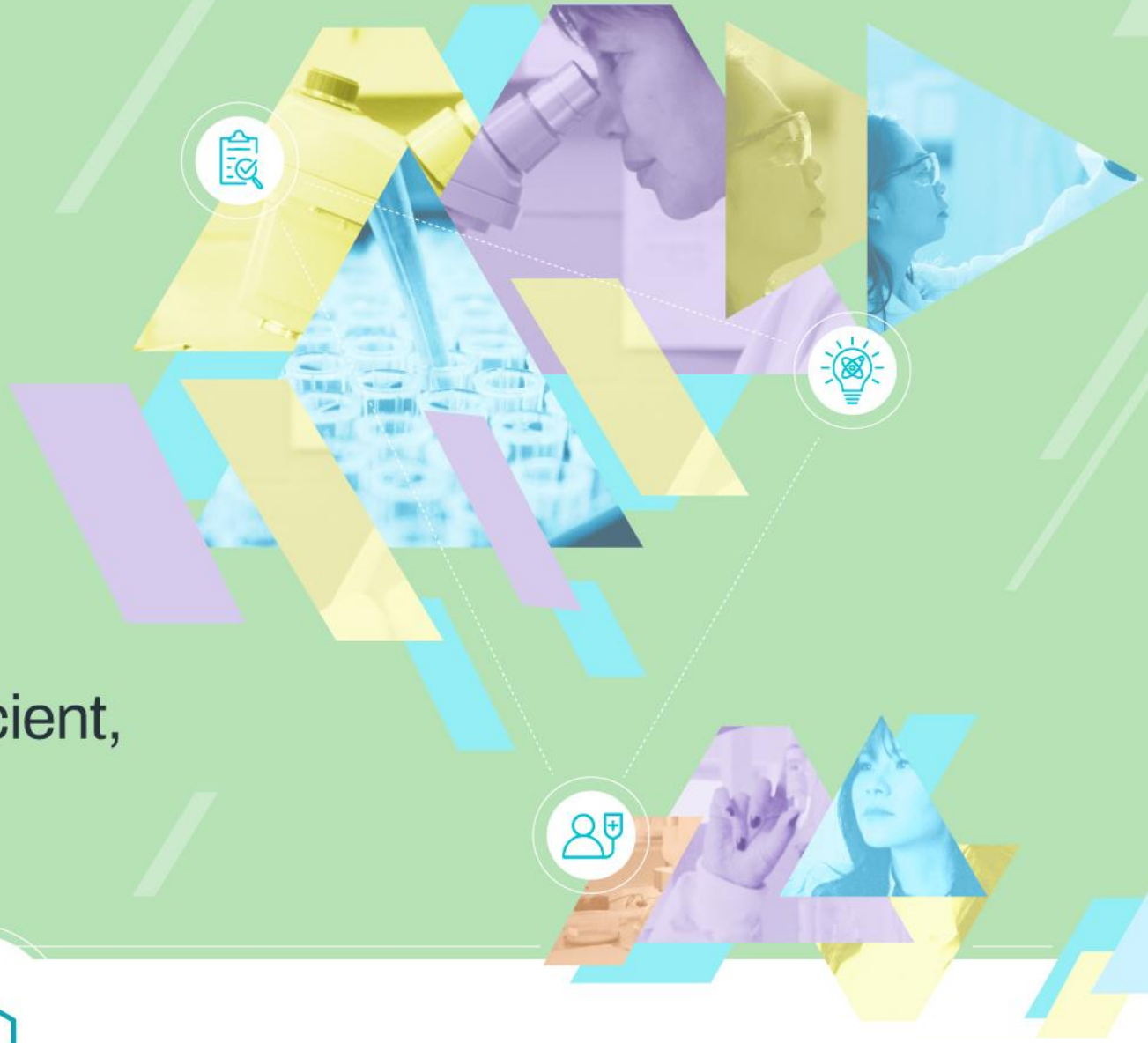
03-06 December 2024

ARC 2024

ASIA REGULATORY CONFERENCE

EVOLVING LANDSCAPES

Asia's role in driving a more efficient, innovative and patient-centric regulatory environment



Organized by IFPMA

In partnership with Medicines Australia

03-06 December 2024

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Asia's role in driving a more efficient, innovative and patient-centric regulatory environment

Welcome to Day 4

ICH Day

Organized by IFPMA

In partnership with Medicines Australia

Thank you for joining! A few guidelines for participants

The conference is held in English.

The detailed conference programme and speakers' biographies are available on arc.ifpma.org.

All participants are muted. Please use the Q&A box to raise questions to the speakers. If a question you would like to ask has already been raised, you can also "like" that question.

Polls will be used during the sessions to get feedback from participants. These will appear on screen.

The conference is recorded. All speaker presentations and videos will be made available on the website after the conference.

ICH: Driving Global Harmonization to Advance Global Health

Session Moderator

Kum Cheun Wong

Head Asia Pacific Regulatory & Development Policy at Novartis, on behalf of SAPI

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Benefits of ICH
&
IFPMA role in ICH

Presented by Angelika Joos

Executive Director Science & Regulatory Policy, MSD

On behalf of IFPMA

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The scope of the ICH

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)…

- **global pharmaceutical regulatory harmonization work in one organization**
- involves **regulators, the pharmaceutical industry, and other stakeholders**
- **transparent platform for discussions**
- science-based, **consensus** driven, and has clear governance

Promoting public health through international harmonization accomplished through Technical Guidelines that are implemented by regulatory authorities

ICH history snapshot

- Founded in 1990
- Initiated by the regulators and the industries of the US, EU and Japan
- IFPMA and the WHO as Observers
- Reformed and established as a non-profit legal entity in October 2015

https://admin.ich.org/sites/default/files/2024-06/OverviewOfICH_2024_0617_0.pdf

Global benefits of the ICH, guidelines, and standards

High-quality and safe medicines

ICH guidelines aim at setting harmonized global standards for the adequate **quality, efficacy, and safety** of medicinal products[1].

International harmonization

Harmonization of technical guidelines **increases efficiencies and reduces duplications** for regulators and industry.

For example, GCP and CTD may lead to a **greater acceptance** of data.

Strengthening collaboration

Participation in ICH strengthens **multi-stakeholder collaboration** as well as collaboration among regulators.

Enhanced access for patients

Implementation of harmonized ICH guidelines can lead to faster regulatory approvals and potentially **faster patient access to high-quality medicines**.

[1] This can be very important for countries with sub-optimal resources.

LMICs: Low-and middle-income countries; **GCP**: Good Clinical Practice; **CTD**: Common Technical Document

Progress and key achievements

The ICH has proven to be a successful forum for delivery of harmonized guidelines through dialogue between regulators and industry

Harmonization

- ICH has achieved international harmonization of technical guidelines
- As of November 2024:
  - ***77 guidelines on technical requirements:***
    - *Quality – 26 guidelines*
    - *Safety - 16 guidelines*
    - *Efficacy – 23 guidelines*
    - *Multidisciplinary - 12 guidelines*
  - ***ICH Standards***
    - *ESTRI (providing electronic standards for transferring regulatory information)*
    - *CTD/eCTD*
    - *MedDRA (standardizing medical terminology to facilitate sharing of regulatory information)*

Growth in membership

- Global membership has been increasing following ICH reform
- Member and Observer economies represent approximately two-thirds of the world's population, excluding Regional Harmonization Initiatives (based on 2022 data)
- As of November 2024, there were **23 Members and 38 Observers**

ESTRI: Electronic Standards for the Transfer of Regulatory Information; **CTD**: Common Technical Document; **MedDRA**: Medical Dictionary for Regulatory Activities

https://admin.ich.org/sites/default/files/2024-06/OverviewOfICH_2024_0617_0.pdf; https://admin.ich.org/sites/default/files/inline-files/ICH_leaflet_2022_0318.pdf

Benefits for ICH Observers

No **duties are** imposed on Observers

Observers **attend ICH Assembly meetings**, without voting right. They may nominate one delegate or an alternate to participate in these meetings, if the primary delegate is unavailable

Observers can propose **new topics for harmonization and can appoint experts to participate in the working groups** (with no automatic right to do so), in line with the applicable procedures in the Assembly Rules of Procedure and EWG/IWG Standard Operating Procedures

Standing Observers (WHO and IFPMA) are **granted additional rights** compared to **Observers**, including the ability to attend ICH MC meetings with up to two delegates and an appointed ICH Coordinator

Becoming an ICH Regulatory Member

Becoming a Member comes with many benefits, but some criteria need to be fulfilled first

Commitment of regulators to implement guidelines is expected and an expedited membership procedure is possible for those with high proven record of ICH guidelines implementation

Application and admission

- Any eligible party can apply to become Member or Observer
- Decisions admission is made by the Assembly

Engagement in the ICH process

- Past regular attendance in at least **three ICH meetings** during the previous two consecutive years
- Past **appointment of experts** in at least two working groups

Application of ICH guidelines

- Having implemented <u>at least</u> the following ICH guidelines ("Tier 1") upon application for Membership:
  - *Q1: Stability Testing Guidelines*
  - *Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients*
  - *E6: Good Clinical Practice Guideline*

More details here: https://www.ich.org/page/application-process

IFPMA within the ICH

- **IFPMA represents research-based National Trade Associations (NTAs) in the ICH that operate within the regulatory jurisdiction of ICH Regulatory Members outside EU, Japan, US**
  - IFPMA convenes a **diverse and consensus-driven industry voice** in shaping global regulatory standards and guidelines
  - IFPMA currently **represents trade associations** from Argentina, Brazil, Canada, China, Chinese Taipei, Egypt, Mexico, Republic of Korea, Singapore, Türkiye, and Saudi Arabia

IFPMA within the ICH

- **As a Standing Observer at ICH, IFPMA can:**
  - **Attend meetings** of the Assembly and the Management Committee (MC) without voting rights
  - Nominate up to **2 delegates** to attend the meetings of the Assembly and the MC
  - Appoint **experts to working groups (WGs):** 1 Expert and 1 Alternate
    - Over 40 IFPMA experts and alternates actively represent IFPMA's view in ICH Expert Working Groups (EWGs); ICH Implementation Working Groups (IWGs); Discussion Groups (DGs)
  - Appoint an **ICH Coordinator**
    - Which facilitates communication, coordination, and collaboration between all IFPMA ICH delegates, experts, and NTAs and serves as the main point of contact with the ICH Secretariat

NTAs: National Trade Associations; **MC**: Management Committee

IFPMA Representation in ICH WGs/DGs

Efficacy Topics
E2D(R1) EWG
E6(R3) EWG
E6(R3) Annex 2 Subgroup
E11A EWG
E20 EWG
E21 EWG
E22 EWG

