International Conference, 19-21 September 2022

Collaboration, Innovation and Scientific Excellence: the European Pharmacopoeia 11th Edition

Session 4: Pharmacopoeial harmonisation

Moderator: Cathie Vielle, EDQM, Council of Europe

THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)

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

Overview of PDG

Yujiro Kameyama, Ph.D.
Division of Pharmacopoeia and Standards for Drugs
Office of Review Management
Pharmaceuticals and Medical Devices Agency (PMDA)

Why do we need harmonisation?

If each country/region has own pharmaceutical regulation without harmonisation….

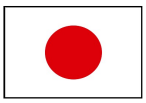
- Pharmaceutical products approved in one country/region that are sold in other countries/regions must meet the quality standards recognised in those countries/regions
- Must conduct similar redundant tests in each country/region, adding no value to the patient or public health

Pharmacopoeial Harmonisation

→ can align test methods and specifications to a common quality standard

The Pharmacopoeial Discussion Group

- Began as an **informal** group in 1989; participants include USP, EP, and JP (WHO joined as an observer in 2001)
- Focuses on selected official, broad-impact **General Chapters** and **excipient** monographs
- Eliminates/minimises need to perform multiple **tests and procedures** and to comply with multiple **acceptance criteria** for the same article
- Detailed official process, with specific **stages** and terminology
- One face-to-face meeting a year, with a video conference in the interim



Japanese Pharmacopoeia (JP)
MHLW/PMDA
Governmental

European Pharmacopoeia (Ph. Eur.)
EDQM
Inter-Governmental

United States Pharmacopeia (USP)
USP
Non-Governmental

PDG Mission
To harmonise pharmacopoeial standards while maintaining a constant level of science with the shared goal of protecting public health.

How PDG works for harmonisation?

Definition of Harmonisation:

A pharmacopoeial general chapter or other pharmacopoeial document is harmonised when a pharmaceutical substance or product tested by the harmonised procedure as published in EP, JP and USP yields the same results, and the same accept/reject decision is reached.

- Text does NOT have to be identical
- Each Pharmacopeia can adapt the text to local style, and take into consideration of local reference standards and reagents

PDG Statement of Harmonisation Policy: https://www.pmda.go.jp/files/000244636.pdf

Harmonisation Process of PDG:

- Harmonisation occurs based on decisions of experts bodies of each pharmacopoeia.
- PDG works transparently in many ways principally including public notice and comment procedures of each pharmacopoeia.
- Each pharmacopoeia does not revise unilaterally after harmonisation. When necessary, revision should be conducted according to the PDG Working Procedures.

PDG Working Procedure: https://www.pmda.go.jp/files/000244637.pdf

Harmonisation by Attributes: How PDG move forward

For the first decade of PDG, **zero** monographs or General Chapters were harmonised!

Harmonisation by Attribute was introduced as an acknowledgement that certain attributes simply cannot be harmonised because of:

- (1) Differing **regulatory** or **legal** requirements
- (2) **Non-harmonised** methodology for procedures
- (3) Differences in **scientific** expert opinions

Acknowledgement that partial harmonisation is preferred to no harmonisation!

PDG Work Program: General Chapters

General Methods Relevant to Q6A:

Q-01 Dissolution
Q-02 Disintegration
Q-03/04 Uniformity of Content/Mass
Q-05a Tests for Specified Microorganism
Q-05b Microbial Enumeration
Q-05c Limits for Non-sterile Products
Q-06 Bacterial Endotoxin
Q-07 Color (Instrumental Method)
Q-08 Extractable Volume
Q-09 Particulate Contamination
Q-10 Residue on Ignition
Q-11 Sterility Test

General Chapters:

G-01 Analytical Sieving
G-02 Bulk Density and Tapped Density
G-03 Conductivity
G-04 Gas Pycnometric Density of Solids
G-05 Powder Flow
G-06 Tablet Friability
G-07 Elemental Impurities*2
G-09 Optical Microscopy
G-10 Powder Fineness
G-11 Specific Surface Area
G-13 Laser Diffraction Measurement of Particle Size

General Chapters:

G-14 X-Ray Powder Diffraction
G-15 Water-solid Interaction
G-16 Thermal Analysis
G-20 Chromatography*1
G-21 Dynamic Light Scattering*2

Methods for Biotechnology Products:

B-01 Amino Acid Determination
B-02 Capillary Electrophoresis
B-03 Isoelectric Focusing
B-05 Peptide Mapping
B-06 Polyacrylamide Gel Electrophoresis

29 of the 31 general chapters have now been harmonised

*1 : Signed-Off in 2021
*2 : Under discussion towards first harmonisation

PDG Work Program: Excipients

E-01 Alcohols
E-02 Dehydrated Alcohol
E-03 Benzyl Alcohol
E-04 Calcium Disodium Edetate
E-05 Calcium Phosphate Dibasic
E-06 Calcium Phosphate Dibasic Anhydrous
E-07 Carmellose Calcium
E-08 Carmellose Sodium*2
E-09 Croscarmellose Sodium
E-10 Microcrystalline Cellulose
E-11 Cellulose, Powdered
E-13 Cellulose Acetate Phthalate
E-14 Citric Acid, Anhydrous
E-15 Citric Acid, Monohydrate
E-16 Crospovidone
E-17 Ethylcellulose
E-18 Hydroxyethylcellulose
E-19 Hydroxypropylcellulose
E-20 Hydroxypropylcellulose, Low Substituted
E-21 Hypromellose
E-22 Hypromellose Phthalate
E-23 Lactose, Anhydrous
E-24 Lactose, Monohydrate
E-25 Magnesium Stearate
E-26 Methylcellulose
E-27 Methyl Paraben
E-28 Petrolatum*1
E-29 Petrolatum, White*1
E-30 Polyethylene Glycol*2
E-31 Polysorbate 80
E-32 Povidone
E-36 Silicon Dioxide*2
E-37 Silicon Dioxide, Colloidal*2
E-38 Sodium Chloride
E-39 Sodium Starch Glycolate
E-40 Starch, Corn
E-41 Starch, Potato
E-42 Starch, Rice
E-43 Starch, Wheat
E-44 Stearic Acid
E-45 Sucrose
E-46 Talc
E-48 Ethyl Paraben
E-49 Propyl Paraben
E-50 Butyl Paraben
E-51 Glycerin*2
E-52 Carmellose
E-54 Copovidone
E-55 Gelatin
E-56 Sucrose
E-58 Mannitol
E-59 Propylene Glycol*2
E-60 Sodium Laurylsulfate
E-61 Starch, Pregelatinized*2
E-62 Sterile Water for Injection*2
E-64 Isomalt
E-65 Isostearyl Alcohol*2
E-66 Myristyl Myristate*2
E-68 Polysorbate 65*2
E-69 Calcium Silicate*2
E-70 Polysorbate 20*2

*1 : Signed-Off in 2021
*2 : Under discussion towards first harmonisation

48 of the 61 excipient monographs have now been harmonised

An Example of PDG Success Story: Chromatography

- The harmonised general chapter **Chromatography** was signed-off by the Pharmacopoeial Discussion Group (PDG) on September 28, 2021.
- During a joint PDG-industry meeting in 2009, the PDG was encouraged to add harmonisation of the three regional chapters on chromatography to the PDG work program. Although the chapters in question differed in content and format, it was considered feasible to develop a chapter describing **core requirements** applicable for TLC, HPLC and GC.
- These harmonised requirements promote the development of individual monographs with a consistent approach and enhance understanding of basic requirements by users in all three regions.

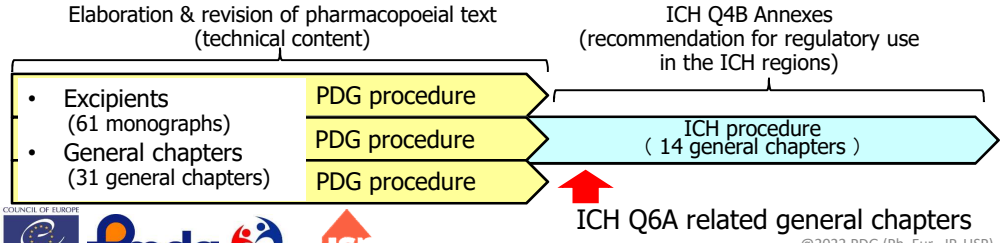
PDG Press Release G-20 Chromatography: https://www.pmda.go.jp/files/000244636.pdf

Interaction of PDG with ICH

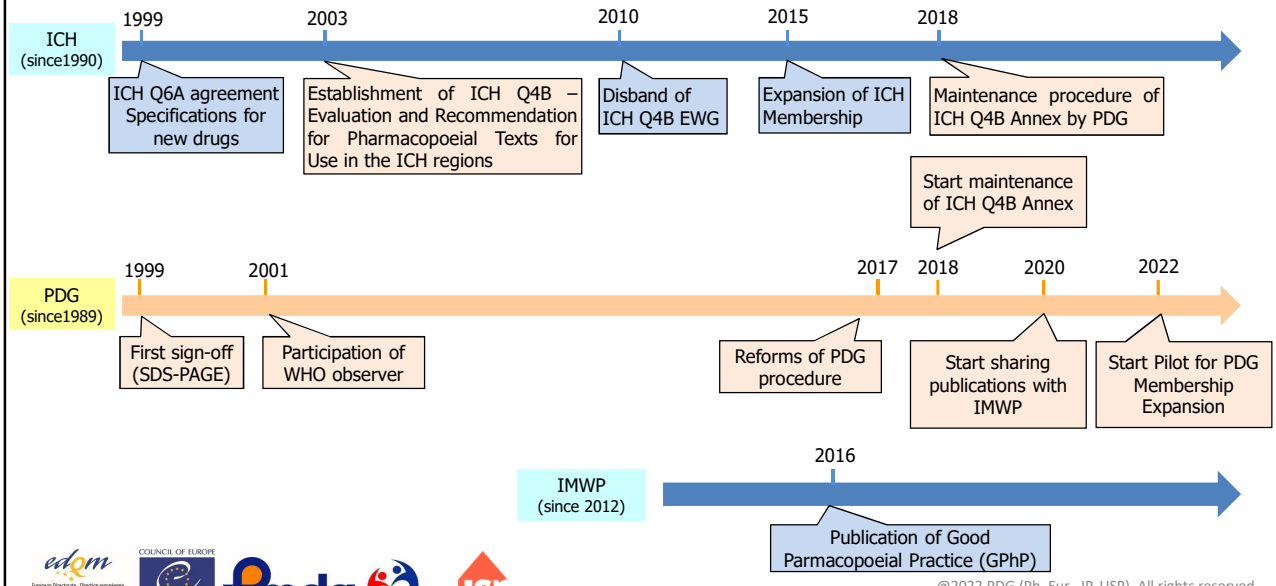
ICH Q4B evaluates and recommends pharmacopoeial texts for use in the ICH regions. Once in agreement as interchangeable, the result was publicised as a guideline.

