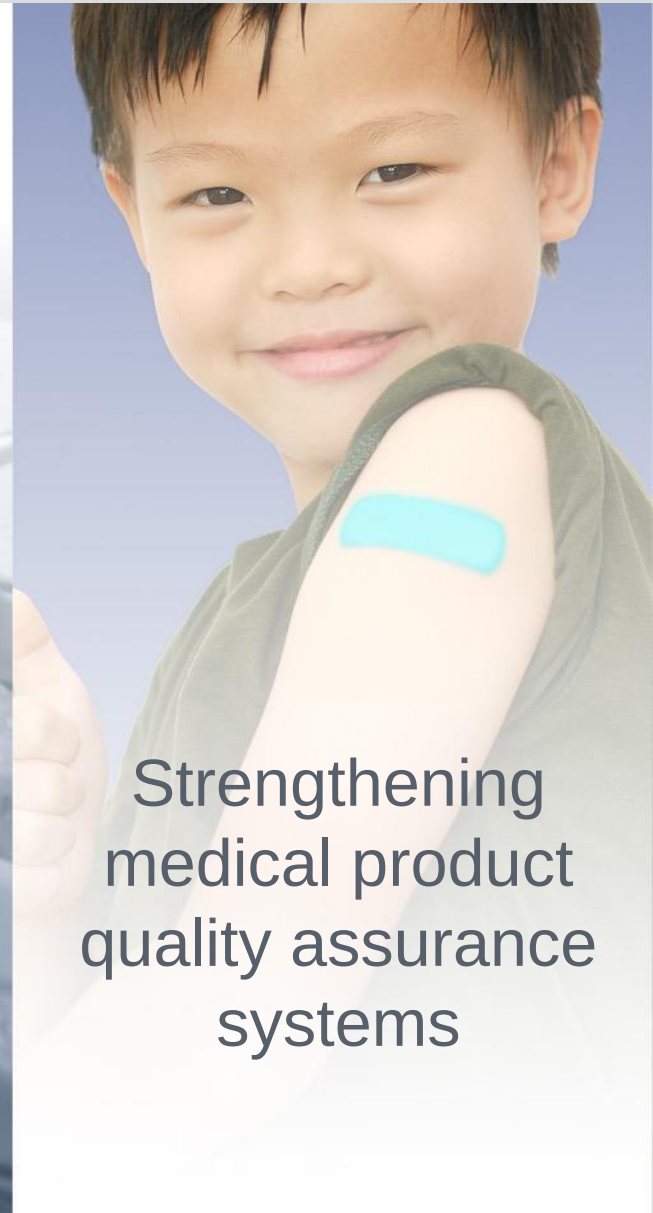
CONVENTION SECTORS: GENERICS | BIOLOGICS | HEALTHCARE PRACTICE | EXCIPIENTS | INNOVATION | DIETARY SUPPLMENTS

We are increasing access to quality medical products

Fostering local manufacturing

Strengthening regulatory and laboratory systems

Optimizing resources and financial structures for sustainability



Strengthening medical product quality assurance systems

More than 9,000 USP standards providing quality benchmarks

USP offer solutions across the supply chain

Suppliers

Manufacturers

Wholesale/ Distributors

Pharmacies/ Hospitals

Healthcare Providers

Patients

General Chapters Monographs Reference standards & materials Nomenclature Labeling Compounding

USP provides flexible solutions

Reference Standards

- Usually referenced in *USP-NF* methods
- Tested in multi-lab studies and approved by USP Expert Committees
- Potential uses: compendial or in-house methods, assay control, control material for method development, standardization testing across laboratories, method transfer, stability testing

Analytical Reference Materials (ARMs)

- Not required for compliance with *USP-NF* methods but sometimes important for verification of methods
- Fit-for-purpose assessments
- Details on testing/application on Product Information Sheet or application notes

USP provides more than just standards

Engagement

Identify and build community
Constructive debate and dialogue
Individual scientific input