Multidisciplinary Topics
M4Q(R2) EWG
M7 Subgroup
M11 EWG
M13 EWG
M14 EWG
M15 EWG

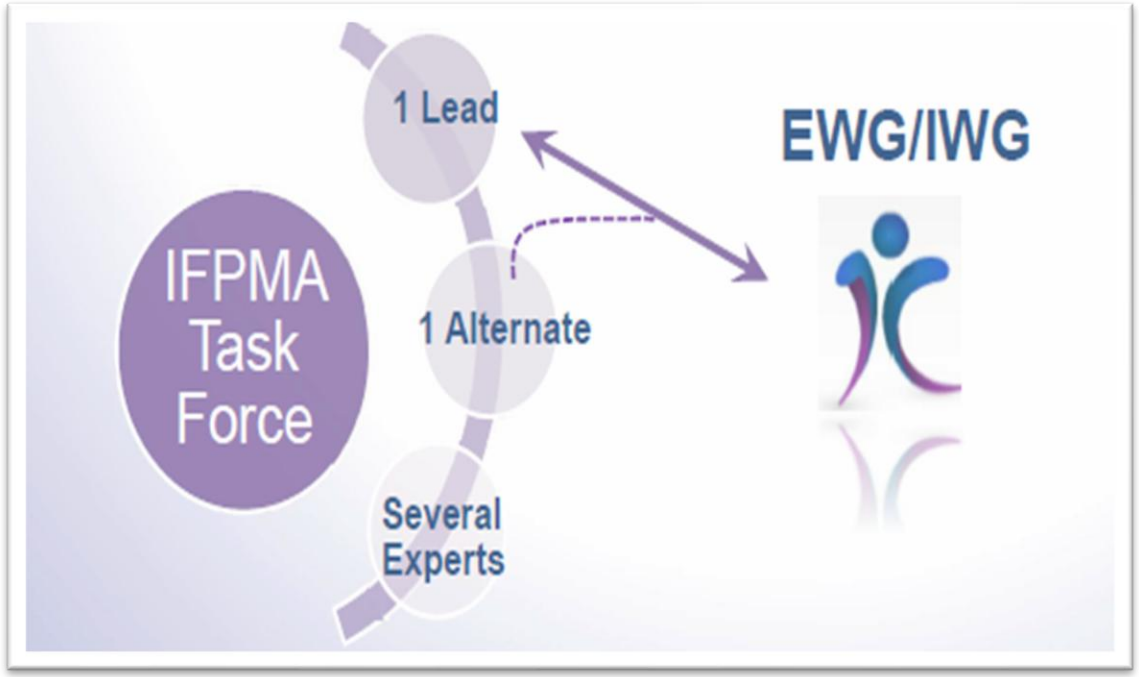
Quality Topics
Q1/Q5C EWG
Q2(R2)/Q14 IWG
Q3E EWG
Q5(R2) IWG
Q6(R1) EWG
Q9(R1) Training Group
Q13 IWG

Safety Topics
S13 EWG

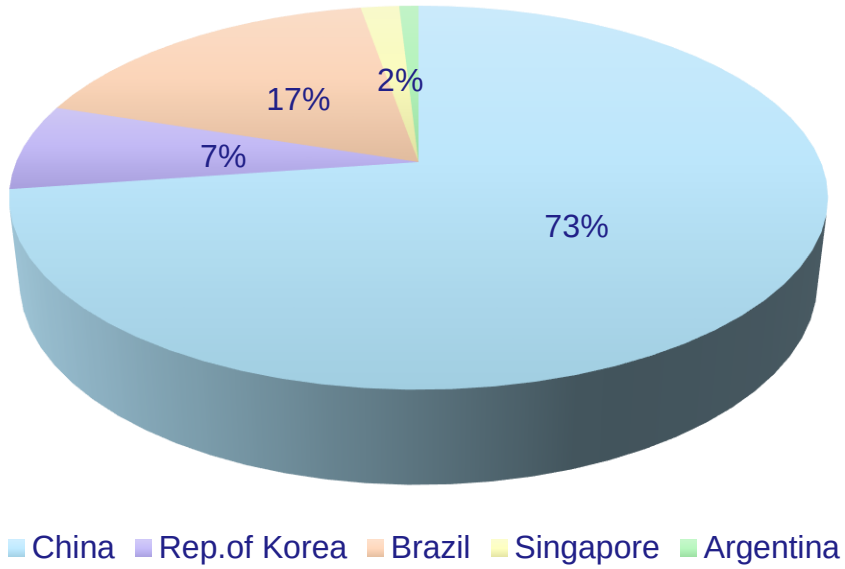
Cell and Gene Therapy Discussion Group (CGTDG)

Making a total of 22 Experts and 20 Alternates across 21 WGs and 1 DG

IFPMA Task Force



IFPMA Task Force (TF) experts should share their Association's views and any feedback on ICH-related topics and support the Lead Expert to prepare for ICH face-to-face meeting and teleconferences.



How IFPMA can support NTAs

The IFPMA may support NTAs in various ways, for instance…

- Assisting NTAs in their national journey of guideline implementation
- Sharing lessons and good practices based on experience collaborating with other NTAs of Member countries
- Representing Members at the ICH Management Committee (MC)
- Ensuring local trades interests are reflected
- NTAs can nominate experts to help develop guidelines and training materials, leverage SME expertise for training support, and assist with country implementation

NTAs: National Trade Associations

More about IFPMA Engagement in ICH

https://www.ifpma.org/publications/how-we-are-contributing-to-global-pharmaceutical-standards/

IFPMA

How we are contributing to global pharmaceutical standards

The evolving global pharmaceutical regulatory environment and the increasing interest of new countries in joining the ICH highlights the importance of maintaining consistent interpretation and implementation of ICH guidelines among industry and regulatory authorities worldwide.

The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), along with other ICH Members and Observers, has an important role in promoting global convergence toward ICH regulatory standards and their harmonized interpretation.

As a Standing Observer of ICH, IFPMA can:

- Attend meetings of the Assembly and the Management Committee (MC) without voting rights
- Nominate up to 2 delegates to attend the meetings of the Assembly and the MC
- Appoint experts to Working Groups (1 expert and 1 alternate per WG)
- Appoint an ICH Coordinator

About ICH

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is a unique platform bringing together regulatory authorities (RAs) and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals, as well as establishing common standards and guidelines.

Implementation of the ICH guidelines supports the alignment of regulatory requirements across regions, reducing duplication of efforts and promoting consistent regulatory standards worldwide. This makes the role of ICH crucial in facilitating the development, registration, and access to safe, effective, and high-quality medicines and vaccines worldwide, contributing to better health outcomes.

JUNE 2024

Thank you

ifpma.org

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Korea’s Journey to ICH :

Advancing Global Harmonisation

Presented by Su Jin KONG

Senior Expert in International Regulatory Affairs , MFDS

6 December 2024

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ASIA REGULATORY CONFERENCE

국민 안심이 기준입니다
YOUR SAFETY IS OUR STANDARD

Ministry of Food and Drug Safety

Korean Regulatory Authority

- Responsible for ensuring public health and safety by regulating food, pharmaceuticals, cosmetics, medical devices and other health-related products
- First established in 1998 & elevated in 2013
- National Institute of Food and Drug Safety (NIFDS)
- 6 Regional Offices of Food and Drug Safety

Status of MFDS in ICH

23 Members

	Regulatory	Industry
Founding members (6)	・EC (Europe) ・FDA (USA) ・MHLW/PMDA (Japan)	・EFPIA ・PhRMA ・JPMA
Standing members (2)	・Health Canada (Canada) ・Swissmedic (Switzerland)	
Members (15)	・ANVISA (Brazil) ・ANMAT (Argentina) ・COFEPRIS (Mexico) ・EDA (Egypt) ・HSA (Singapore) ・JFDA (Jordan) ・**MFDS (Korea)** ・MHRA (UK) ・NMPA (China) ・SFDA (Saudi Arabia) ・TFDA (Chinese Taipei) ・TITCK (Turkey)	・BIO ・Global Self- Care Federation ・IGBA

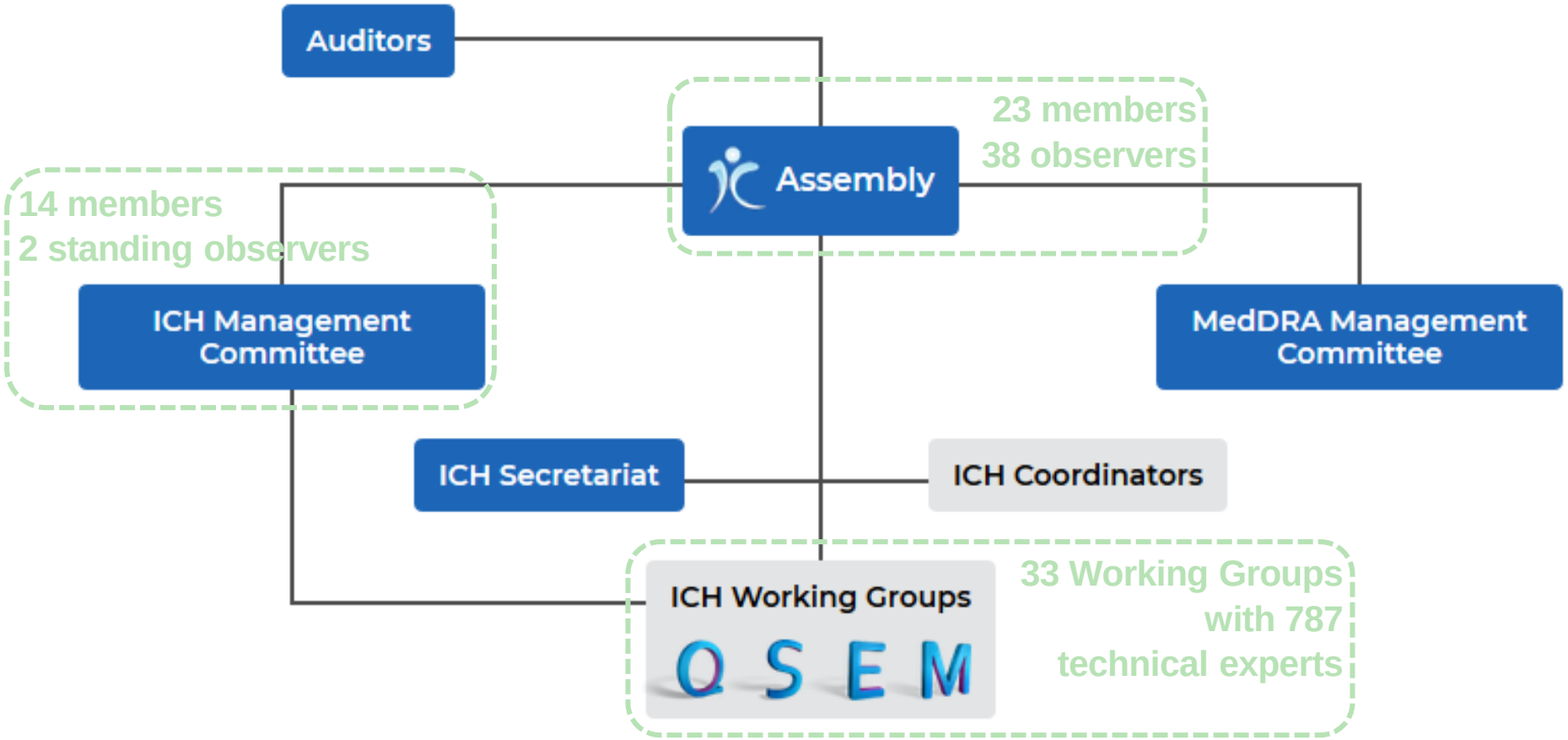
38 Observers

Standing Observers (2)	・IFPMA ・WHO	
Legislative or Administrative Authorities (23)	AEC (Azerbaijan) ANMAT (Argentina) ANPP (Algeria) CDSCO (India) CECMED (Cuba) CPED (Israel) CPPS (Uzbekistan) EDA (Egypt) Indonesian FDA INVIMA (Colombia) JFDA (Jordan) DIGEMID (Peru)	MMDA (Moldova) MOPH (Lebanon) National Center (Kazakhstan) NPRA (Malaysia) NRA (Iran) Roszdravnadzor (Russia) SAHPRA (South Africa) SCDMTE (Armenia) SECMOH (Ukraine) TFDA (Thailand) TGA (Australia)
*RHIs (6)	・APEC ・ASEAN ・EAC ・GHC ・SADC ・PANDRH	
Int'l pharmaceu-tical Ind. Org. (1)	・APIC	
Int'l Org. regulated or affected by ICH (6)	・Bill & Melinda Gates Foundation ・CIOMS ・EDQM ・IPEC ・PIC/S ・USP	