PDG (since 1989)		ICH Q4B (2003 – 2010)
Ph.Eur. (EDQM), JP (MHLW/PMDA), USP (USP)	Participant	Regulatory: EU, MHLW/PMDA, FDA Industry: EFPIA, JPMA, PhRMA
Harmonisation of Science (Analytical Method, Acceptance Criteria)	Activity	Regulatory Harmonisation Regulatory Guideline
31 general chapters, 61 monographs*	Target	14 general chapters*
Harmonised pharmacopoeial texts	Outcome	Guideline = Recommendation for regulatory use in the ICH regions

*As of August 2022



PDG Collaborative Activities with ICH and IMWP



Future of PDG: three strategic discussions

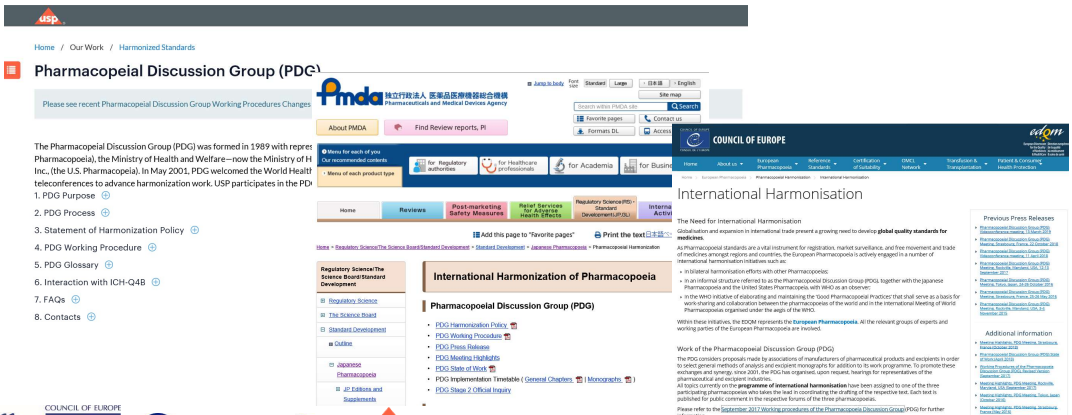
- The PDG is currently investigating and engaging in three strategic discussions designed to enhance the global reach and impact of international harmonisation of quality standards:
  - Engagement with Regulators: The PDG is investigating ways to improve interaction with regulators by a better anticipation of items critical for regulators and better reactivity in case of identifying potential issues.
  - Engaging Industry: The PDG is considering the development of a concept paper to improve early engagement of industry stakeholders and to reach further stakeholders than usually involved. This concept paper would also consider the Interaction with Regulators. It has been agreed to test this new approach using *Polysorbate 20*.
  - Engagement of other Pharmacopoeias: The PDG is working on ways to further improve interactions with other pharmacopoeias (e.g. Sharing PDG publications with IMWP, Pilot for PDG membership expansion)

Publication of Harmonisation Status

EP：https://www.edqm.eu/en/international-harmonisation-614.html

JP：https://www.pmda.go.jp/rs-std-jp/standards-development/jp/0005.html

USP：https://www.usp.org/harmonized-standards/pdg



Thank You for Your Attention

PDG projects involving other pharmacopoeias

20 September 2022

Dr Dirk Leutner, EDQM, on behalf of PDG

Engagement of other pharmacopoeias

- **Setting together strong science-based standards**
- PDG developed and rolled out initiatives for **cooperation on specific texts with more pharmacopoeias** taking into account different situations of other pharmacopoeias

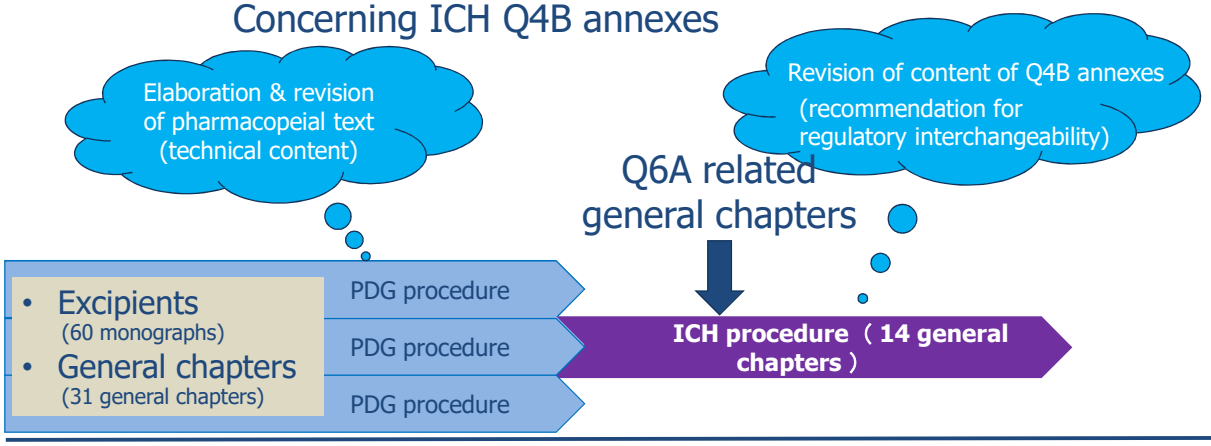
3 major projects:

1. Maintenance of **ICH Q4B** Annexes
2. **exchange of texts** with world pharmacopoeias
3. **PDG expansion**

Maintenance of ICH Q4B Annexes

Clarification of scope of Q4B and its annexes

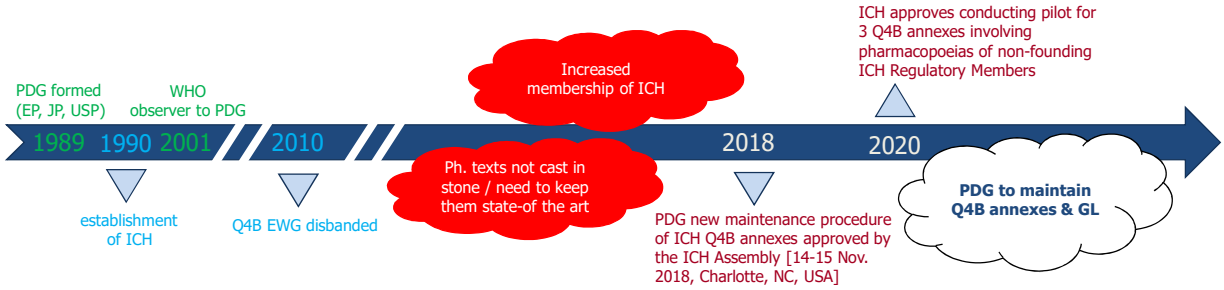
- **Declarations of Interchangeability by ICH regulatory members**
- **Relevant for pharmacopoeias from ICH regulatory members**



Why a new maintenance procedure? Some history

Founding Regulatory Members: EC, Europe; FDA, United States; MHLW/PMDA, Japan;
Standing Regulatory Members: Health Canada, Canada*; Swissmedic, Switzerland**
* No active Ph. – ** member of the Ph. Eur.

Regulatory Members: ANVISA, Brazil; HSA, Singapore*; MFDS, Republic of Korea; NMPA, China; TITCK, Türkyie**, TFDA, Chinese Taipei; MHRA, UK**, SFDA, Saudi Arabia*, COFEPRIS, Mexico
* No active Ph. – ** member of the Ph. Eur.