Standard Setting

Monographs
General Chapters
Reference Standards and Materials
Guidelines

Education

Build awareness
Education, training, tools

USP Supports Innovation

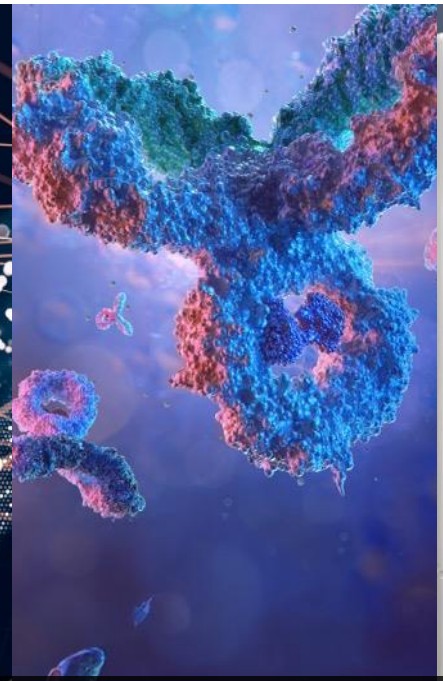
- **New Products and Modalities**
  - Complex generics
  - Gene and Cell Therapies
  - Combination Products
- **New Technologies**
  - Advanced manufacturing
  - Process Analytical Technologies
  - Advanced analyticsl technologies (qNMR, UPLC, MAM)
- **Digital tools and solutions**

USP’s 2025-2030 Cycle Mission Commitments

Enable greater availability of the world’s most relied-upon medicines

Solve pervasive quality challenges that impact medicines, supplements, and foods

Strengthen resilience of the global pharmaceutical supply chain



Expand global availability of and access to quality-assured biologics products

Advance quality through the increased use of digital technologies

Foster environmental sustainability across the pharmaceutical life cycle

Enhancing availability of global medicines

Enable greater availability of the world's most relied-upon medicines

- Continuing our mission to support stakeholders with standards that help ensure the quality medicines to meet the needs of patients globally
  - Developing new public standards for medicines that will have the greatest impact and ensure the relevancy of USP (~1300 monographs/~10 years)
  - Improving the design of standards to increase their effectiveness at ensuring medicine quality
    - e.g. mutagenic impurities, complex generic products
  - Evolving standards to make them easier to use, provide more information, allow greater flexibility (when appropriate) to ensure medicine quality
  - Creating new approaches/tools beyond traditional standards (e.g. emerging standards)

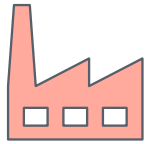
Fostering Environmental Sustainability

Note: Focus on environmental efforts; access to medicines and DEIB related initiatives are excluded.
Source: Interviews of ESG Leads, Sept 2022

Solving pervasive quality challenges that impact medicines, supplements, and foods

Discovery and Design

- Development and characterization of novel therapies
- Detection and characterization of impurities



Manufacturing/ Production

- Raw material variability and quality
- Complex manufacturing processes
- Reproducibility and scalability
- Adoption of new technologies

Product Testing and Release

- Quality by Design (QbD)
- Validation of analytical methods
- Detecting contaminants
- Standardization of food ingredients

Regulatory Compliance

- Regulatory divergence
- Regulatory adaptation to advanced technologies
- Regulatory frameworks for advanced therapies
- Regulatory variability for dietary/herbal supplements and foods

Storage/ Distribution

- Stability and shelf life
- Traceability
- Temperature control and monitoring
- Serialization and anti-counterfeiting measures
- Global distribution networks

Dispensing

- Pharmacy practice standards
- Direct-to-patient distribution models
- Medication errors
- Combating Antimicrobial Resistance (AMR)
- Personalized medicine quality