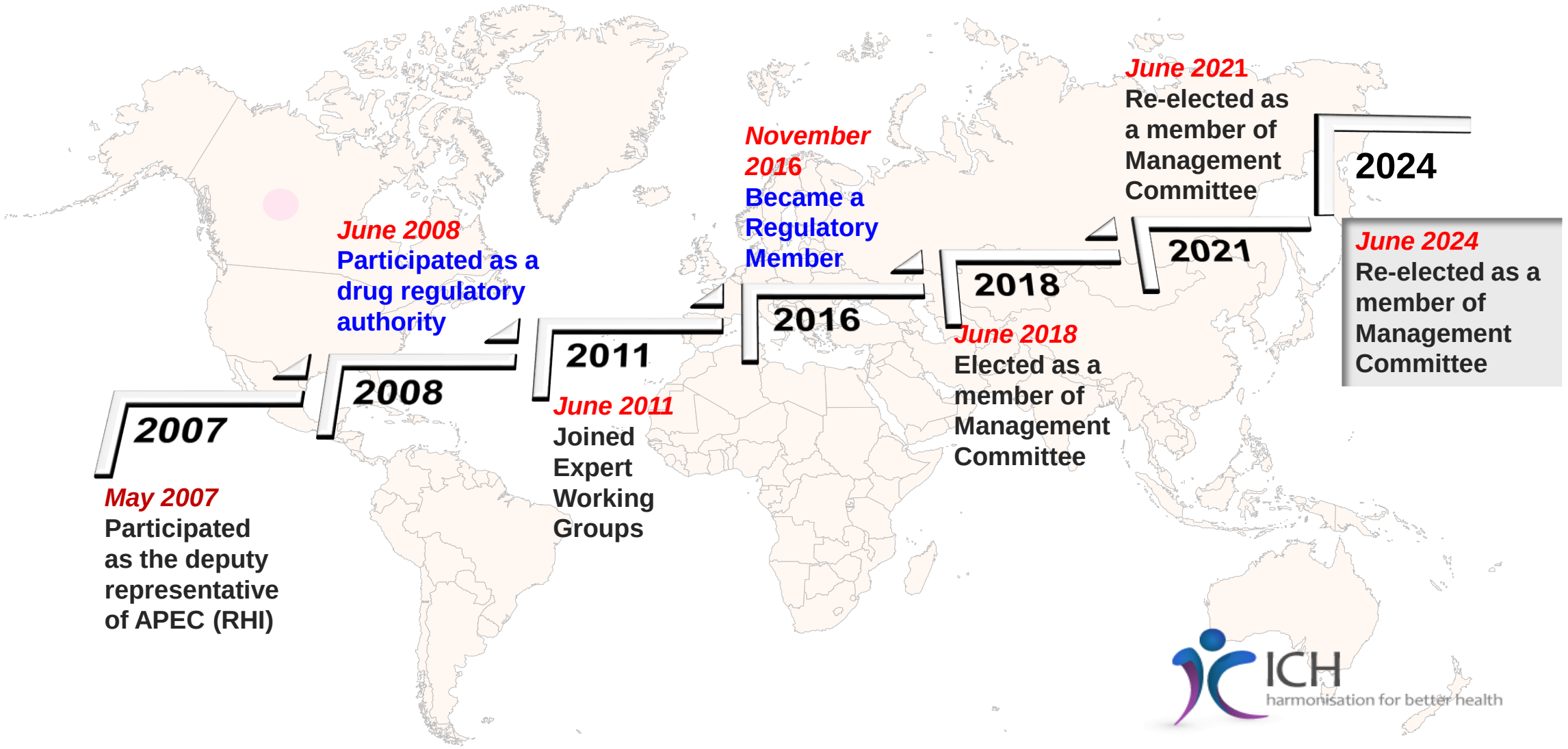
ICH Membership Eligibility for Regulators

- **Recognized Authority**
  - Has a legal personality
  - Responsible for regulation of pharmaceuticals for human use
- **Engagement in the ICH Process**
  - Past regulator attendance in the at least 3 ICH meetings during the previous 2 consecutive years
  - Past appointment of experts in at least 2 Working Groups
- **Application of ICH Guidelines**
  - Having implemented at least the following ICH Guidelines upon application for Membership
    - Q1 : Stability Testing Guidelines
    - Q7 : Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
    - E6 : Good Clinical Practice Guideline

ICH Structure and Governance



Milestones for MFDS Participation in ICH



MFDS as an elected member of Management Committee*.

	Founding Members (6)	Standing Members (2)	Standing Observers	Members (6)
Regulatory Authorities	EC (Europe) FDA(United States) MHLW/PMDA(Japan)	Health Canada(Canada) Swissmedic(Switzerland)	WHO IFPMA	ANVISA(Brazil) **MFDS(Korea)** NMPA(China) SFDA(Saudi Arabia)
Industry Association	EFPIA JPMA PhRMA			BIO IGBA
	Standing MC Members & Observers			**Elected MC Members**

**** Management Committee** is:*
The body that oversees operational aspects of the Association on behalf of all Members, including administrative and financial matters and oversight of the working groups.

ICH Guidelines Finalized

Tier 1 Guidelines
Q1, Q7, E6

Tier 2 Guidelines
E2A, E2B, E2D, M4 (CTD), M1 (MedDRA)

Safety

- S1A – S1C: Carcinogenicity studies (3)
- S2: Genotoxicity studies (1)
- S3A – S3B: Toxicokinetics and Pharmacokinetics (2)
- S4: Toxicity Testing (1)
- S5: Reproductive toxicology (1)
- S6: Biotechnology products (1)
- S7A – S7B: Pharmacology studies (2)
- S8: Immunotoxicology studies (1)
- S9: Nonclinical evaluation for anticancer pharmaceuticals (1)
- S10: Photosafety evaluation (1)
- S11: Nonclinical Pediatric Safety (1)
- S12: Nonclinical Biodistribution Considerations for Gene Therapy Products (1)

Quality

- Q1A – Q1E: Stability (5)
- Q2: Analytical validation (1)
- Q3A – Q3D: Impurities (4)
- Q4 – Q4B: Pharmacopoeias (1)
- Q5A – Q5E: Quality of biotechnology products (5)
- Q6A – Q6B: Specifications (2)
- Q7: Good Manufacturing Practice (1)
- Q8: Pharmaceutical development (1)
- Q9: Quality risk management (1)
- Q10: Pharmaceutical quality system (1)
- Q11: Development and manufacture of drug substances (1)
- Q12: Lifecycle management (1)
- Q13: Continuous Manufacturing of Drug Substances and Drug Products (1)
- Q14: Analytical Procedure Development (1)

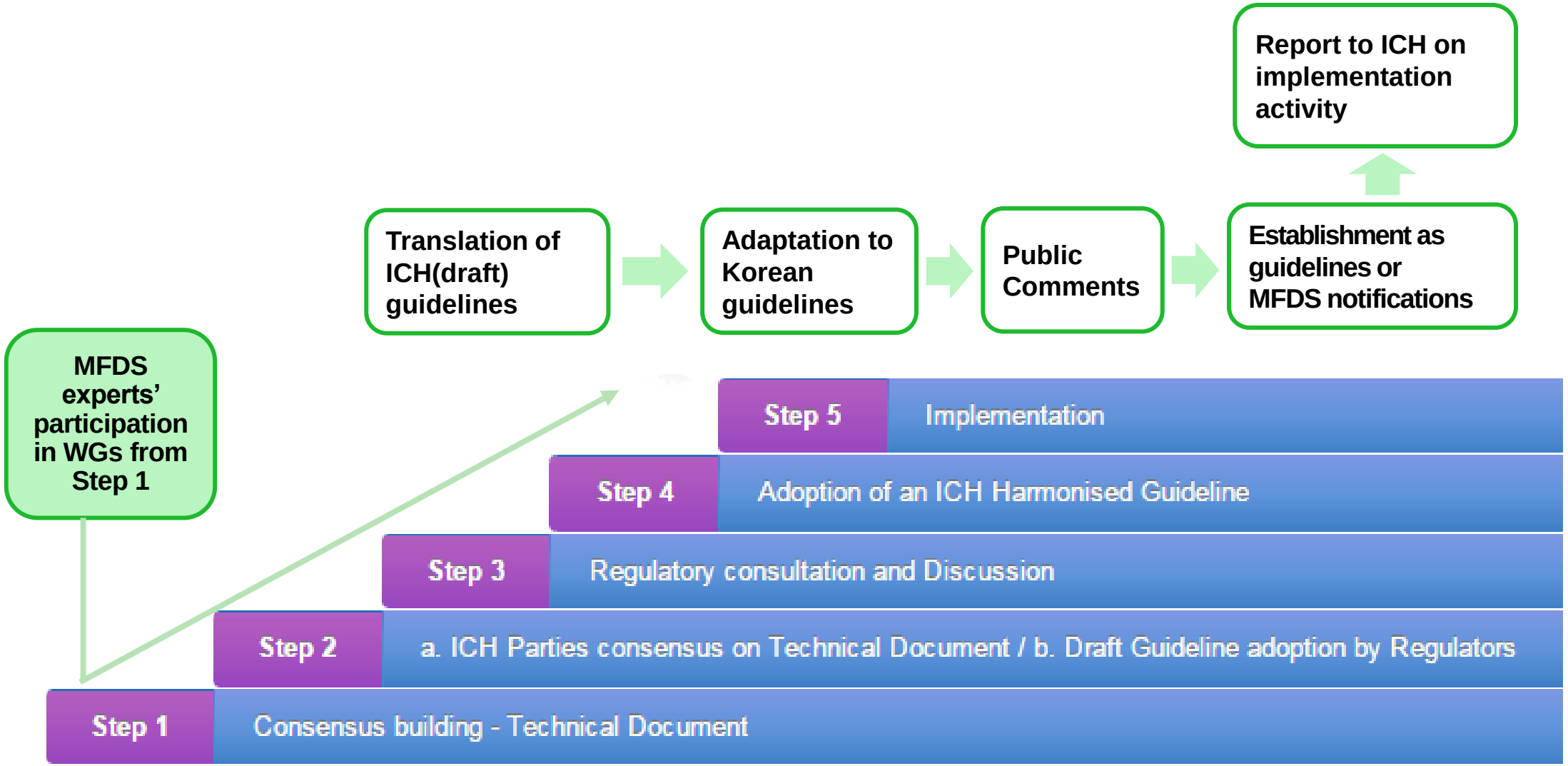
Efficacy

- E1: Clinical safety (1)
- E2A – E2F: Pharmacovigilance (6)
- E3: Clinical study reports (1)
- E4: Dose-response studies (1)
- E5: Ethnic factors (1)
- E6: Good Clinical Practice (1)
- E7, E8, E9, E10, E11-E11A: Clinical Trials (5)
- E11A: Pediatric Extrapolation (1)
- E14: Clinical evaluation (1)
- E15: Definitions in Pharmacogenomics (1)
- E16: Qualification of Genomic Biomarkers (1)
- E17: Multi-Regional Clinical Trials (1)
- E18: Genomic Sampling (1)
- E19: Safety Data Collection (1)