Involved other Pharmacopoeias of ICH regulatory members

- ***Pilot phase:***
- **FB, Brazil**
- **ChP, People's Republic of China**
- **KP, Republic of Korea**
- **TWP, Chinese Taipei**

In future:

- **FEUM, Mexico**

Implementation of Q4B Annexes in new ICH Jurisdictions

- Approval by ICH Assembly to conduct a **pilot phase** → proof-of-concept on **3 annexes**
- **Pharmacopoeia of non-founding ICH Regulatory Member**
  - **evaluated own text** vs. PDG-harmonised text,
  - inform PDG about own understanding of harmonisation status
  - provided PDG with **English copy** of its Ph. Text, harmonisation status (incl. potential residual discrepancies)
- **Technical Review by PDG**. internal PDG evaluation and exchanges with involved pharmacopoeias
- PDG will draft and submit **revised Q4B Annexes** to the ICH Assembly before consultation of regulators
- **Goal of wider regulatory interchangeability**

Interaction of PDG with other world pharmacopoeias

IMWP History and setup

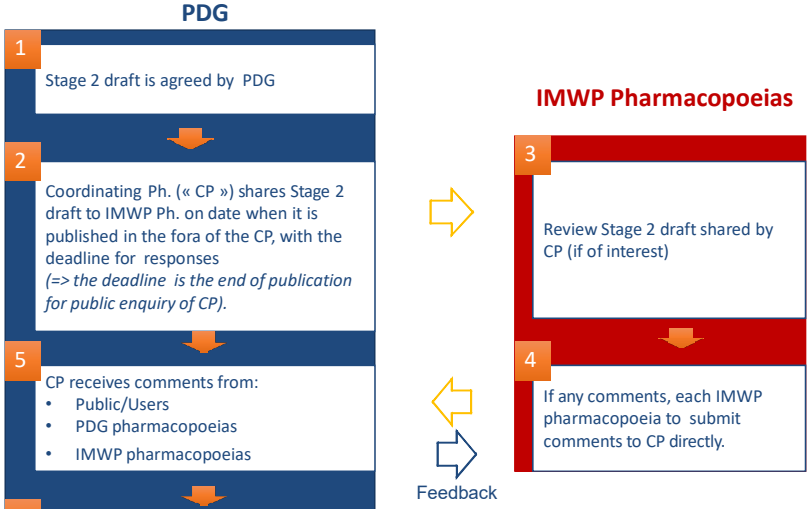
- **Started in 2012**, meetings organised by WHO together with host
- **for all interested world pharmacopoeias**
- **Yearly face-to-face meetings** to exchange on on-going topics (since 12th meeting in 2021 as videoconference); usually **15-30 representatives**
- Elaboration of **Good Pharmacopoeial Practices (GPhP)**
- "**pharmacopoeial alert system**" – COVID-19 response (work on Favipiravir IMWP monographs)

How PDG interacts with IMWP

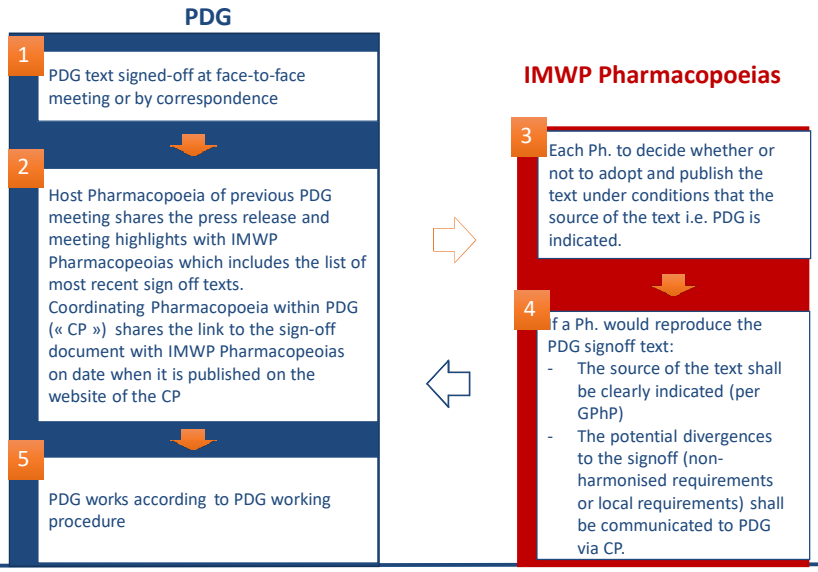
- PDG committed to **support pharmacopoeial harmonisation** of quality standards by **liaising** with other world pharmacopoeias (e.g. via IMWP) and by **exchanging PDG texts** with all IMWP ph. :
  - **at public consultation** stage **for comments** and
  - **after sign-off** for optional implementation following GPhP

- **PDG sees IMWP as discussion and information sharing forum** to
  - **get to know** peers
  - **build trust** among pharmacopoeias
  - **exchange information, knowledge and expertise**, e.g. to inform each other of recent challenges and share solutions found

Interaction PDG-IMWP: PDG Stage 2 (Official Inquiry)



Interaction PDG-IMWP: Stage 4 (sign-off by PDG)



PDG Pilot Expansion

Kevin Moore, Ph.D
Sr. Manager, Ph. Collaboration

Value of Effective Pharmacopeial Collaboration

PROMOTE

Access to Quality medicines leveraging global expertise

INCREASE

Value of public quality standards

FACILITATE

Global access to state of the industry technology

PRIORITIZE

Balance current paradigms and future trends

ENABLE

Global pharmaceutical trade

The Pharmacopeial Discussion Group (PDG)

- Began as an **informal** group in 1989; participants include USP, EP, and JP (WHO joined as an observer in 2001)
- Focuses on selected official, broad-impact **General Chapters** and **excipient** monographs
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JP (MHLW/PMDA)

Ph. Eur. (EDQM)

USP

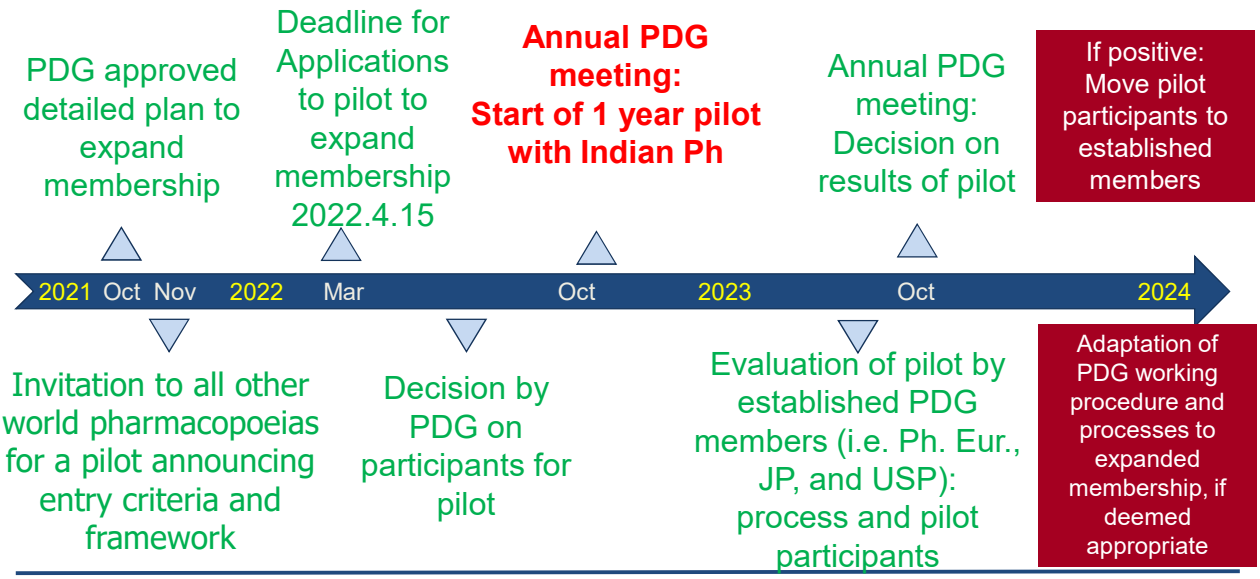
PDG Mission

To harmonize pharmacopeial standards while maintaining a constant level of science with the shared goal of protecting public health.

Global Expansion of PDG

- Landmark decision by PDG to launch a pilot for the first expansion of membership in 32 years.
- Critical first step in PDG's commitment to expand recognition of harmonized pharmacopeial standards
- Global Pharmacopeias interested were invited to submit applications to evaluated against objective entry criteria
- Pilot scheduled to begin Fall 2022 with the Indian Pharmacopeial Commission (IPC) invited to join.

Pilot phase for Expansion of PDG 2021 - 2023



Pilot and Evaluation Phase for PDG

- IPC to become a **regular participant** in all PDG activities **for a period of one year,** beginning at the 2022 Fall PDG Meeting
- Established PDG members **evaluate** pilot participants and resources/performance of PDG during the one year period following the 2022 Fall PDG Meeting
- Discussion by established members in two areas
  - Pilot Member: **Indian Pharmacopeial Commission**
  - Resources/Performance of the **PDG**:
    - Discuss lessons learned and changes needed to the PDG process and model

Next Steps: Annual meeting Fall 2023

Established PDG members to decide by consensus on the outcome of the evaluation of the two areas

- If deemed appropriate, **adapt PDG structure** for pharmacopoeial harmonisation based on lessons learned
- Evaluate effectiveness of current "informal model" in the context of lessons learned from pilot
  - Potential next steps include:
    - **Change** in Model and/or criteria
    - Pilot participant moved to **established** member
    - **Continue** pilot for another year
    - **Terminate** pilot and evaluate next steps.
- PDG commits to transparency in the decisions and outcomes of the pilot to all stakeholders, including other interested pharmacopeias who may be interested to participate in potential future collaborative areas with PDG.

USP Vision for Convergence – Alignment with PDG

- **Driving global convergence of pharmaceutical quality standards through collaboration to increase patient access to quality medicines**
- **Changing landscape and implications**
  - **Continued globalization of the pharmaceutical industry – rising importance of new regions.**
  - **Rising tide of nationalism – Importance of driving collaboration**
  - **More opportunities for harmonization than ever – new ways to approach this problem**

Questions

Empowering a healthy tomorrow

Pharmacopoeial harmonization: perspectives from WHO

Luther Gwaza PhD.

Team Lead Norms and Standards for Pharmaceuticals

World Health Organization

World Health Organization

Global Health Priorities

WHO Triple Billion Targets

Healthier populations — One billion more people enjoying better health and well-being.