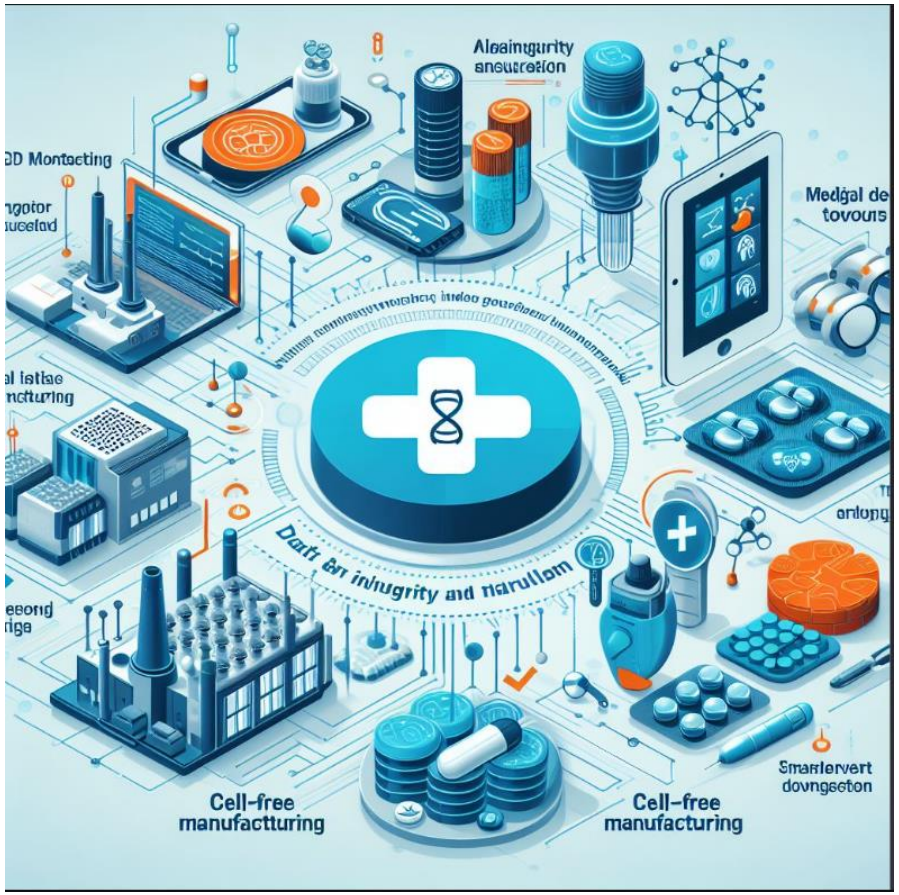
Post Market

- Counterfeit medicines
- Adverse event monitoring
- Real-World Evidence

Pervasive challenges such as sterility, adulteration and impurities, persist across the supply chain

Looking forward

- Medical Devices Standards and AI Utilization
- Multilingual Monographs with Voice Over:
- Development of Green Methods and Scoring System
- Multi-Attribute Methods
- Collating Information on FDA Warning Letters
- Alignment with Industry4.0
- Monograph Modernization and MODR Models
- 3D printing of solid biologics
- Cell-free manufacturing
- Xenotransplantation (transgenic animals)
- Smart pills, Microneedles, Films, Extended release devices
- Digital Therapeutics, Precision Therapies, Gene Editing



Expert Volunteers help power USP's impact on global public health

Serving on Expert Committees, Panels and Sub-Committees, they collaborate to develop quality standards and other solutions that help build a more resilient supply of quality medicines.

Apply and amplify your impact

Thank You

The standard of trust

Pharmacopoeial Discussion Group (PDG) stakeholder event - The PDG is going global

World Health Organization (WHO)
Herbert SCHMIDT

Update on The International Pharmacopoeia

PDG Open Stakeholder Event

3 October 2024

World Health Organization

75 HEALTH FOR ALL

Pharmacopoeias establish quality standards for pharmaceutical products ensuring their safe and effective use

Pharmacopoeias define the quality of medicines by setting **appropriate quality standards** for pharmaceutical products.

Regulatory agencies use pharmacopoeias to **evaluate and approve new medicines and monitor the quality** of medicines already on the market.

Pharmacopoeias provide information on accepted processes, tests and limits to **support product development and manufacturing of medicines**

(1) Not all countries or regions maintain or publish pharmacopoeias

(2) Shortfall in monographs of relevance for LMIC such as antimalarials, neglected or tropical diseases, are not covered

(3) Need to harmonize or unify quality standards to streamline regulatory requirements and to facilitate production of essential medicines

World Health Organization

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The International Pharmacopoeia and its role in public health

- *The International Pharmacopoeia* addresses the needs of all WHO Member States, including LMIC
  - priority is given to medicines listed on
    - WHO Model List of Essential Medicines (EML),
    - Invitations to submit EOI for product evaluation to Prequalification Team – Medicines
    - guidelines of WHO/UN specific disease programmes
  - focus on medicines with the indications
    - antimalarial, antiviral (incl. antiretrovirals), antituberculosis medicines
    - medicines against tropical diseases
    - medicines for maternal, newborn, child and adolescent health


World Health Organization

The International Pharmacopoeia
11th Edition – 2022

Enter

The International Pharmacopoeia (Ph. Int.) constitutes a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances and dosage forms that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. The pharmacopoeia, or any part of it, shall have legal status, whenever a national or regional authority expressly introduces it into appropriate legislation. Further explanation or the role of *The International Pharmacopoeia* is provided in the paragraphs entitled "Scope and function" at the end of the Preface of this edition.

The history of *The International Pharmacopoeia* dates back to 1874 when the need to standardize terminology and to specify dosages and composition of medicines led to this international pharmacopoeial compendium. The first World Health Assembly in 1948 established with the resolution WHA1.27 the Secretariat of *The International Pharmacopoeia* and the "Expert Committee on the Unification of Pharmacopoeias of the World Health Organization", which later became the "Expert Committee on Specifications for Pharmaceutical Preparations".

Compared to other pharmacopoeias, priority is given to medicines included in the WHO Model List of Essential Medicines and to medicines which are important for WHO health programmes and for which other pharmacopoeias do not offer any test specifications. The quality control specifications published in *The International Pharmacopoeia* are developed independently via an international consultative procedure. The needs of developing countries are taken into account. The ultimate goal of *The International Pharmacopoeia* is to provide quality control specifications so as to help enabling access to quality medicines worldwide.