Multidisciplinary

- M1: MedDRA
- M3: Nonclinical safety studies (1)
- M4, M4Q, M4S, M4E: CTD (4)
- M7: Genotoxic impurities (1)
- M9: Biopharmaceutics Classification System-based Biowaivers (1)
- M10: Bioanalytical Method Validation and Study Sample Analysis (1)
- M12: Drug Interaction Studies (1)
- M13A: Bioequivalence for Immediate release Solid Oral Dosage Forms (1)

ICH and MFDS Guideline Process

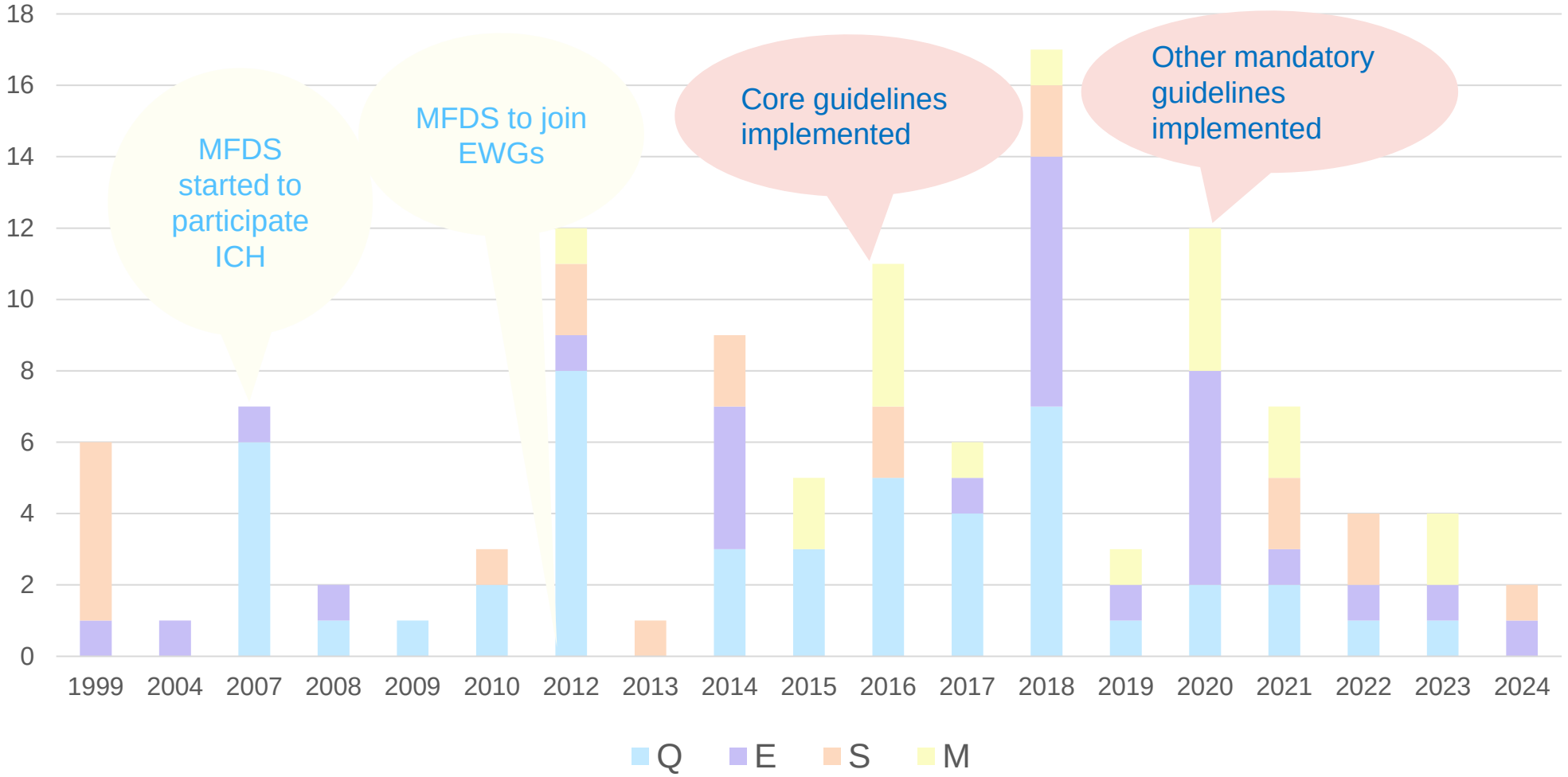


MFDS' Participation in Working Groups

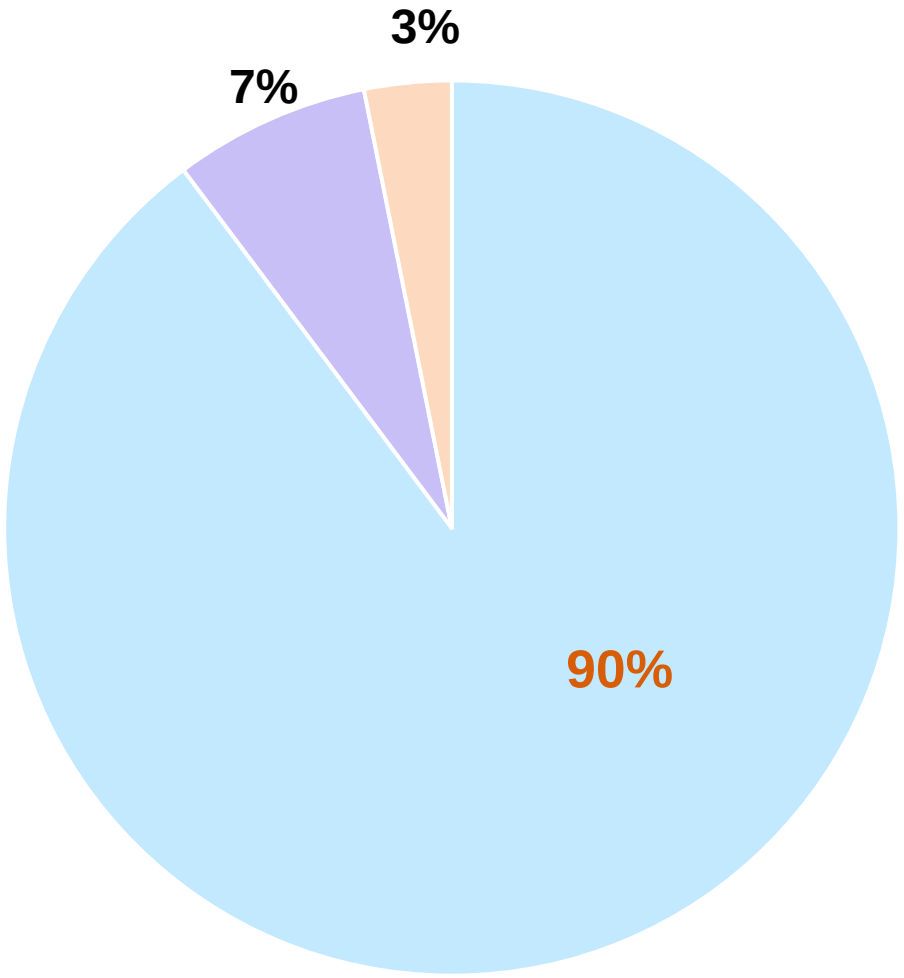
- Currently **33** Expert Working Groups & Implementation Working Groups are active in the ICH level.
- MFDS is participating **16** working groups

Quality	Efficacy	Safety	Multi-disciplinary
Q1/Q5 Q3E Q5A(R2) Q6(R1) Q12 Q13	E11A E21 E2B(R3)	S5(R4)	M1 M4Q(R2) M8 M13 M14 M7
6	3	1	6

MFDS's implementation of ICH Guidelines

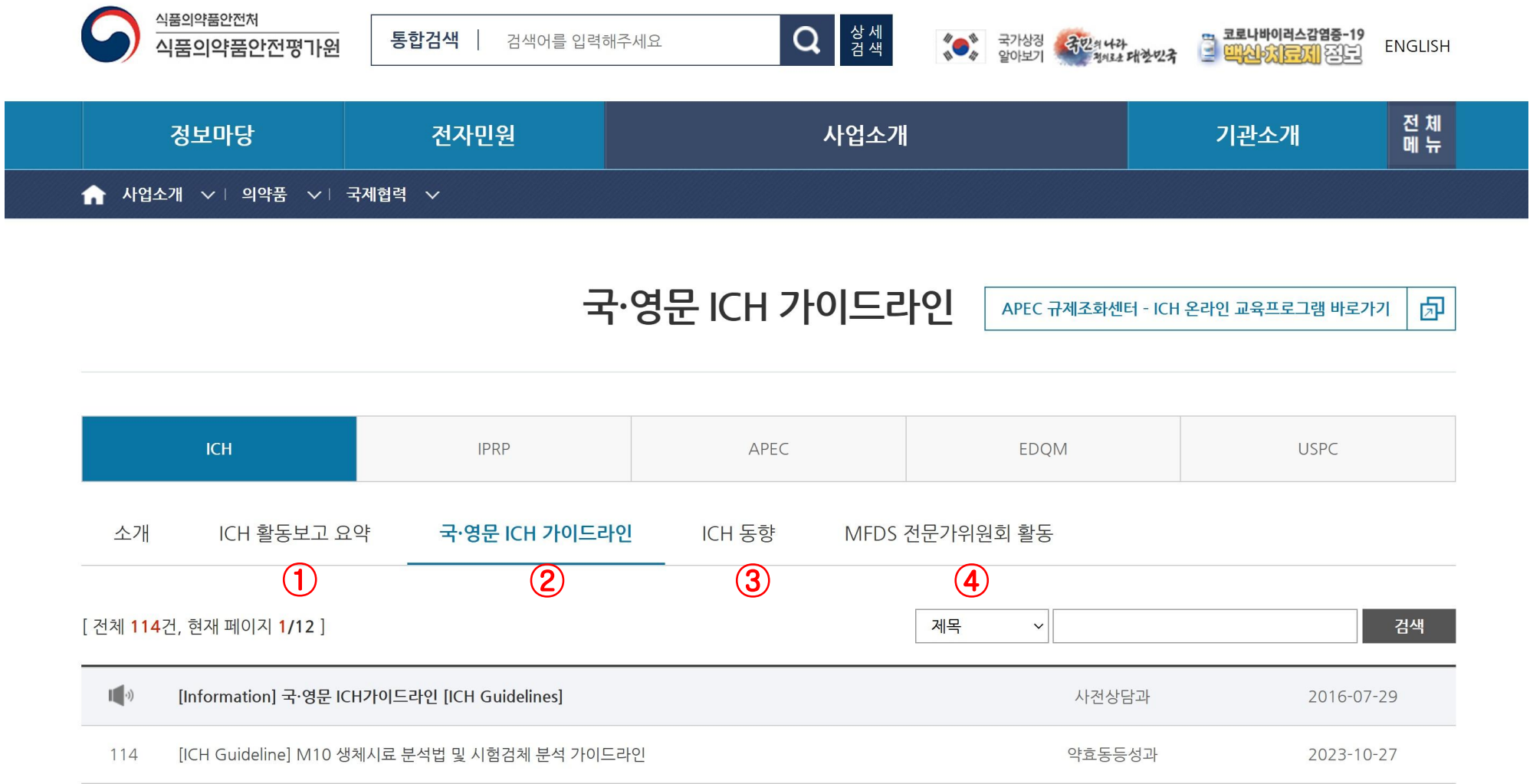


MFDS Implementation of the Guidelines(as of September 2024)



※ 4 out of 9 Guidelines in the process of implementation are planned to be implemented by the end of 2024.