Universal health coverage — One billion more people benefitting from universal health coverage.

Health Emergencies — One billion more people better protected from health emergencies.

UN Sustainable Development Goals (SDGs)

Unification of pharmacopoeias

History on international cooperation to unify pharmacopeial standards goes back to 1874 – need to standardize terminology and to specify dosages and composition of medicines

World Health Organization

(*Article 2 (u) ..to* develop, establish and promote international standards with respect to food, **biological, pharmaceutical** and similar products;

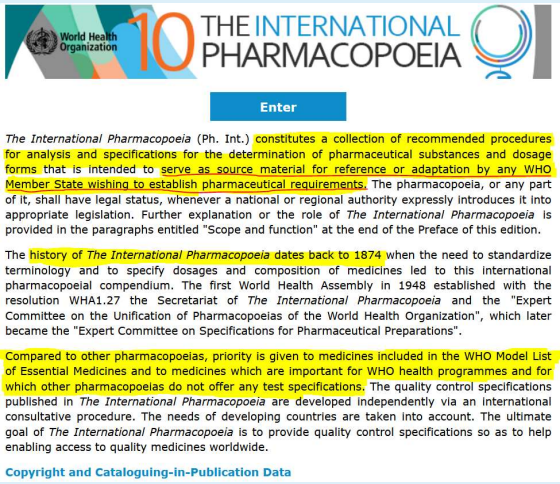
The first World Health Assembly established :

- The Secretariat of *The International Pharmacopoeia*
- "Expert Committee on the Unification of Pharmacopoeias"

World Health Organization

First World Health Assembly (WHA1), Palais des Nations, Geneva, 24 June - 24 July 1948. Left to right: Dr Brock Chisholm, first Director-General of WHO, Dr Andrija Stampar, M. Henri Laugier, Assistant Secretary-General of the UN.

The International Pharmacopoeia



World Health Organization 10 THE INTERNATIONAL PHARMACOPOEIA

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

Focus on:

- **WHO Model List Of Essential Medicines (EML) and EMLc;**
- **on the invitations to manufacturers to submit an expression of interest (EOI) to the WHO Prequalification Unit;**
- **United Nations (UN)/WHO documents recommending the use of medicines for the treatment of specific diseases and/or for use by treatment programmes.**

The International Pharmacopoeia online

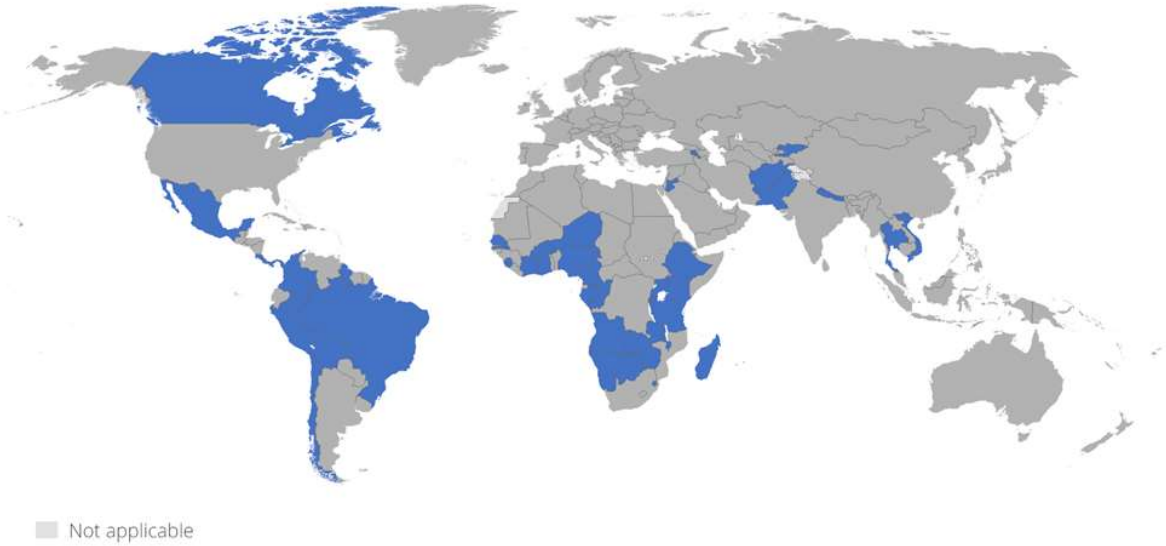
World Health Organization

Acceptable specifications should be relevant/applicable to all WHO Member States, current and accessible to all users (e.g., quality control laboratories, NRAs, generic manufacturers).

"The Ph.Int. (…) 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."

World Health Organization

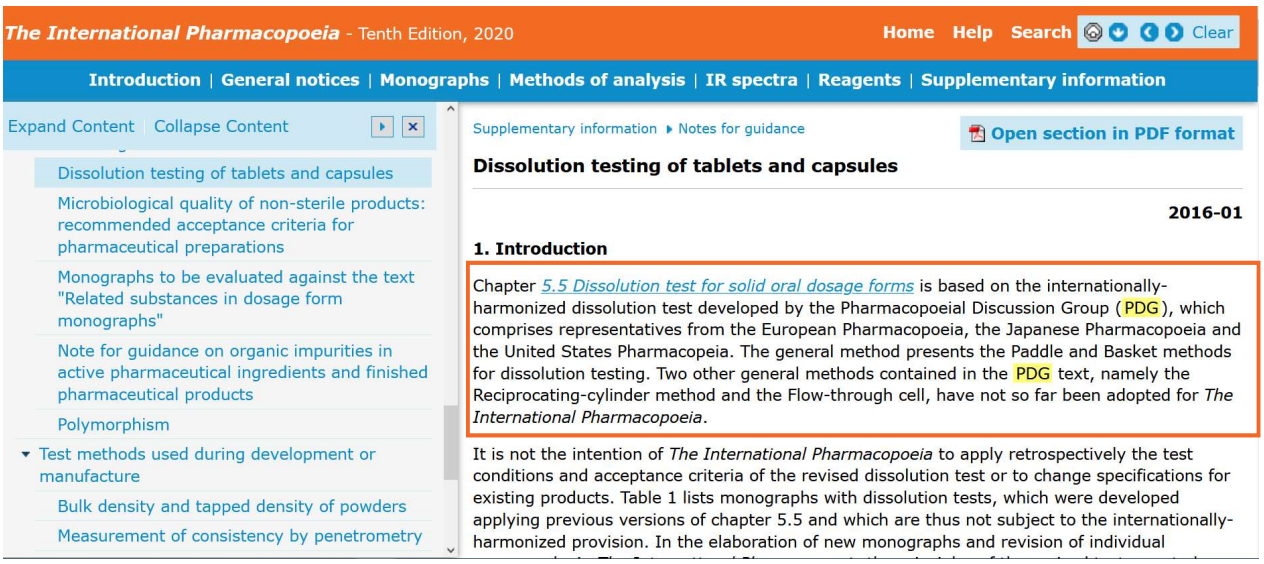
Member States referring to The International Pharmacopoeia



International collaboration and harmonization

- **Pharmacopeial Discussion Group (PDG)**
  - works to harmonize excipient monographs and general chapters.
  - Ten harmonized texts included in Ph. Int
- **International Meeting of World Pharmacopoeias (IMWP)**
  - Good Pharmacopoeial Practices (GPhP)
  - Pharmacopoeial Alert System
  - IMWP monographs (Favipiravir and on Favipiravir tablets)
- **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)**
  - ICH guidelines, e.g., related to the control of impurities, the development and validation of analytical methods
- **Bilateral Agreements and collaboration**
  - E.g., EDQM serves as custodian for the International Chemical Reference Substances (ICRS) and International Standards for Antibiotics (ISA)

World Health Organization



Foreword in the Report to the First World Health Assembly in 1948
by A.STAMPAR, M.D, Chairman of the Interim Commission

Thank you

For more information, please contact:
Name: Luther Gwaza PhD
Title: Team Lead, Norms and Standards for Pharmaceuticals
Email: gwazal@who.int

World Health Organization

INDIAN PHARMACOPOEIA COMMISSION

(Ministry of Health & Family Welfare, Government of India)
Sector 23, Raj Nagar, Ghaziabad 201002 (U.P.), India
E-mail: lab.ipc@gov.in; Website: www.ipc.gov.in

Motivation and Expectations for Harmonization from the Indian Pharmacopoeia

20 September 2022
Strasbourg, France

Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Directo
Indian Pharmacopoeia Commissio

Outline

- Background: Harmonisation
- Motivation for Pharmacopoeial Harmonisation
- Advantage of Pharmacopoeial Harmonisation
- Harmonisation Efforts by Indian Pharmacopoeia
- IPC participation in PDG
- IPC Monograph/ General Chapter (GC) Harmonisation process
- PDG Excipients and General Chapters
- Expectations from Harmonisation

INTRODUCTION

The Govt. of India has created a dedicated and autonomous institution - Indian Pharmacopoeia Commission (IPC) to be custodian of Indian Pharmacopoeia (IP), the official book of standards for drugs included therein, in terms of the Second Schedule to the Drugs and Cosmetics Act, 1940. It came into existence on 1st January 2009 as an Autonomous Institute

Indian Pharmacopoeia (IP) specifies the Standards of Quality (identify, purity and strength) of the drugs imported, manufactured for sale, stocked or exhibited for sale or distributed in India.