Copyright and Cataloguing-in-Publication Data

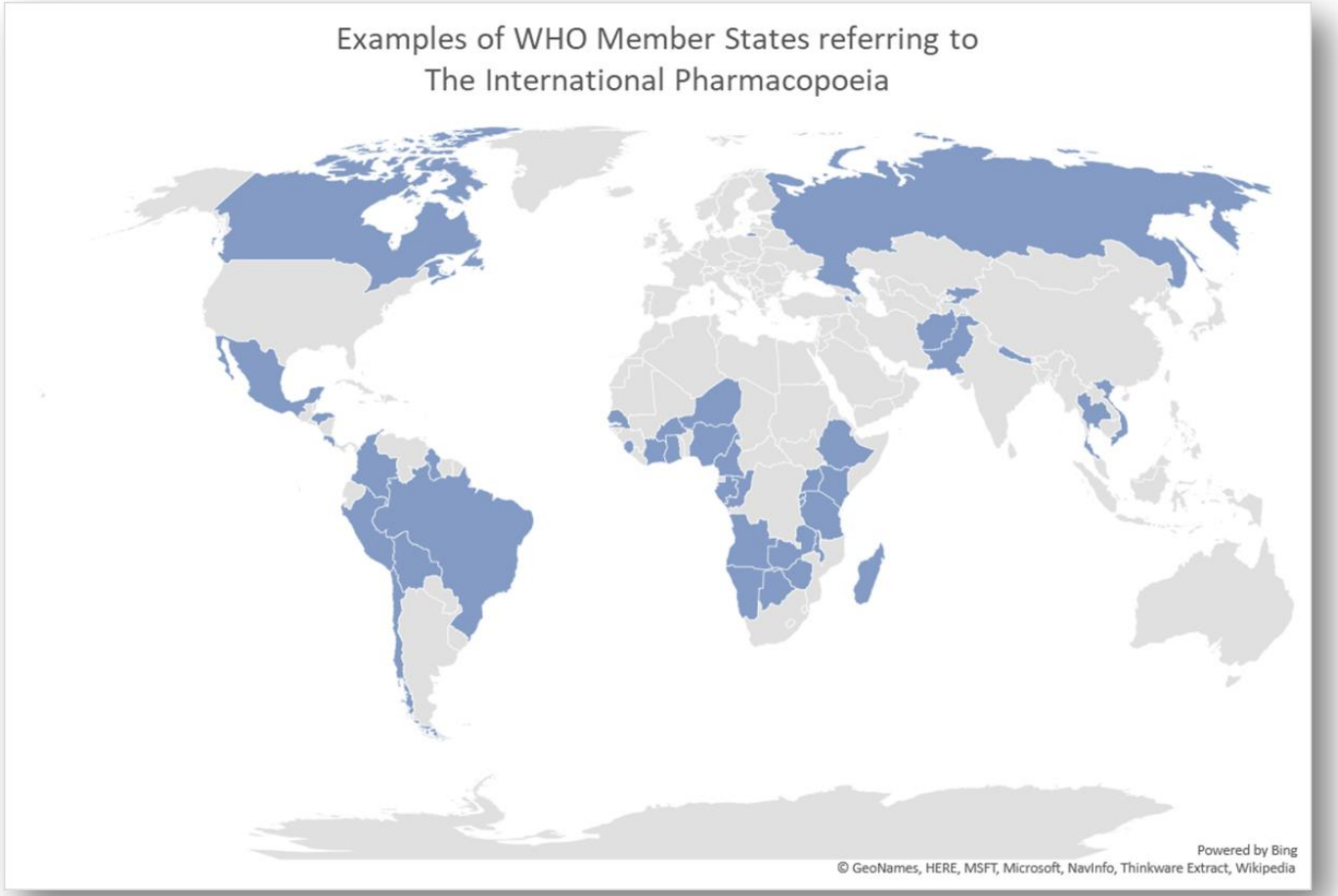
About this Library

This Library contains the Tenth Edition of *The International Pharmacopoeia*.

This Library was produced by WHO Department of Essential Medicines and Health Products with the help of Human Info NGO/WIT and its logistic partner HumanityCD Ltd, and the University of Waikato, New Zealand, using the Greenstone software of the New Zealand Digital Library. It also includes Mozilla Firefox, distributed by Human Info NGO/WIT.