Up-to-date information for Public and Industries



① ICH activities ② ICH Guideline(Korean/English) ③ ICH Updates ④ MFDS EWG Activities

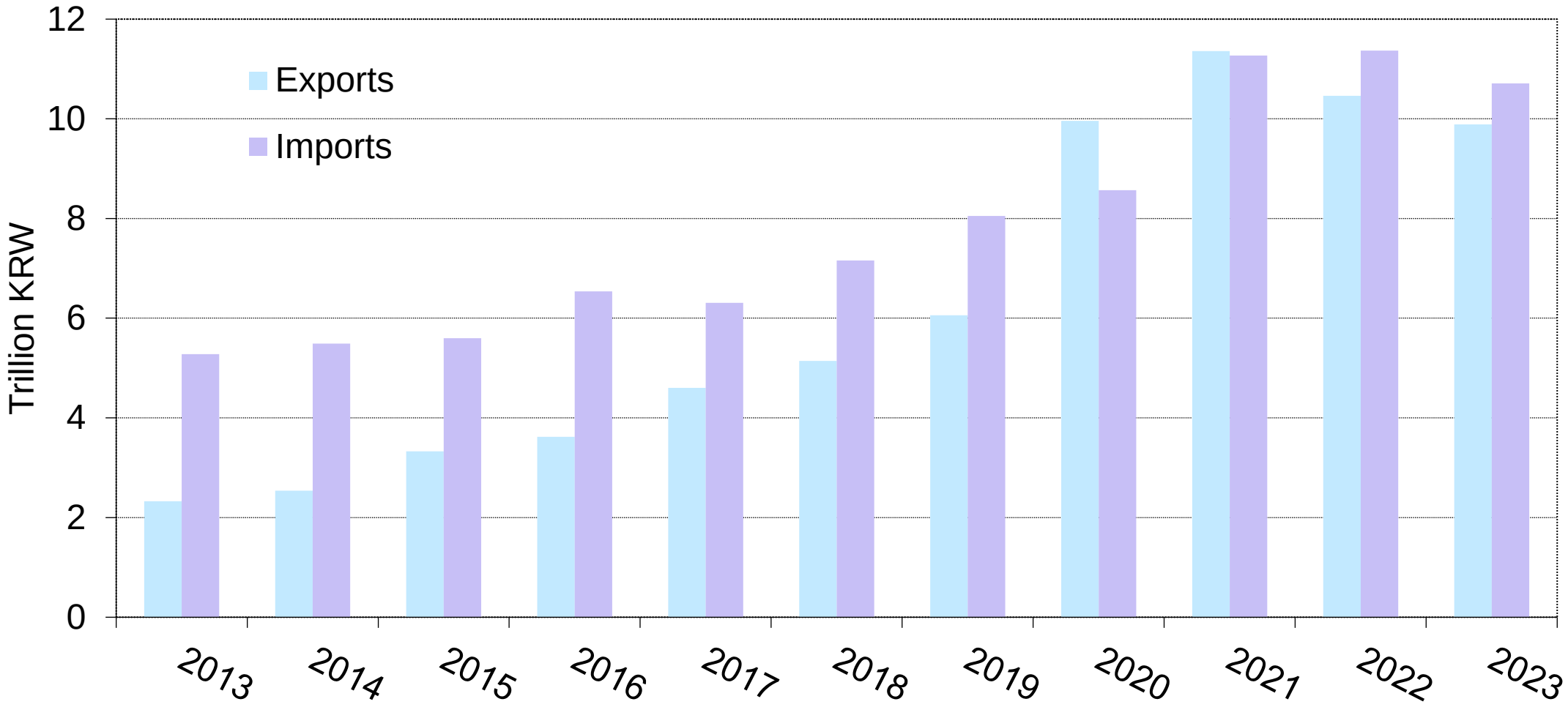
ICH Training Cluster

- Initiated from 2017
- Consisted of 4 clusters (Quality, Efficacy, Safety, Multi-disciplinary)
- Cluster members are regulators, industry experts and academic experts
- The purpose of the cluster is
  - To discuss the ICH guideline issues(establishment, revision, implementation) and
  - To develop the ICH training program agenda

ICH Training Program

- Started to run from 2018~
- 2~4 days program/Annual basis
- Training agenda
  - All ICH guidelines that were proposed by Korean stakeholders
- 2024 Program
  - 2024.9.30~10.1 (2 days)
  - 400 Participants, 23 Lectures, Program Satisfaction Rate 4.23/5

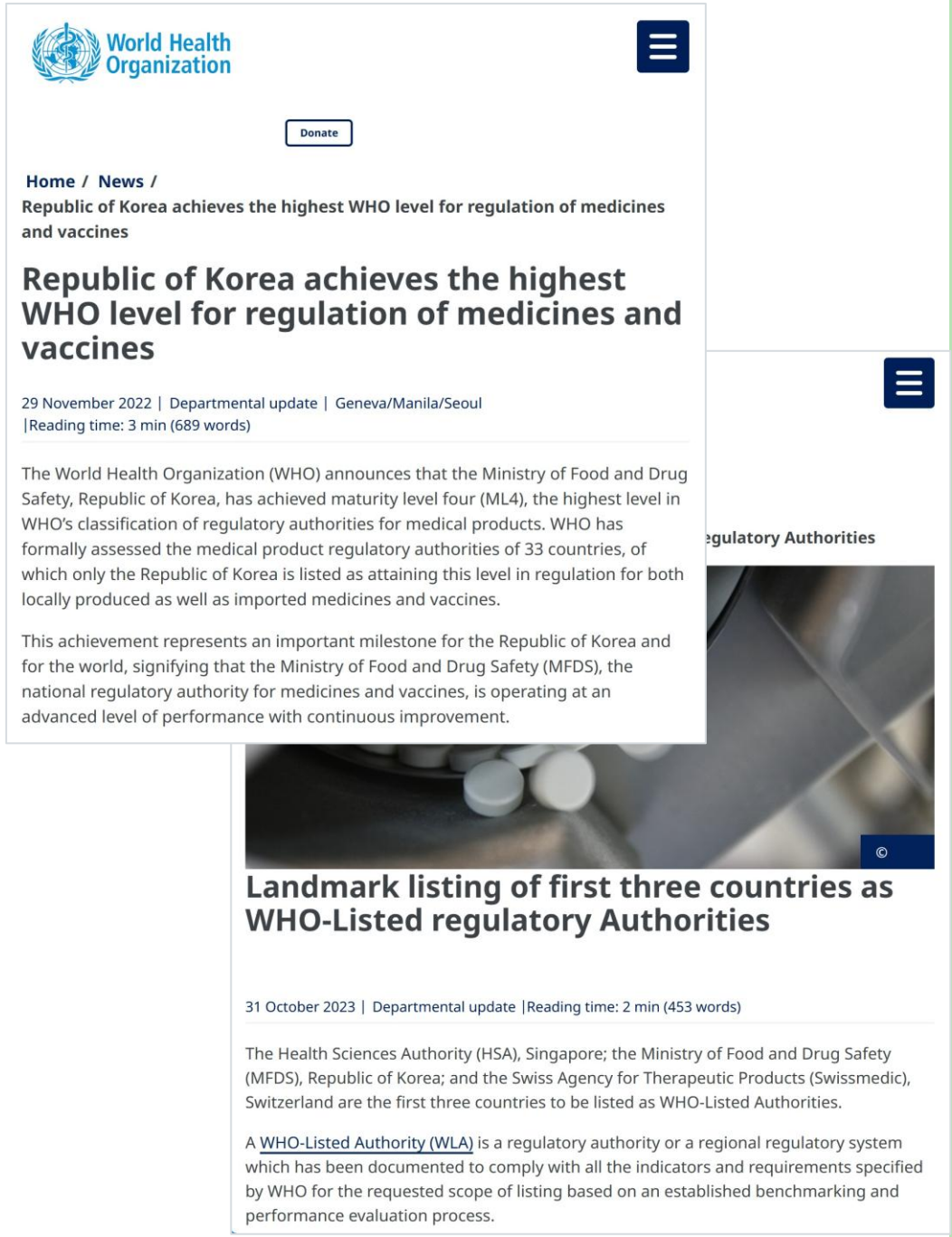
Korea’s Pharmaceutical Trade Trends (2013-2023)



Source : Ministry of Food and Drug Safety, Pharmaceutical Trade Statistics

Pains and Gains in Joining ICH

- **Pains**
  - Resource intensity
  - Learning curve
  - Resource constraints
  - Language accessibility
- **Gains**
  - Improved efficiency and consistency
  - Global collaboration in guideline developments
  - Enhanced regulatory maturity
  - Proactive adaptation to innovations
  - Predictability and certainty
  - Market access and trade facilitation
  - Strengthened public health



World Health Organization

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Republic of Korea achieves the highest WHO level for regulation of medicines and vaccines

Republic of Korea achieves the highest WHO level for regulation of medicines and vaccines

29 November 2022 | Departmental update | Geneva/Manila/Seoul
|Reading time: 3 min (689 words)

The World Health Organization (WHO) announces that the Ministry of Food and Drug Safety, Republic of Korea, has achieved maturity level four (ML4), the highest level in WHO's classification of regulatory authorities for medical products. WHO has formally assessed the medical product regulatory authorities of 33 countries, of which only the Republic of Korea is listed as attaining this level in regulation for both locally produced as well as imported medicines and vaccines.

This achievement represents an important milestone for the Republic of Korea and for the world, signifying that the Ministry of Food and Drug Safety (MFDS), the national regulatory authority for medicines and vaccines, is operating at an advanced level of performance with continuous improvement.

egulatory Authorities

Landmark listing of first three countries as WHO-Listed regulatory Authorities

31 October 2023 | Departmental update |Reading time: 2 min (453 words)

The Health Sciences Authority (HSA), Singapore; the Ministry of Food and Drug Safety (MFDS), Republic of Korea; and the Swiss Agency for Therapeutic Products (Swissmedic), Switzerland are the first three countries to be listed as WHO-Listed Authorities.

A WHO-Listed Authority (WLA) is a regulatory authority or a regional regulatory system which has been documented to comply with all the indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process.

Thank you for your attention!