JOURNEY 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
Addendum in 2008

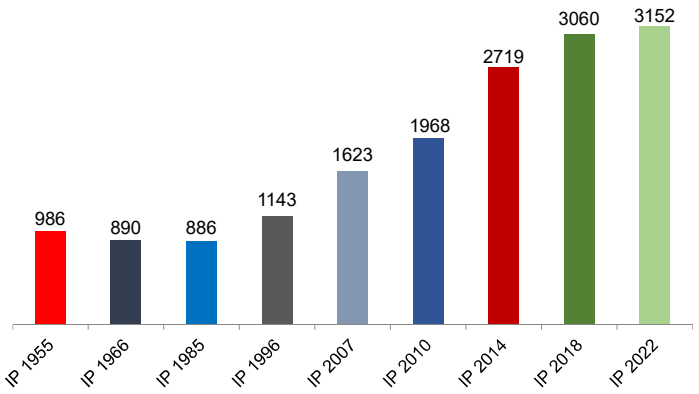
2010 – Sixth Edition
3 Volumes
Published by IPC
1968 Monographs
Biotech Monographs Incorporated
Addendum in 2012

2014 – Seventh Edition
4 Volumes
Separate Veterinary Volume
2586 Monographs
Radiopharmaceutical Monographs Incorporated
Addenda in 2015 & 2016

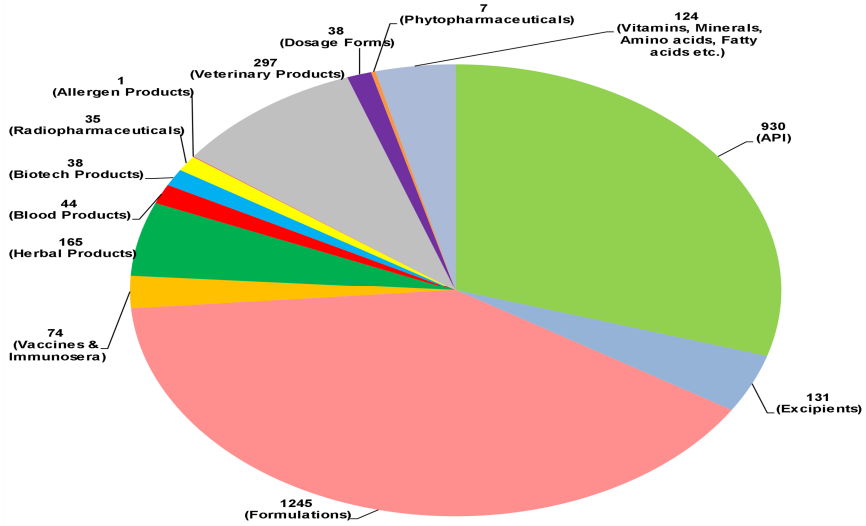
2018 – Eighth Edition
4 Volumes
3060 Monographs
Allergen Monograph Incorporated
Addenda in 2019 & 2021

2022 – Ninth Edition
4 Volumes
Separate Veterinary Volume
3284 Monographs
Radiopharmaceutical Monographs Incorporated
Addenda in 2019 & 2022

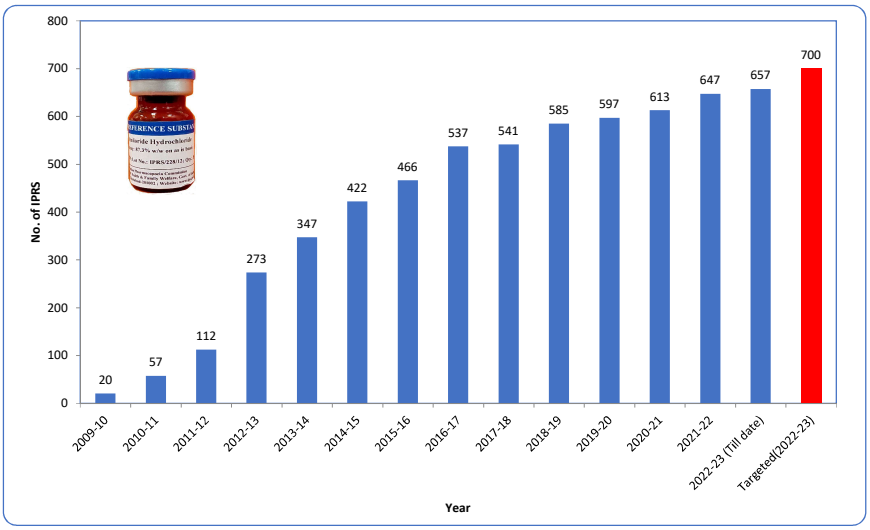
IP Monograph Development



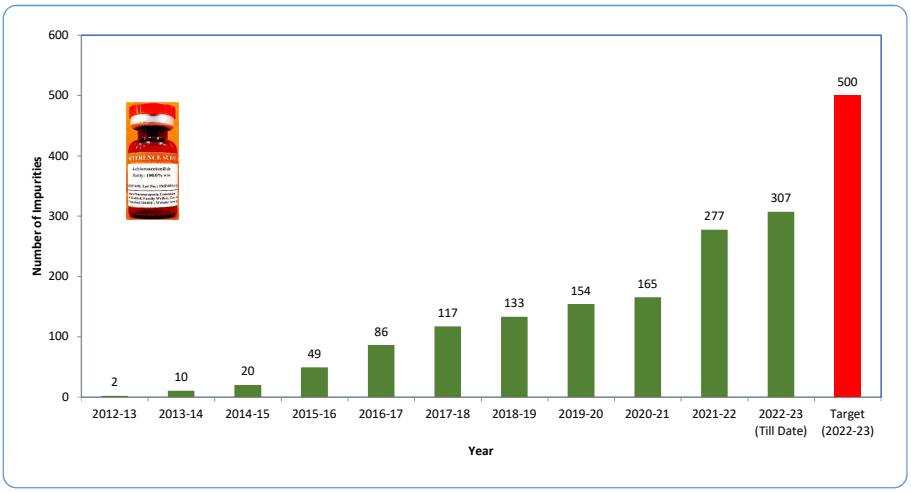
IP 2022 : Monograph Status



Built-up of IPRS Inventory



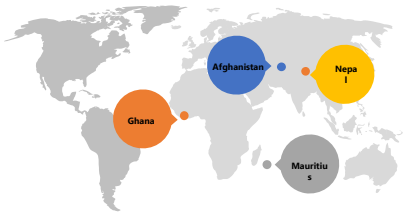
Built-up of Impurity Standard Inventory



NEW INNITIATIVES AT IPC WITH HIGH IMPACT ON PUBLIC HEALTH

1	DIGITAL IP – SHOULD BE AVAILABLE BY END OF FY'23
2	INCREASING INVENTORY AND STAKEHOLDER AWARENESS ON IMPURITY STANDARDS USE AND IMPORTANCE
3	BRINGING DISSOLUTION TESTING IN PROLONGED RELEASE FORMULATION MONOGRAPHS
4	IMPURITY LIMITS HARMONIZED WITH ICH RECOMMENDATION
5	JOINING PDG PILOT – GLOBAL INITIATIVE TOWARDS HARMONIZATION OF PHARMACOPOEIA
6	NEW MoU BEING SIGNED WITH Ministry of AYUSH and NIPER GUAHATI

RECOGNITION OF IP IN FOREIGN COUNTRIES



IP has been accepted as a book of standards in a total of four countries

Background: Harmonisation

- **Objective**: to have aligned test methods and specifications to a common standard
- **Participating countrie** JP (MHLW/PMDA) Ph. Eur. (EDQM) USP
- Harmonisation is embedded in development and history of pharmacopoeias and Pharmacopoeias are themselves embedded within current regulatory and legal framework of the country or region in which they are applicable.
- Pharmacopoeial harmonization provides support to global regulatory agencies.
- It address global manufacturing and supply chain which ultimately benefits global patients health.

Motivation for Pharmacopoeial harmonisati

01 Value for Patients Health

- Access to high quality, safe and effective medicines worldwide
- Dissemination, recognition and adoption of best practices and assurance of high quality standards
- Reduction of Unnecessary Testing in Animals and Humans
- Promote Innovation and Development of Medicines for Unmet Medical Needs
- Impact in control of Medicine quality & Safety
- Assist in achievement of UN Sustainable Development Goals (SDG)

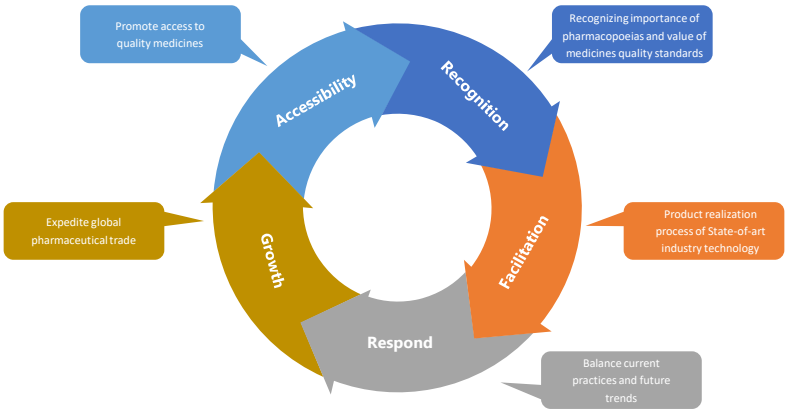
02 Value for regulators

- Helps in managing increased globalization and new technology change
- Facilitates regulatory communication & information sharing
- Improves consistency, efficiency, and transparency of review and promote faster access of life-saving medicines to patients
- Leverage international expertise and keep up with international best practices
- Decreases duplication of activities and facilitates work sharing and optimization of resources

03 Value for Industry

- Enables industry to reduce development times by removing the duplication of studies that was previously required to gain global market approval for a new medicine.
- Reduces cost, time and resources associated with multiple lot release
- Reduces testing of same product batch and in-country testing of each lot
- Facilitates global development plan supporting global registration

Advantage of Pharmacopoeial harmonisati



Harmonisation Efforts by Indian Pharmacop

- **Pharmacopoeial Discussion Group (PDG) accepted IPC** to pilot for global expansion of membership
- **Bilateral Memorandums of Understanding with Pharmacopoeias** United States Pharmacopoeia (USP) and British Pharmacopoeia (BP) on exchange of knowledge and pharmacopoeial standards.
- **Participation in International Meeting of World Pharmacopoeias–**
  - New-Delhi, India, April 2013, co-organised by IP and WHO
  - Suzhou City, China, Sept. 2015, co-organised by ChPh and WHO
  - Tokyo, Japan, September 2016, co-organised by JP and WHO
  - Brasilia, Brazil, July 2017, co-organised by ANVISA and WHO
  - Geneva, Switzerland, March 2019 organized by WHO

Harmonisation Efforts by Indian Pharmacopoeia (C

- **Work for International Pharmacopoeia-**
  Participated regularly for the development of the monographs related to Anti-retroviral, Anti-tubercular and Radio pharmaceutical for the WHO/International Pharmacopoeia from time to time.