The International Pharmacopoeia and its role in public health

- *The International Pharmacopoeia* provides international standards for global use
  - Our provisions are integrated and referred to in many regulatory guidelines and legislations of WHO Member States



World Health Organization

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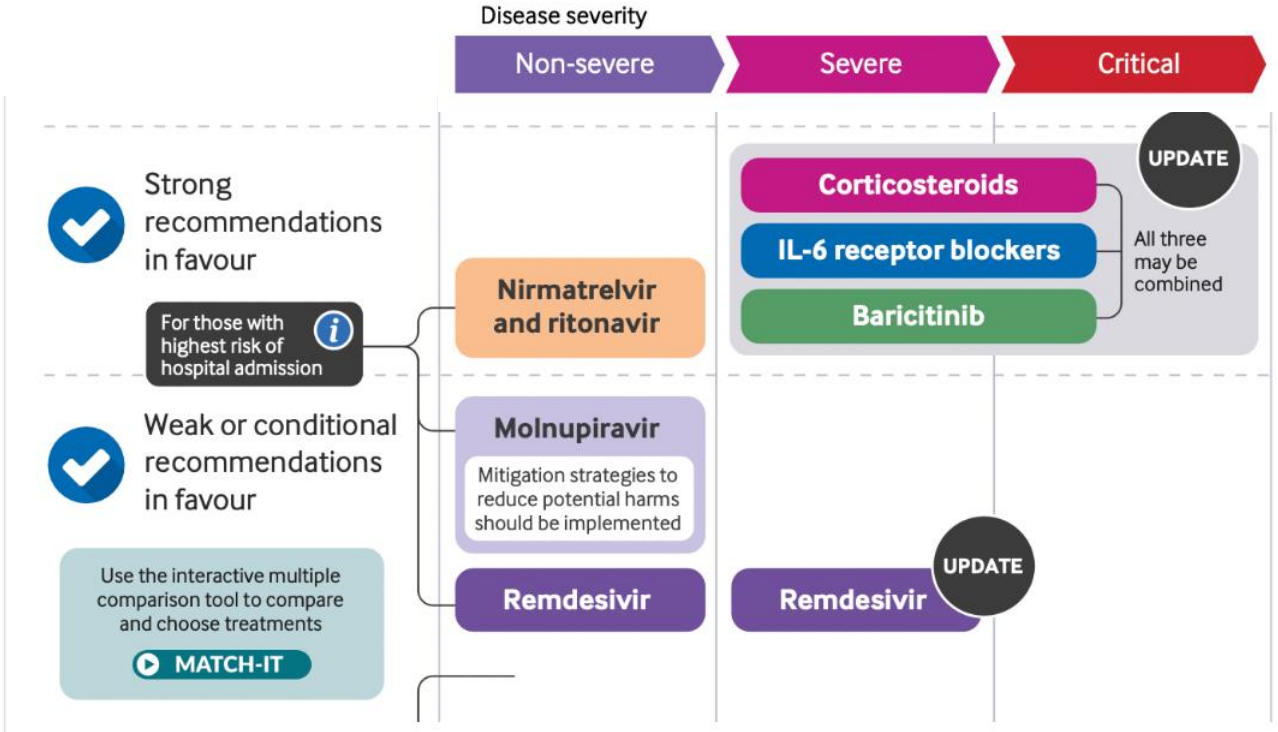
The International Pharmacopoeia and its role in public health

- *The International Pharmacopoeia*
  - supports key WHO activities and
    - WHO Prequalification Programme (https://extranet.who.int/prequal/)
      - by articulating their expectations regarding the quality of medicines
    - WHO Global Surveillance and Monitoring System (GSMS) (https://www.who.int/who-global-surveillance-and-monitoring-system)
      - by defining appropriate quality standards for essential medicines to allow following-up on incidents reported to GSMS
    - WHO Global Health Emergency Response (https://www.who.int/emergencies/overview)
      - by providing public standards on COVID-19 therapeutics to safeguard patients from substandard and falsified medicines and facilitate their registration, production and distribution.

Support of WHO´s response to COVID-19

- 11th Edition, 2022
  - Monographs on Remdesivir and Remdesivir intravenous infusion
- September 2023
  - Remdesivir ICRS, Remdesivir for system suitability ICRS
- August 2024
  - Molnupiravir ICRS
- 12th Edition, 2024
  - Monographs on Molnupiravir, Molnupiravir capsules, Nirmatrelvir, Nirmatrelvir tablets
- Under establishment
  - Nirmatrelvir ICRS



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Support of WHO´s response to COVID-19

- Public standards facilitate the production and registration of multi-source products
  - Patent holders (Gilead Sciences, Merck Sharp & Dohme, Pfizer Limited) and Medicines Patent Pool signed voluntary licensing agreements to facilitate global access to generic therapeutics.
  - Generics are available at reduced prices - Estimates from Harvard University

Treatment course with	Originator (in US)	Costs in US
Remdesivir	USD 4680 (in 2020)	n.a.
Molnupiravir	USD 700	USD 14.16
Nirmatrelvir and ritonavir	USD 530	USD 73.15

Barber MJ, Gotham D. Estimated cost-based generic prices for molnupiravir for the treatment of COVID-19 infection. Cambridge, MA: Harvard University; 2022).