Contact info sujinkong@korea.kr

QUESTIONS AND ANSWERS

We encourage you to use the Q&A box to raise questions to the speakers.

If a question you would like to ask has already been raised, you can also “like” that question.

KEY TAKEAWAYS AND INSIGHTS

•**Regulatory Alignment**: The adoption of ICH guidelines promotes harmonized regulatory standards, reducing inefficiencies, enhancing predictability, and ensuring that medicines meet consistent quality, safety, and efficacy requirements across markets.

•**Mutual Benefits for Regulators and Industry**: ICH membership strengthens regulatory systems by providing clear, harmonized frameworks, reducing duplication, and fostering global collaboration. For both regulators and industry, this translates into streamlined processes, better resource utilization, and faster patient access to medicines.

•**Collaborative Implementation Drives Success**: The effective implementation of ICH guidelines depends on robust engagement between regulators and industry, ensuring shared understanding of expectations and enabling the seamless adoption of new standards within national regulatory frameworks.

•**Capacity Building and Global Health Impact:** ICH plays a critical role in enhancing regulatory capacity through training, knowledge sharing, and the adoption of harmonized guidelines. This strengthens regulatory systems worldwide, ensuring better health outcomes by improving access to safe, effective, and high-quality medicines.

Thank you

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eCTD Harmonization in Asia: Unlocking the Benefits of Standardized Submissions

Session Moderator

Asst. Prof. Tan-Koi Wei Chuen
Lead of Regulatory Systems Strengthening at
Centre of Regulatory Excellence, Duke-NUS Medical School

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Advancements in Regulatory Agility, Regional Collaboration, and Digital Transformation: Insights from the Asia Partnership Conference of Pharmaceutical Associations (APAC)

Focusing on paperless e-submission and best practices in eCTD implementation

Dr. Sannie SF Chong

Senior Director, APAC Regional Lead

Merck Sharp & Dohme (MSD), on behalf of IFPMA

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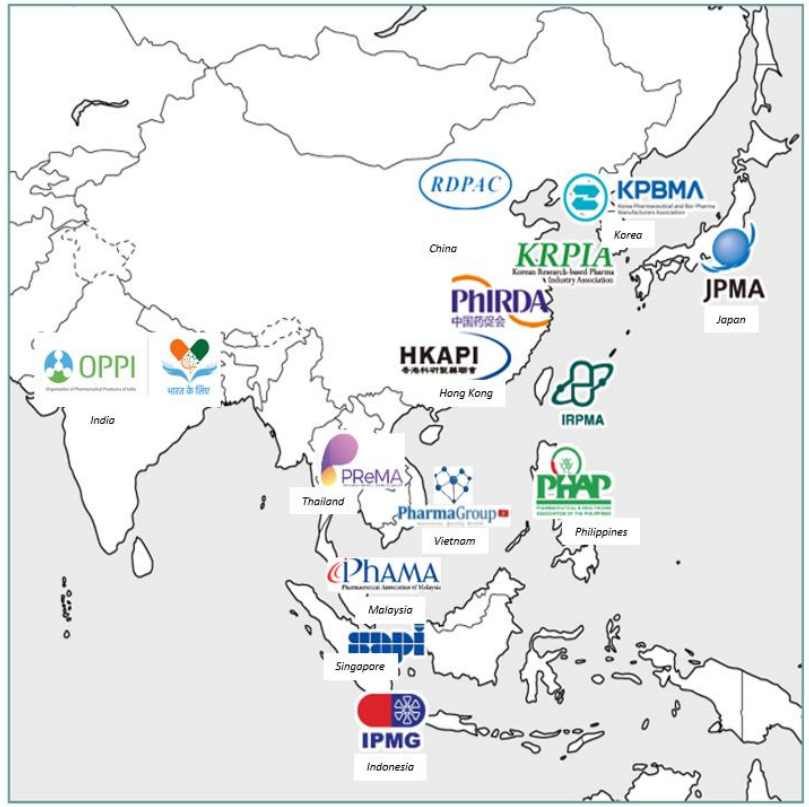
2nd APAC Paper accepted for publication by American Association of Pharmaceutical Scientists (AAPS) Open

Advancements in Regulatory Agility, Regional Collaboration, and Digital Transformation: Insights from the Asia Partnership Conference of Pharmaceutical Associations (APAC)

Sannie Siaw Foong Chong[1*] · Stephanie Hui Min Ong[2] · Siew Mei Long[3] · Masaaki Kanno[4]. Usanee Harnpramukkul[5] · Kum Cheun Wong[6]· Asawari Sathaye[7] Mamta Singh[8]. Manish Paliwal[9]· Huyen Do[10]· Helene Sou[11]· Richard Simon R. Binos[12]

The Asia Partnership Conference of Pharmaceutical Associations (APAC) examines recent developments in regulatory practices across Asia, focusing on regulatory agility, regional collaboration, and digital transformation.

The paper identifies key improvements made by national regulatory authorities (NRAs) in adopting regulatory agilities over a two-year span. It also suggests optimizing regional reliance pathways and recommends best practices for implementing e-submission, real-world evidence (RWE), decentralized clinical trials (DCTs), and paperless e-labelling.



14 APAC member associations from across Asia

Insights from APAC: #1
58% of NRAs implement entirely paperless e-submission

All twelve economies permits e-submissions.

In China, India, Indonesia, Japan, the Philippines, Singapore, and Vietnam, e-submissions are entirely paperless.

In contrast, the remaining economies still require some form of physical documentation to be submitted.

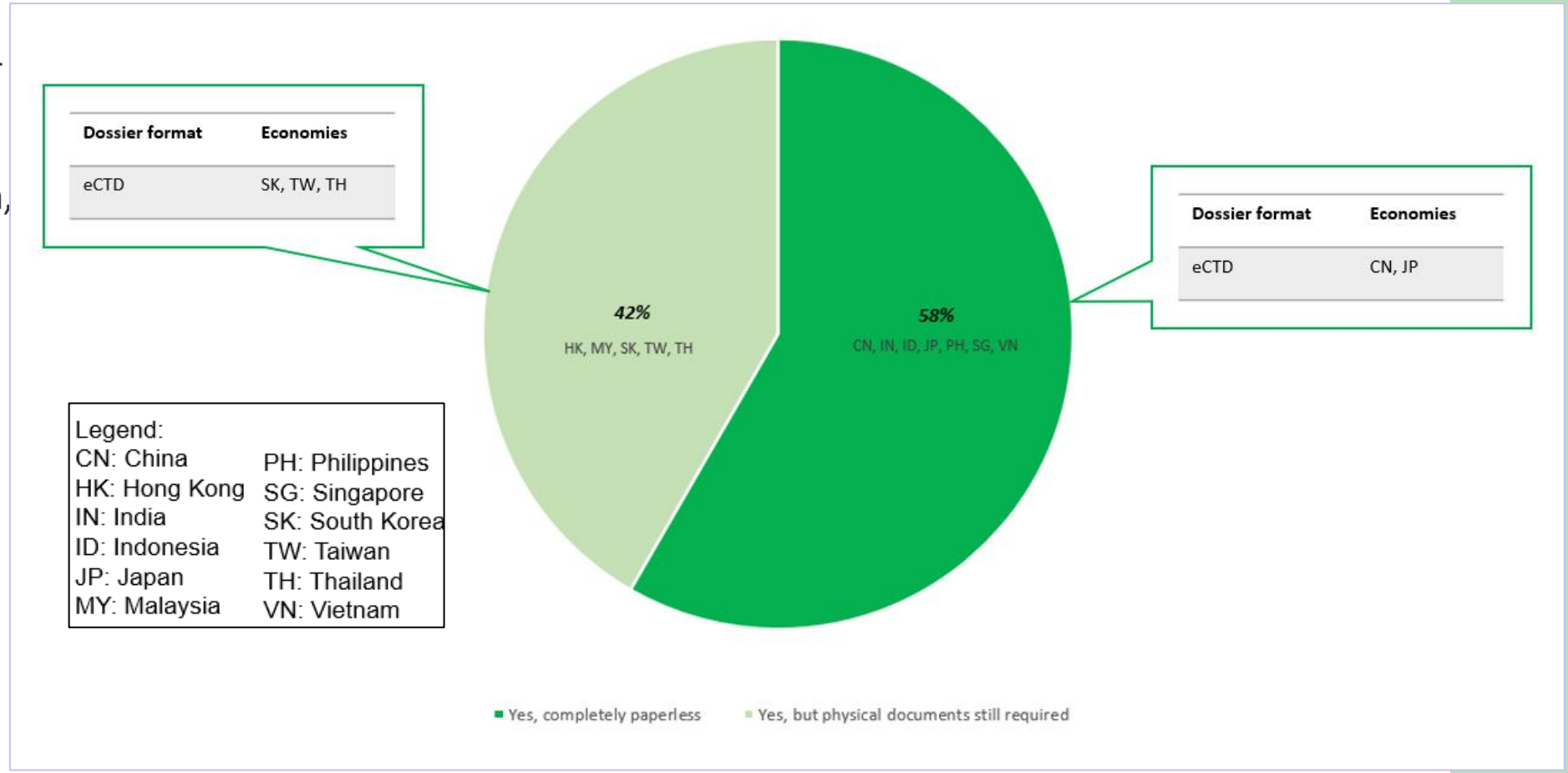


Figure 5: 58% of NRAs implement entirely paperless e-submission.

Insights from APAC: #2
42% of NRAs accept ICH eCTD

The ICH eCTD format is implemented in China, Japan, South Korea, Taiwan, and Thailand, which constitutes **42%** of NRAs.

Hong Kong accepts the ICH CTD format as is, while India mandates country-specific customization of the dossier.

The dual system for pharmaceutical registrations, which accepts both ICH and ACTD formats, is implemented in Malaysia, the Philippines, Singapore, Vietnam, and Indonesia.