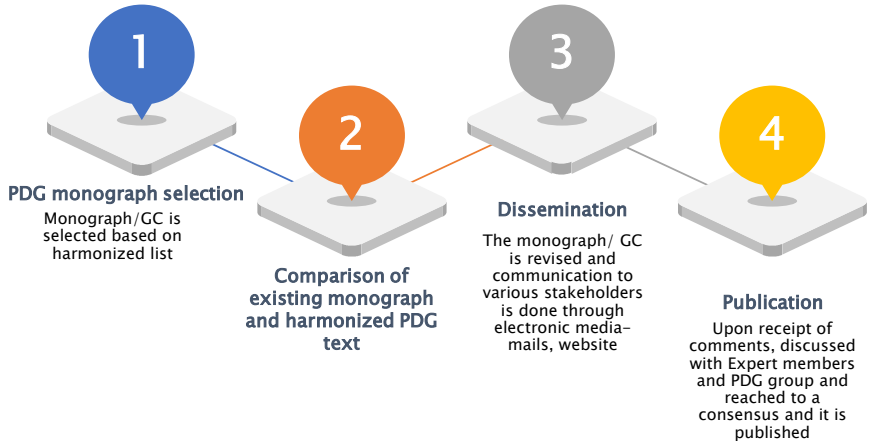
- **Observer status in European Directorate of Quality of Medicines (EDQM) and participates in the meetings-**
  - 154th session, Strasbourg, France, 15th -16th March, 2016
  - 160th session Strasbourg, France, 20th - 21st March, 2018
  - 164th session Strasbourg, France, 18th -19th June, 2019

- Conducted IPC-EDQM Symposium on Drug Standards and Regulatory Updates Hotel Courtyard Marriot, Mumbai, India, 26th- 27th April, 2018

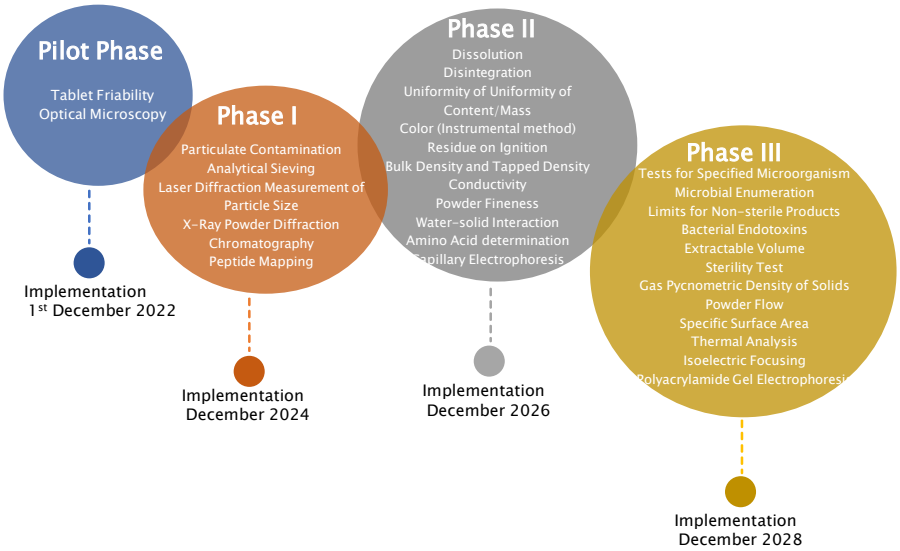
IPC participation in PDG

- **India** participated in **PDG pilot phase for global expansion (Dec 13, 2021)**
- IPC gave intent to participate in **pilot phase (Dec 31, 2021)**
- IPC staff participated in **informational follow-up videoconferencing (Feb 28, 2022)**
- Submitted application for **PDG pilot for global expansion of membership (April 6, 2022)**
- Responded to **additional clarifications on application (June 7, 2022)**

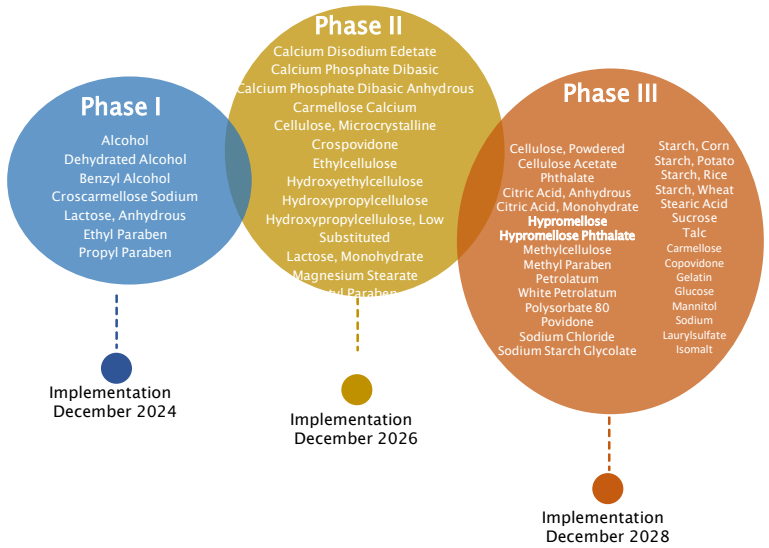
IPC Monograph/ General Chapter (GC) Harmonisation pro



PDG General chapters



PDG Excipient Monographs



Expectations from Harmonisation

- Harmonization with ICH and other worldwide authorities will position India as one of new key countries for pharmaceutical companies.
- Avoids **repetition in drug development** activities.
- **Decrease the drug development** delays and ensures availability of key medicines to patients.
- **Enhance the functioning of regulatory** systems and harmonization of pharmaceutical regulations
- High level of **engagement** among stakeholders
- Scope of accommodating local issues
- Discourage **unethical activities such as**:
  - Production and import of substandard medicine
  - Conduct of unethical trials
  - Corruption
  - Irrational prescribing and dispensing practices

Thank You

USE OF IP & IPRS IS SOCIAL AND LEGAL OBLIGATION FOR "IP" PRODUCTS

ChP's Perspective for standards harmonisation

2022 EDQM Conference to mark the launch of
11th Edition European Pharmacopoeia

Chinese Pharmacopoeia Commission

20th Sept. 2022

国家药典委员会
Chinese Pharmacopoeia Commission

ChP and EDQM

- The 1st CHP-EDQM Joint Workshop (about the special topic on pharmaceutical excipients standards) was held at EDQM headquarters in October 2016
- The 2nd CHP-EDQM Joint Workshop (about the special topic on impurity control and detection technology) was held at Jinan in July 2019

Signature of the CHP-EDQM MOU

国家药典委员会
CHINESE PHARMACOPOEIA COMMISSION

The overview of ChP international cooperation

The Chinese Pharmacopoeia Commission has good cooperation with the World Health Organization (WHO) and Pharmacopoeia agencies of the EU, the US, the UK, Japan, India, Kazakhstan and other countries.

——Active participation in IMWP activities under the WHO framework

——Signing bilateral MOUs with counterpart agencies of the US, the UK, the EU, Japan and Kazakhstan to gradually promote international cooperation on drug standards

——Collaboration with the French Pharmacopoeia, the US Pharmacopoeia and the British Pharmacopoeia: joint development of standards for Chinese crude drug, excipients, packaging materials and biological products

——FHH (China, Japan, South Korea, Singapore, Vietnam, Australia, Hong Kong 6+1, forum for the harmonisation of herbal medicines) Sub-Committee I: Pharmacopoeia

——Recommendation of international experts: USP, EP

——Recommendation of Chinese crude drug standards to Pharmacopoeias of other countries

ChP Since 1950

Main content

- Harmonisation of *the Chinese Pharmacopoeia* with ICH Guidelines
- ChP's Perspective for standards harmonisation

China's accession to ICH

- In June 2017, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) officially approved the former China Food and Drug Administration (CFDA) as its 8th regulatory member.
- On 7th June 2018, the National Medical Products Administration (NMPA) was elected member of ICH management committee.


国家食品药品监督管理总局 CFDA
China Food and Drug Administration

国家食品药品监督管理总局成为国际人用药品注册技术协调会成员

2017年06月19日 发布

2017年5月31日至6月1日，国际人用药品注册技术协调会（ICH）2017年第一次会议在加拿大蒙特利尔召开。会议通过了中国国家食品药品监督管理总局的申请，总局成为国际人用药品注册技术协调会正式成员。

The International Council for Harmonization (ICH) met in Montreal, Canada from May 31 to June 1, 2017. The ICH Assembly approved the China Food and Drug Administration as a new Regulatory Member.