Barber MJ, Gotham D. Estimated cost-based generic prices for nirmatrelvir/ritonavir (Paxlovid). Cambridge, MA: Harvard Univesity; 2022

Support of WHO´s response to the surge of EG/DEG contaminations of oral liquids in 2022

- Response to current wave of EG/DEG contaminations of oral liquids
  - Number of reported EG/DEG contaminations has increased over the last 3 years.
  - WHO Medical Product Alerts
    - The Gambia – 5 October 2022
    - Indonesia – 2 November 2022
    - Uzbekistan, Cambodia – 11 January 2023
    - Marshall Island, Micronesia – 6 April 2023
    - Cameroon – 19 July 2023
    - Iraq – 7 August 2023
    - Maldives, Pakistan – 7 December 2023

Medical Product Alert N°8/2023: Substandard (contaminated) syrup and suspension medicines

Substandard (contaminated) syrup and suspension medicines identified in the WHO Regions of the Americas, Eastern Mediterranean, South-East Asia and Western Pacific

7 December 2023 | Medical product alert | Geneva |Reading time: 3 min (731 words)

Alert Summary

This WHO Medical Product Alert refers to five different syrup and suspension medicines initially detected in the Maldives and Pakistan and notified to WHO on 8 November 2023. Some of the affected products have also been detected in Belize, Fiji and Lao People's Democratic Republic.

The five products are ALERGO Syrup, EMIDONE Suspension, MUCORID Syrup, ULCOFIN Suspension and ZINCELL Syrup. A total of 23 batches of these products are affected. The stated manufacturer of all the affected products is PHARMIX LABORATORIES (PVT.) LTD (Pakistan).

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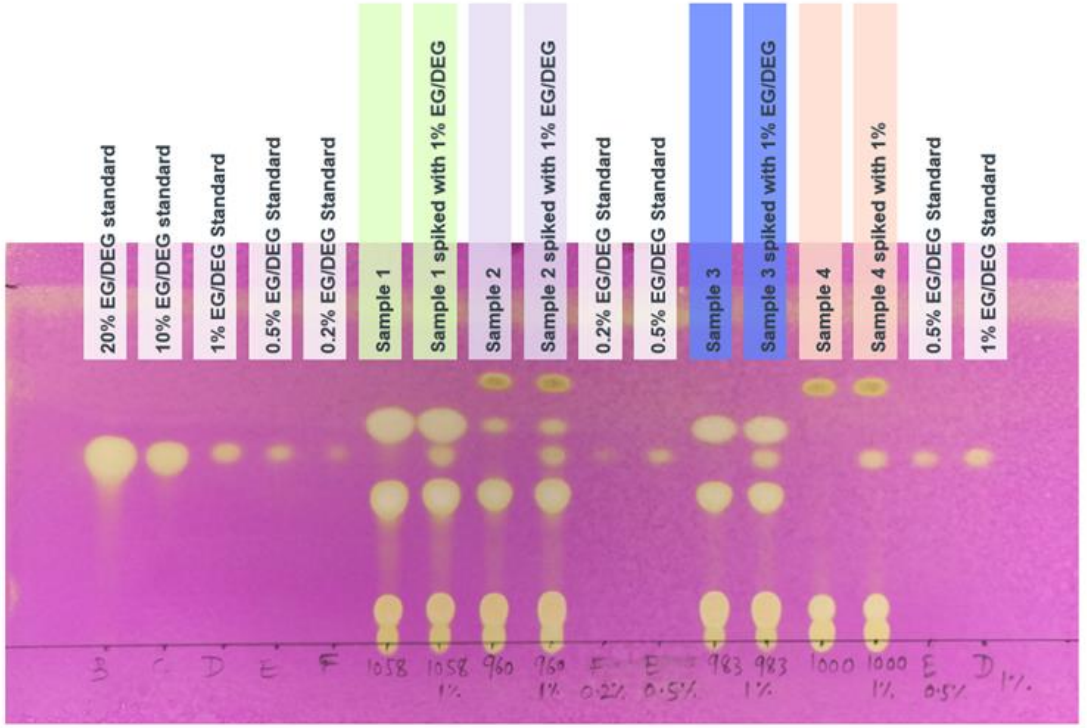
Support of WHO´s response to the surge of EG/DEG contaminations of oral liquids in 2022

- Response to EG/DEG contaminations of oral liquids
  - Two-level approach for the detection of DEG and EG in liquid preparations for oral use
    - To enable Member Stats to detect contaminants in finished products and to respond to current Medical Product Alerts
    - Comprises of a screening for non-compliance by thin-layer chromatography and a confirmatory testing by gas chromatography.
  - Save limit
    - The minimum safe levels for humans for ingested DEG and EG are not known with certainty, but it is generally recognized that a detection level of 0.10% for each substance is considered adequate for screening raw materials and finished products for these substances from a safety point of view.