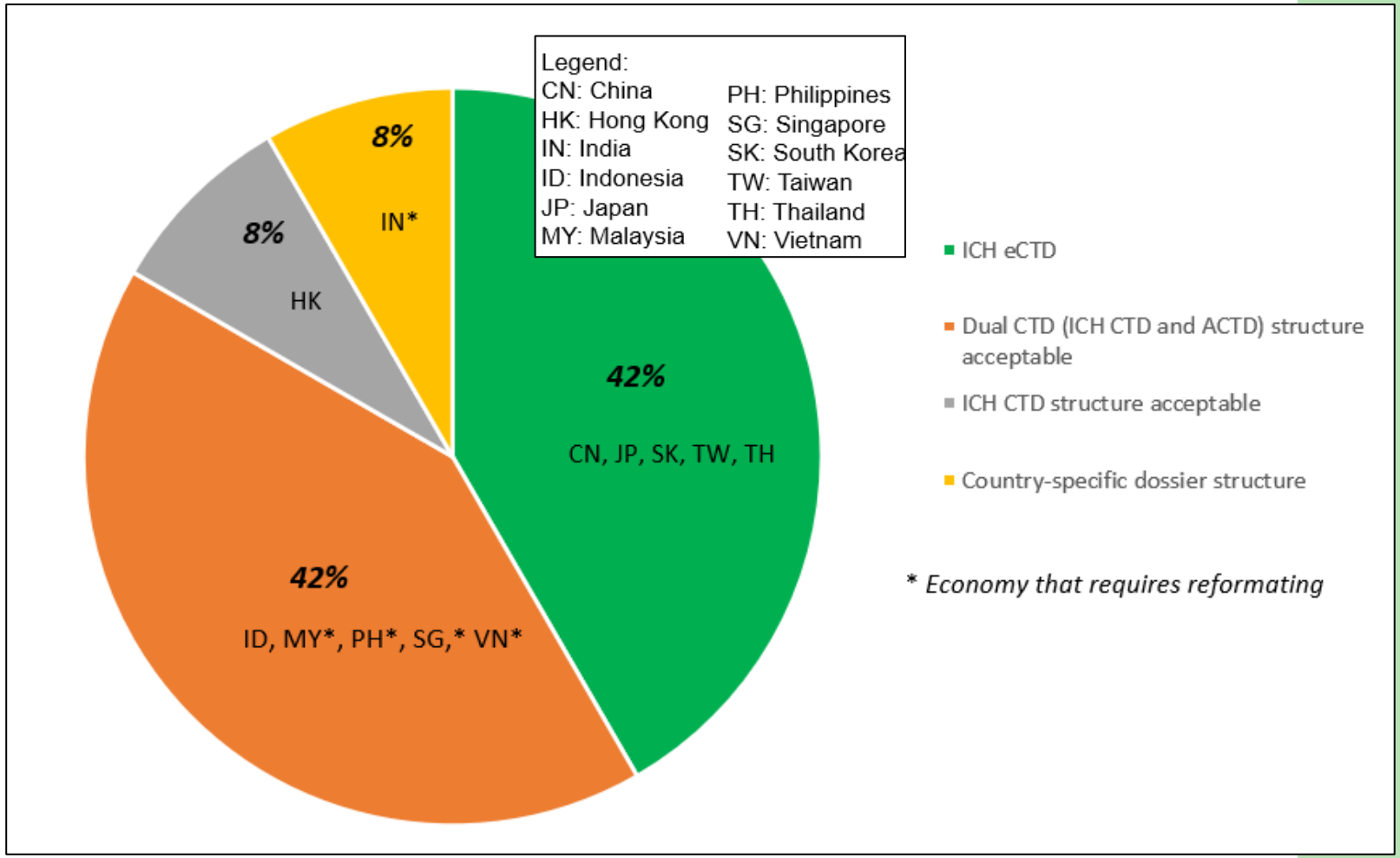


Figure 6: 42% of NRAs accept ICH eCTD.

Insights from APAC: #3
Not mandating baseline requirement for existing products

More than 50% of NRAS do not mandate a baseline requirement for existing products to support the transition to e-submission.

China, Japan, Malaysia, Philippines, Singapore, South Korea, and Taiwan did not mandate baseline requirement when e-submissions were applied retrospectively into existing products

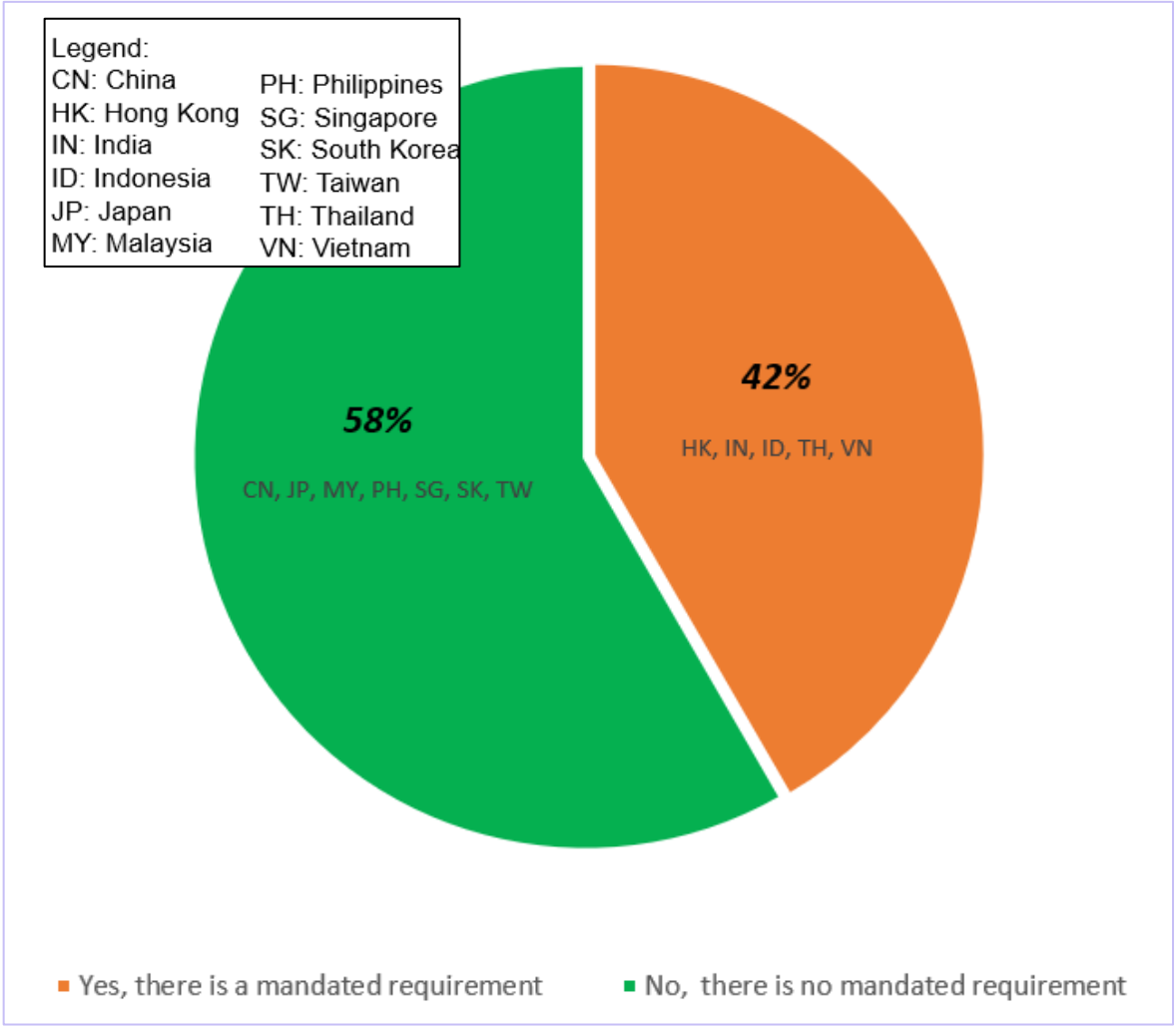
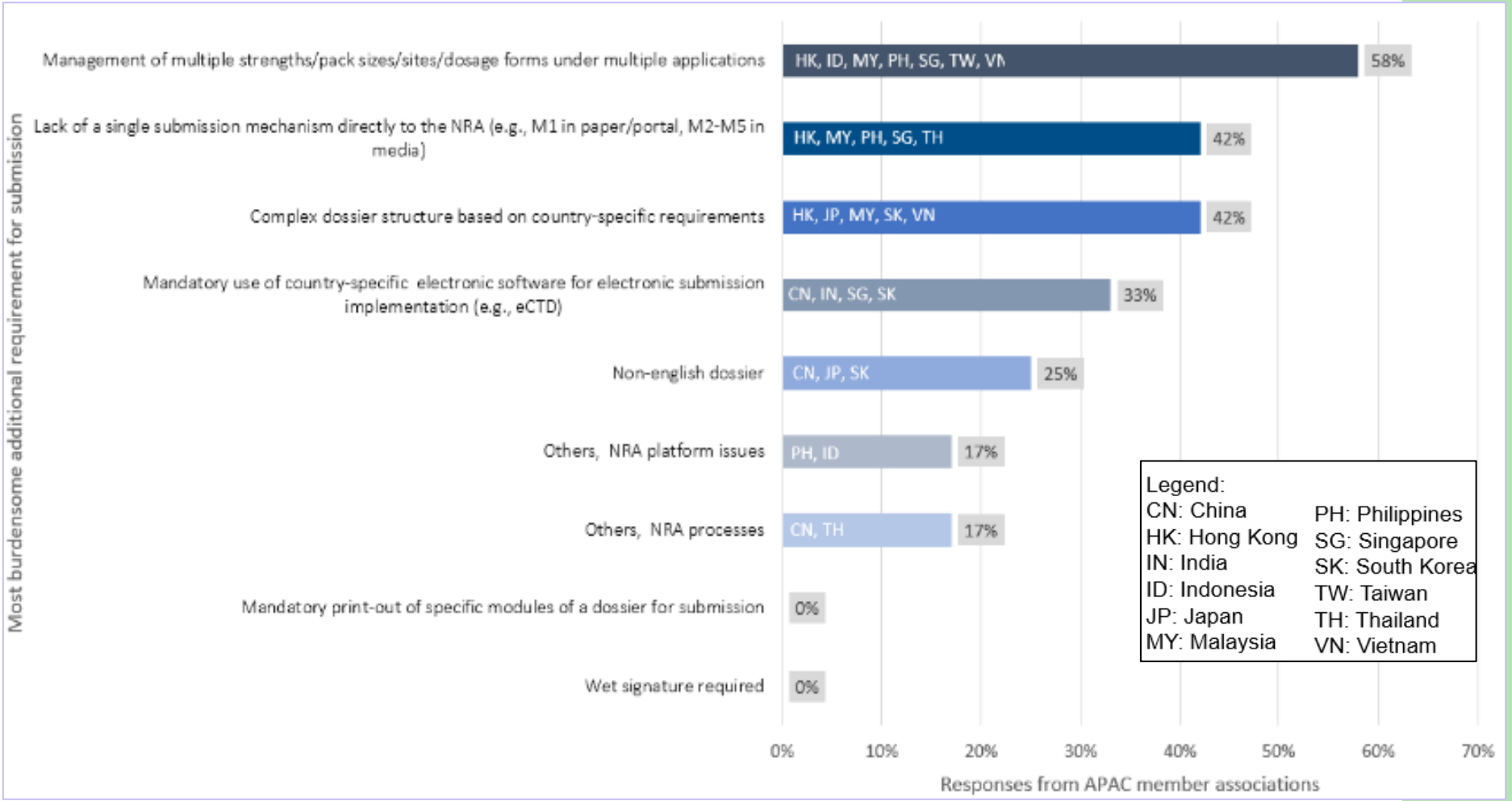


Figure 7: More than 50% of NRAS do not mandate a baseline requirement for existing products to support the transition to e-submission.