国家药品监督管理局 国家市场监督管理总局

中国国家药品监督管理局当选为国际人用药品注册技术协调会管理委员会成员

2018年06月01日 发布

当地时间5月31日下午1点30分，在日本横户举行的国际人用药品注册技术协调会（ICH）2018年第一次大会上，中国国家药品监督管理局当选为ICH管理委员会成员。

国家药典委员会 CHINESE PHARMACOPOEIA COMMISSION

ICH guidelines

- As a technical, non-governmental international organisation established by the drug regulatory agencies and industry associations of the US, the EU and Japan
- the basic purpose of ICH is to harmonise and establish international technical standards and regulations on the safety, efficacy and quality of drugs in the field of drug registration.

- Q category deals with quality assurance, 44 guidelines
- S category deals with preclinical studies, 16 guidelines
- E category deals with clinical studies, 30 guidelines
- M category deals with multidisciplinary topics, 12 guidelines

ICH guidelines on quality	
Q1 Stability	Q8 Pharmaceutical development
Q2 Analytical validation	Q9 Quality risk management
Q3 Impurities	Q10 Pharmaceutical quality system
Q4 Pharmacopoeias	Q11 Development and manufacture of drug substances
Q5 Quality of biotechnological products	Q12 Lifecycle management
Q6 Specifications	Q13 Continuous manufacturing of drug substances and drug products
Q7 Good Manufacturing Practice (GMP)	Q14 Analytical procedure development

- In March 2018, according to the principle of "the organiser takes charge" made by the ICH Office of NMPA, ChP is responsible for the conversion and implementation of ICH Q4.
- Considering the high complexity and wide impact of implementing ICH Q4 in China, this guideline is defined as tier 3 guideline by the ICH Office, and there is no clear time frame and task requirements for implementation at present.

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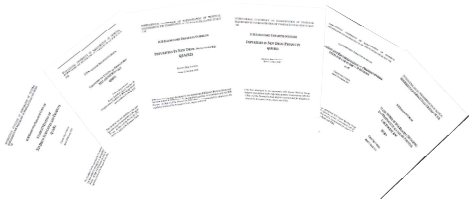
Other ICH guidelines

- *The Chinese Pharmacopoeia* also involves harmonisation with ICH guidelines Q1, Q2, Q3, Q5, Q6, M7, M10, etc.

ICH guidelines	ChP guidelines
Q1 Stability	9001 Guideline for stability testing of drug substances and products
Q2 Analytical Validation	9101 Guideline for analytical validation
Q3 Impurities	0861 Residual solvent determination method, 0821 Heavy metal examination method 9102 Guideline for the analysis of pharmaceutical impurities
Q5 Quality of Biotechnological Products	Examination methods related to biological products
Q6 Specifications	Q4-related testing methods
M7 Mutagenic Impurities	9306 Guideline for the control of genotoxic impurities
M10 Bioanalytical Method Validation	9011 Guideline for human bioavailability and bioequivalence testing of pharmaceutical products

Harmonisation of *the Chinese Pharmacopoeia* (2020 edition) with ICH

1. Revised guideline for stability testing of drug substances and products — ICH Q1
2. Revised guideline for analytical validation — ICH Q2
3. Revised guideline for the analysis of pharmaceutical impurities — ICH Q3
4. Revised residual solvent determination method — ICH Q3C
5. New Flow-Through Cell and reciprocating cylinder apparatus — ICH Q4
6. New bulk density and tapped density determination method — ICH Q4
7. New guideline for the control of genotoxic impurities — ICH M7



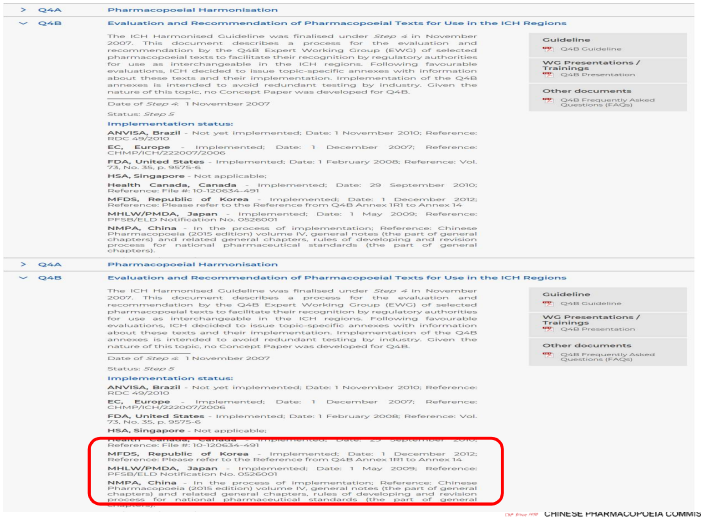
- Combining the current situation of drug manufacture and quality control in China
- Considering the applicability of marketed products
- Conformity with the scope and specifications of the pharmacopoeia
- Mainstream pharmacopoeias around the world are revised according to ICH guidelines

New: as consistent as possible
Revision: harmonised as far as possible

ICH website published ChP's implementation status of ICH Q4

- From 2017 to 2020, ChP submitted the implementation status of 16 pharmacopoeial analytical methods of ICH Q4 in China, technical differences as well as comments and suggestions on revising ICH Q4 to ICH office of NMPA.

In 2020, for the first time, all 14 annexes of ICH Q4B on the ICH website incorporated the implementation status of the ChP.



ChP Since 1950

Main content

- Harmonisation of *the Chinese Pharmacopoeia* with ICH Guidelines
- ChP's Perspective for standards harmonisation

国家药典委员会
Chinese Pharmacopoeia Commission

The assessment of the difference between ChP and ICH Q4

—Similarity: All the methods in Q4B annexes are included in *the Chinese Pharmacopoeia* (2020 edition) and are generally consistent in terms of technical requirements.
—Difference: There are differences in instrument parameters, determination methods and results determination. The differences in residue on ignition test, disintegration test, content uniformity test and dissolution test are relatively big.

No.	Testing methods	Harmonisation assessment	Main difference
Q4B1	Residue on ignition test	Relatively big difference	The amount of sulphuric acid added, ignition temperature, conditions for ending test
Q4B2	Test for extractable volume of parenteral preparations	Generally consistent	Different sampling methods, different specific operations
Q4B3	Insoluble particulate matter test	Generally consistent	Different determination methods of water for particulate matter, different sampling methods, different methods of determining the results of 100ml volume
Q4B4A	Microbiological examination of non-sterile products: microbial enumeration test	Generally consistent	Differences in some validated strains, control media, operational details, etc.
Q4B4B	Microbiological examination of non-sterile products: tests for specified micro-organism	Generally consistent	Differences in some validated strains, control media, operational details, determination results, etc.
Q4B4C	Microbiological examination of non-sterile products: acceptance criteria for pharmaceutical preparations and substances for pharmaceutical use	Generally consistent	Significant differences in scope of application, requirements for Salmonella testing, microbiological limits for small dosage formulations such as patches, standards for traditional Chinese medicine (botanical drug), etc.
Q4B5	Disintegration test	Relatively big difference	Different apparatus and result determination methods

The assessment of the difference between ChP and ICH Q4

No.	Testing methods	Harmonisation assessment	Main difference
Q4B6	Content uniformity test	Relatively big difference	Different apparatus and result determination methods
Q4B7	Dissolution and release test	Relatively big difference	Different examination methods and result determination methods
Q4B8	Sterility test	Generally consistent	Slight differences in strains, number of tests and washout volumes
Q4B9	Tablet friability test	Generally consistent	Slight differences in apparatus and points for attention
Q4B10	Polyacrylamide gel electrophoresis	Generally consistent	ICH method is more flexible and detailed
Q4B11	Capillary electrophoresis	Generally consistent	The description in ChP is more explicit (isolation mode, apparatus)
Q4B12	Analytical sieving	Generally consistent	ICH has more detailed rules on different sieve sizes, how to choose the right sieve in accordance with different sample sizes, and sample weight
Q4B13	Bulk density and tapped density	Consistent	/
Q4B14	Bacterial endotoxins test	Generally consistent	Slight difference in method description

Are the methods with small differences equivalent/interchangeable? i.e. do these differences affect the ability to produce the same results of acceptance and rejection? —Extensive validation, statistical comparison

The conversion of Q4B annexes in ChP

Steadily forging ahead Implementation of the Chinese Pharmacopoeia (2025 edition)

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Challenges

General chapters	Year of first inclusion in *the Chinese Pharmacopoeia*	Number of references to monograph standards in *the Chinese Pharmacopoeia*
Residue on ignition test	1953	791
Test for extractable volume of parenteral preparations	1995	356
Insoluble particulate matter test	1977	≫142,
Microbiological examination of non-sterile products: microbial enumeration test/tests for specified micro-organism/acceptance criteria for pharmaceutical products and substances for pharmaceutical use	1995	37 dosage forms, ≫81
Disintegration test	1953	1068
Content uniformity test	1985	347
Dissolution test	1985	657
Sterility test	1953	15 dosage forms, ≫746
Tablet friability test	2000	/
Polyacrylamide gel electrophoresis	1990	62
Capillary electrophoresis	2000	3
Analytical sieving	2000	273
Bulk density and tapped density determination method	2020	/
Bacterial endotoxins test	1993	＞589