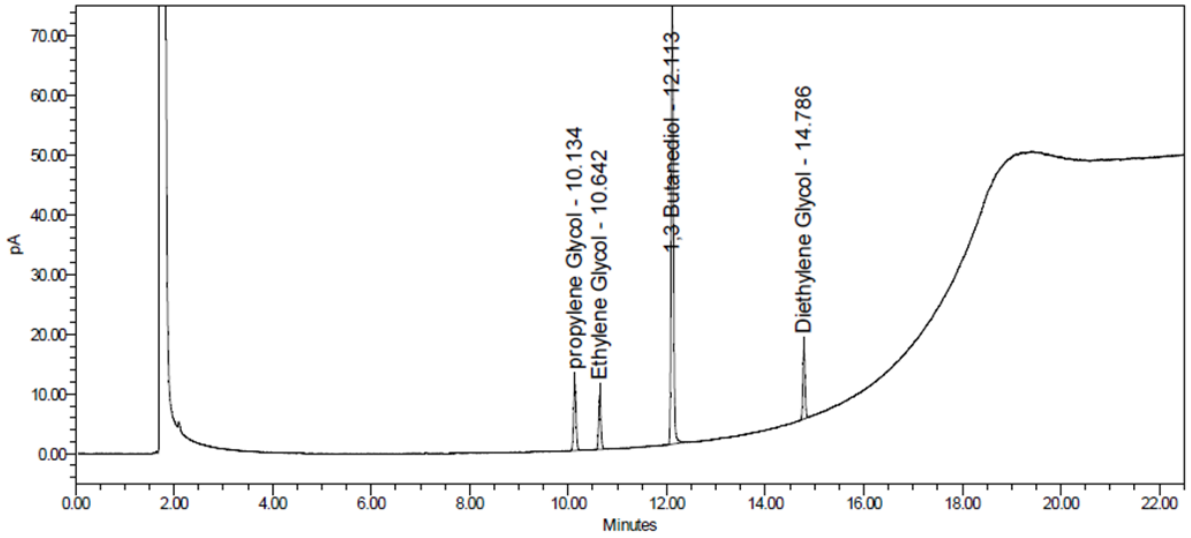
Support of WHO´s response to the surge of EG/DEG contaminations of oral liquids in 2022

- Screening for non-compliance by TLC
  - Limit of detection DEG/EG about 0.2% (m/m)
  - EG/DEG have similar Rf values
    - 50:50 (m/m) EG/DEG mixture used as ref. solutions
  - Separation of EG/DEG from PG and glycerol
  - Optimized by InphA, TGA, NIFDC
  - Suitable for the intended use:
    - screening for non-compliance by NQCL without access to GC
    - Semiquantitive, sufficiently sensitive, discriminative (DEG/EG vs PG, G), robust, easy to perform, cheap, generic.



Support of WHO´s response to the surge of EG/DEG contaminations of oral liquids in 2022

- Confirmatory testing by GC
  - Discrimination between DEG and EG
  - Limit of detection below 0.10%
  - Parameters of the method were optimized by HSA, TGA, NIFDC
  - Suitable for intended use
    - Routine and confirmatory testing of finished products for laboratories able to perform GC testing
    - Quantitative, sensitive, discriminative (DEG vs EG), robust, generic.



World Health Organization

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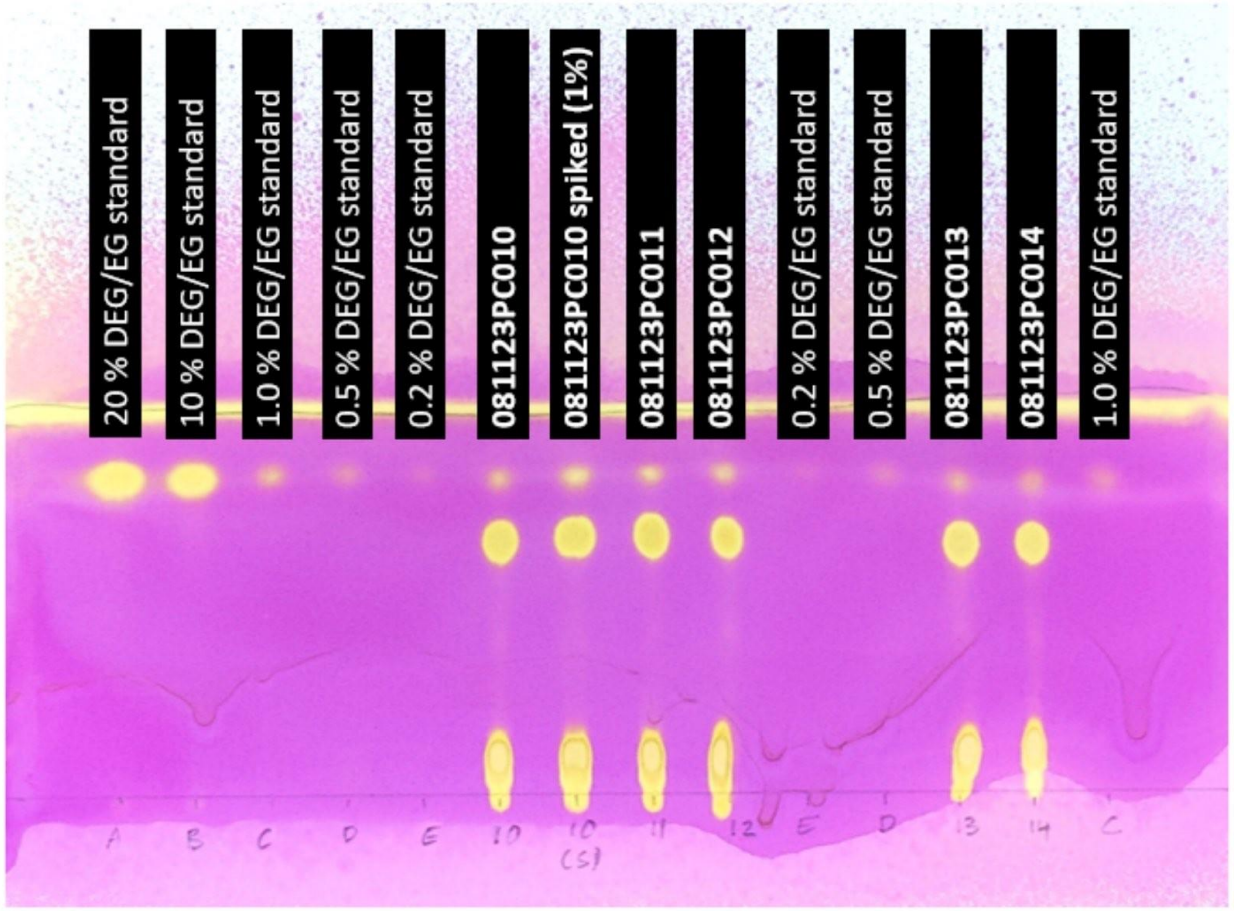
Support of WHO´s response to the surge of EG/DEG contaminations of oral liquids in 2022

- Screening for non-compliance by TLC performed by NQCL of the Maldives
  - Identification of 5 samples from the local market suspicious of EG/DEG contamination
  - TGA performed confirmatory testing by GC
  - Contamination with EG confirmed
    - Determined concentrations ranging between 0.63% and 0.82%.



The International Pharmacopoeia and its role in public health

- Harmonization and convergence of pharmacopoeial requirements leads to
  - Standardization of quality requirements across regions
  - Increased regulatory efficiency
  - Reduced of costs associated with the development and approval of medicines
  - Facilitate exchange of medicines between countries
  - Facilitate market access for generic medicines
  - Improved access to quality assured essential medicines.

The International Pharmacopoeia and its role in public health

PDG texts included in *The International Pharmacopoeia*

- General chapters
  - Chromatography
  - Capillary electrophoresis
  - Sulfated ash
  - Test for sterility
  - Microbial enumeration tests
  - Tests for specified microorganisms
  - Test for bacterial endotoxins
- Disintegration test for tablets and capsules
- Dissolution test for oral dosage forms
- Extractable volume for parenteral preparations
- Tests for particulate contamination/Subvisible particles
- Microbiological quality of non-sterile products: recommended acceptance criteria for pharmaceutical preparations
- Tablet friability

The International Pharmacopoeia and its role in public health

PDG texts included in *The International Pharmacopoeia*

- Excipient monographs
  - Hydroxypropylcellulose, low-substituted
  - Sodium laurilsulfate
  - Sodium starch glycolate

Thank you

World Health Organization

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