Long history of use

Lots of varieties in use

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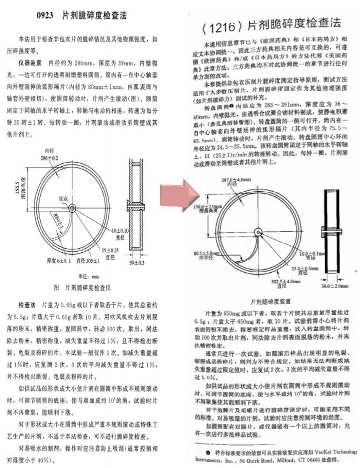
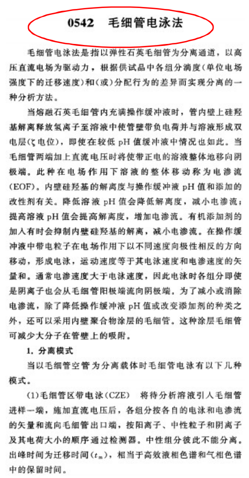
Methods for harmonisation and conversion

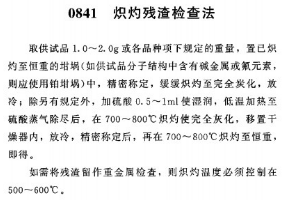
1. Substitution of the original text



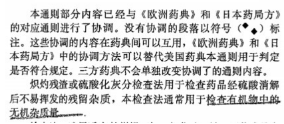
2. Substitution of the original text + special consideration



3. 原文+协调案并行



+ ICH Q4B annex 1 method



Retaining the style of Chinese Pharmacopoeia with modifications to the text

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Methods for harmonisation and conversion

Gradually less difficult to harmonise

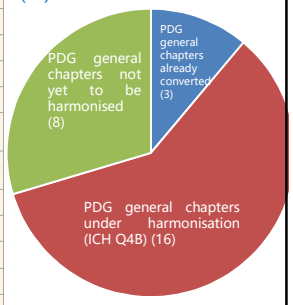
Name of methods	Principle of application						Initial intentional approach
	Number of variety reference	Time since first inclusion (20 years)	Reference of TCM variety	Formal differences in style, presentation, etc.	Substantial differences affecting result determination	ChP is more advanced	
Dissolution test	Big	Long	Yes	Small	Big	None	Original text in parallel
Insoluble particulate matter test	Big	Long	Yes	Small	Medium	None	Original text in parallel
Disintegration test	Big	Long	Yes	Small	Big	None	Original text in parallel
Analytical sieving	Big	Long	Yes	Big	Big	None	Original text in parallel
Residue on ignition test	Big	Long	Yes	Small	Big	None	Original text in parallel
Capillary electrophoresis	Small	Medium	None	Big	None	Yes	Substitution of the original text + sepcial consideration/revision
Tablet friability test	None	Medium	None	Small	Small	None	Substitution of the original text/substitution+ revision
Bulk density and tapped density determination method	None	Small	None	Small	None	None	Substitution of the original text

Harmonisation of PDG harmonisation programmes

Harmonisation programme No.	Content of PDG harmonisation	Harmonisation programme No.	Content of PDG harmonisation
G01	Analytical sieving (8/5/2007)	G21	Dynamic light scattering (under harmonisation)
G02	Bulk density and tapped density determination method (6/11/2013)	Q01	Dissolution test (10/6/2010)
G03	Electrical conductivity test (13/9/2017)	Q02	Disintegration test (30/10/2007)
G04	Gas pyknometer method for solid density (8/5/2007)	Q03/04	Content uniformity test (9/11/2010)
G05	Powder flowability test (10/6/2007)	Q05a	Specified micro-organism test (5/6/2008)
G06	Tablet friability test (18/2/2004)	Q05b	Microbial enumeration test (10/6/2009)
G07	Metallic impurities (under harmonisation)	Q05c	Limits of non-sterile products (27/6/2013)
G08	Inhalation products (removed from PDG plan)	Q06	Bacterial endotoxins test (16/6/2011)
G09	Optical microscope (10/6/2004)	Q07	Colour instrumentation examination method (26/10/2016)
G10	Powder fineness test (8/5/2007)	Q08	Test for extractable volume of parenteral preparations (9/11/2010)
G11	Specific surface area test (10/11/2003)	Q09	Insoluble particulate matter test (6/6/2012)
G12	Porosimetry (8/5/2007)	Q10	Residue on ignition test (4/8/2005)
G13	Light scattering test for particle size (11/11/2008)	Q11	Sterility test (10/6/2009)
G14	X-ray powder diffraction method (30/10/2007)	B01	Amino acid determination (28/4/2017)
G15	Water-solid interation (10/9/2002)	B02	Capillary electrophoresis (9/6/2010)
G16	Thermal analysis (26/6/2014)	B03	Isoelectric focusing electrophoresis (9/9/2002)
G17	Delivery dosage uniformity of inhalation products (under harmonisation)	B04	Protein test (removed from PDG plan)
G18	Solution calorimetry for crystallinity determination (16/6/2011)	B05	Peptide map method (10/9/2002)
G19	Solid density test (3/6/2008)	B06	Polyacrylamide gel electrophoresis (26/6/2014)
G20	Chromatography (under harmonisation)	…	

PDG harmonisation programmes (39 general chapters)

PDG general chapters included in the Chinese Pharmacopoeia (27)



PDG general chapters not included in the Chinese Pharmacopoeia (10)

2 removed from PDG plan

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Overview of PDG general chapters included in the Chinese Pharmacopoeia

No.	Testing methods	Main difference
B03	Isoelectric focusing electrophoresis	The PDG harmonisation programme focuses on the elaboration of principles and theories. The introduction of electrophoresis apparatus does not include detailed operation and is not for specific varieties. However, the Chinese Pharmacopoeia has detailed description of electrophoresis process and are specific to some varieties.
G16	Thermal analysis	The structure of the text is different, the Chinese Pharmacopoeia has a clearer structure while the analysis of low eutectic impurities in the PDG harmonisation programme is more specific.
Q07	Colour instrumentation examination method	The principles of the method are basically the same, but there are differences in the method of determination, calibration of the instrument, general requirements for the instrument, text structure and description.
G20	Chromatography	Differences in text structure, requirements for trailing factors, formulae for calculating separation degree, range of adjustment of chromatographic parameters, calculation of signal-to-noise ratio
G13	Light scattering test for particle size	1. Different text structure. The method is the 3rd method of light scattering in ChP 0982 particle size and particle size distribution test, which is more focused on practical applications, while PDG is a separate harmonisation programme; 2. PDG harmonisation programme is a separate method in pharmacopoeias of many countries, which is more focused on theoretical introduction.
G14	X-ray powder diffraction method	Different text structure. The Chinese Pharmacopoeia is more focused on practical applications and is divided into the first method of single crystal X-ray diffraction and the second method of powder X-ray diffraction; the PDG hharmonisation programme is more focused on theoretical introduction, which is divided into sections on introduction, basic principles, instrumentation, sample preparation, instrument performance, qualitative and quantitative analysis, estimation of amorphous and crystallinity, and single crystal structure.

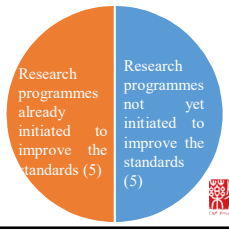
➢ PDG general chapters not included in *the Chinese Pharmacopoeia*

1. Research programmes already initiated to improve the standards

Research programmes have already been initiated to improve the standards for 5 PDG methods, including B01 amino acid determination, G05 powder flowability test, G07 metallic impurities, G15 water-solid interation and G21 dynamic light scattering.

2. Research programmes not yet initiated to improve the standards

No research programmes have been initiated to improve the standards for the other 5 PDG methods, including G03 electrical conductivity test, G09 optical microscope, G10 powder fineness test, G12 porosimetry and G18 solution calorimetry for crystallinity determination.



PDG general chapters not included in the Chinese Pharmacopoeia (10)

国家药典委员会 CHINESE PHARMACOPOEIA COMMISSION


Looking forward to
collaborating with EP
Thank you!
国家药典委员会
Chinese Pharmacopoeia Commission

- An API of a certain quality is always of the same quality, regardless of how it is tested. Nevertheless, there are numerous (small and big) differences between the pharmacopoeial monographs for the API.
- The use of the different methods and/or calculations does not contribute to the quality and/or the safety of the API.
- For Industry it is hard to see why so much differences are there and why it is apparently so difficult to harmonize.
- Regulatory agencies all around the world often require compliance with the local pharmacopoeia, without recognition of other pharmacopoeia.
- Even for “new”topics (think nitrosamines as an example) it turns out to be impossible to have a harmonized approach.

International Federation
of Pharmaceutical
Manufacturers & Associations

IFPMA

Talking Points on Pharmacopoeia Harmonization for the September EDQM Conference

Manufacturing and Quality Working Group

20 Sep 2022

Stephen Corrigan, Amgen

Thoughts on Pharmacopeial Harmonization

IFPMA

Opportunities implementing reliance approaches

- Overarching patient focus by acceptance of demonstrated equivalence
- Expansion of the Pharmacopeial Discussion Group (PDG) to involve new ICH members
- Collaborating and work-sharing to increase of efficiency of the process
- Continuous improvement towards alignment of general chapters

Observation

Complementary standards by national pharmacopoeia

- Not harmonized methods and specification limits
- Execute multiple testing programs for individual compendial monographs
- Individual methods - slightly differently executed - achieve comparable results

Definitions

- **Same text: Harmonization**
  Align individual monographs and general chapters by collaboration (e.g., ICH Q4B)
- **Accept equivalence: Reliance**
  Recognizing the pharmacopeial standards from another country benefiting from reduced resources, (including environmental, time, bureaucracy).
- **Recognize similarities: Convergence**
  Independent development of similarities between separate pharmacopoeias