Insights from APAC: #4
The most burdensome additional requirements that impact the full benefits of e-submission

The most burdensome additional requirements that limit the benefits of e-submission include, but are not limited to:

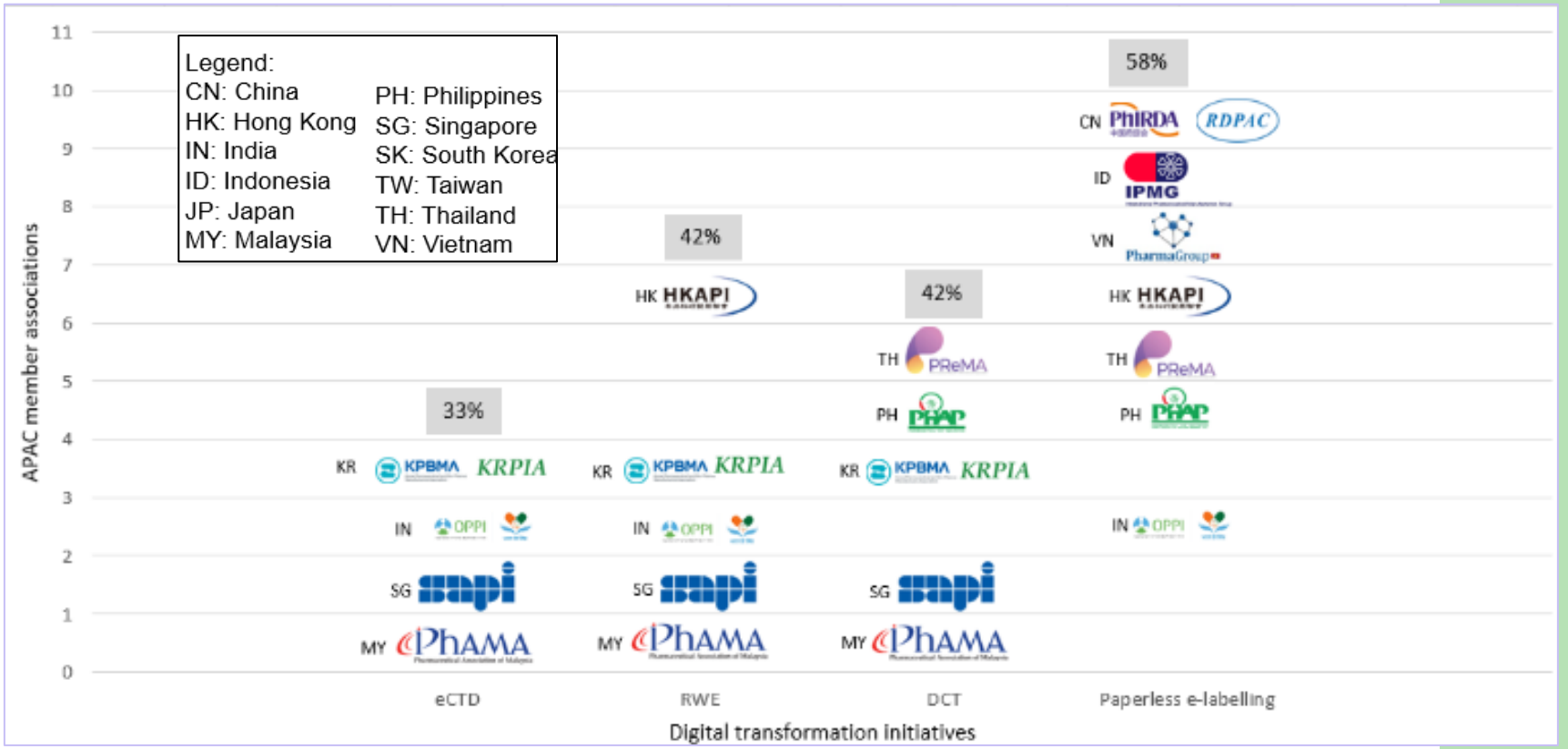
- managing multiple strengths, pack sizes, sites, and dosage forms under multiple applications
- the lack of a unified submission mechanism directly to the NRA from both a management and system perspective
- a complex dossier structure based on country-specific requirements
- mandatory use of country-specific electronic software, and
- additional tools such as non-English dossiers



Priorities (digital) of APAC member associations for engaging with local regulators to develop guidelines or approaches over the next 1 to 3 years

APAC member associations in Japan and Taiwan have reported that guidelines for e-submission, RWE, DCTs, and paperless e-labelling are already in place locally. For the remaining ten economies, paperless e-labelling is the top priority, with 58% of APAC industry members planning to engage local NRAs on this issue in the next 1 to 3 years

APAC member associations from India, Malaysia, South Korea, and Singapore have also prioritized the implementation of ICH eCTD in their engagements with NRAs over the next 1 to 3 years.



Recommendations

On e-Submissions: 42% of NRAs continue to require paper documents as part of the process. Another observation is the use of varying dossier formats. Submission in country specific format requires reformatting dossiers originally prepared in ICH CTD, **which increases workload and resource demands.** To streamline processes and align with international best practices while preventing the proliferation of divergent formats, **APAC advocates for a fully paperless system and a single globally harmonized structure based on the ICH CTD.** It is recommended that countries convert to ICH CTD **sooner rather than later**, before the process becomes more complex with additional applications and technical requirements, particularly with the upcoming implementation of eCTD v4.0 in 2026, which may intensify the need for non-eCTD countries to align with major ICH market standards.

On eCTD: Several submission requirements significantly impact the effectiveness of e-submissions, making them cumbersome. **It is highly recommended that NRAs take steps to address, as well as harmonise eCTD requirements and process with major ICH regulators to fully realize the benefits of eCTD.** Among these, the most burdensome requirement is submitting separate applications for each strength, site, dosage form, and pack size. **eCTD is designed to consolidate these into a single application, leading to significant efficiencies** as seen in regions like the EU, Gulf Cooperation Council, and Australia. **This consolidation reduces administrative burden and review time by presenting common documents only once, which simplifies the process for all users.** Including region and ICH metadata—such as drug substance, manufacturer, and dosage form—within the same eCTD application also clarifies the submission's scope. NRAs planning to implement eCTD should adopt this approach to maximize benefits as intended.

More than 50% of NRAs do not require a baseline for existing products when transitioning from paper to electronic dossiers. Baseline should not be expected when transiting from paperless e-submission to eCTD. Baselines involve submitting current registered documents, previously provided in paper format, via eCTD. **APAC supports not mandating baselines**, particularly for older products with minimal activity. If baselines are required, flexibility should be allowed (partial baselines, formatting of legacy documents (e.g., scanned documents)), to enhance the regulatory submission process, reviews, and dossier maintenance.

Conclusions

The shift towards digital transformation is evident, with 50% adoption of paperless e-labeling and 100% adoption of e-submissions, though not all processes are paperless with the use of ICH CTD dossier format.

We recommend:

✓An entirely paperless e-submission/eCTD system

✓A single CTD dossier structure based on ICH

✓A pragmatic phased approach in retrospective update of existing products without mandatory requirement of baseline.

APAC supports and values partnerships with NRAs in implementing eCTD, to enable full benefits of digital efficiency and standardization that facilitates work-sharing/reliance across multiple regulators, thereby expediting the launch of innovative medicines for people in Asia.

Thank you

Acknowledgements

The authors acknowledge the submission of the India and Vietnam case studies to the India DCGI and the Vietnam DAV, respectively. Special thanks are extended to Anil Matai and Thuy Nguyen for their writing support.

We extend our gratitude to Junko Tsukada, Shinji Hatakeyama, Mari Okada, and Erina Yamada of APAC for assisting in the preparation of the APAC paper, and to all 14 APAC member associations for their survey responses and funding towards the publication of the paper.

The authors also recognize the invaluable input from Tim Powell*, Anna Sokolowicz*, Andrew Deavin*, Lada Leyens, Eileen Soo, Jing Yi Teoh, and Stephanie Chen for sharing their expert opinions.

*EFPIA eCTD SME/colleague

Advancements in Regulatory Agility, Regional Collaboration, and Digital Transformation: Insights from the Asia Partnership Conference of Pharmaceutical Associations (APAC)

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QUESTIONS AND ANSWERS

We encourage you to use the Q&A box to raise questions to the speakers.

If a question you would like to ask has already been raised, you can also “like” that question.

KEY TAKEAWAYS AND INSIGHT

Towards one ICH eCTD submission to benefit patients' access & global collaboration

- **Paperless Submissions and Sustainability**

Moving toward fully electronic, paperless systems is a shared vision that offers significant efficiency and sustainability benefits.

- **Harmonizing Dossier Formats**

Aligning with ICH CTD standards can streamline submissions, reduce reformatting efforts, and support smoother transitions to eCTD while addressing regional needs and capacities.

- **Simplifying and Consolidating Submissions**

Consolidating applications—such as multiple strengths, pack sizes, or dosage forms—within eCTD to fully benefit from eCTD's efficiency and effectiveness that it intended for all stakeholders.

- **Collaboration With Pragmatic Approach is Key**

Early conversation and pragmatic approach during the transition to eCTD—such as not mandating baseline submissions—can ease challenges for all stakeholders. **Collaboration** - Enable full benefits of eCTD digital efficiency and standardization that facilitates work-sharing/reliance across multiple regulators, thereby expediting the launch of innovative medicines for people in Asia.

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03-06 December 2024

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Asia's role in driving a more efficient, innovative and patient-centric regulatory environment

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Virtual coffee/tea break

Advancing Clinical Trials: The Impact of E6(R3) Guideline

Session Moderator

Sally (Ping) Zhang
Executive Director, Head of R&D Quality Assurance APAC at AstraZeneca

IFPMA Experts on ICH E6(R3)

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Overview of ICH E6(R3) Guideline Revisions

Eriko Yamazaki

Pharmaceuticals and Medical Devices Agency (PMDA)

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Disclaimer

The speaker is affiliated with Pharmaceuticals and Medical Devices Agency.

The views expressed in this presentation are those of the author and do not necessarily reflect the official views of Pharmaceuticals and Medical Devices Agency.

ICH-E6: An Important Global Standard for Clinical Trial Conduct

https://www.ich.org/news/ich-reflection-gcp-renovation-modernization-ich-e8-and-subsequent-renovation-ich-e6

E8 clinical trial design principles

↕

E6 GCP clinical trial conduct principles

- **E6: Good Clinical Practice (GCP) – finalised in 1996**
  - Described the responsibilities and expectations of stakeholders in the conduct of clinical trials;
  - Covered aspects of monitoring, reporting, and archiving of clinical trials; and
  - Included sections for essential documents and investigator brochures
- **E6 (R2) – finalised in 2016**
  - Included integrated addendum to encourage implementation of improved and more efficient approaches to GCP, while continuing to ensure human subject protections; and
  - Updated standards for electronic records.

Background to E6(R3) Renovation

Updated open Letter to EMA & ICH: From ~~2~~ 5 research organisations and

an international consortium of ~~84~~ 119 health researchers in ~~19~~ 22 countries

Signatories listed at end:

Original signatories of 31st January letter shown in black with

new signatories of this letter shown in red

Contemporary Clinical Trials Communications 29 (2022) 100983

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Stakeholders' views on the most and least helpful aspects of the ICH E6 GCP guideline and their aspirations for the revision of ICH E6(R2)

Carrie Dombeck[a,b], Teresa Swezey[a,b], Annemarie Forrest[a], Pamela Tenaerts[a], Amy Corneli[a,b,c,*]

[a] Clinical Trials Transformation Initiative, Duke University, Durham, NC, USA
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[c] Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9468347/pdf/main.pdf

GCP Renovation

Interim analysis, external control, observational study, pragmatic elements…

The goal is to provide updated guidance that is both appropriate and flexible enough to address the increasing diversity of clinical trial designs and data sources

CRF, electronic health records, hospital discharge summaries, claims data, patient/disease registries…

<ICH Reflection on ‘’GCP Renovation’’>

- Modernization of ICH E8 (General Considerations for Clinical Trials) and subsequent renovation of ICH E6
- Seek outside stakeholder comment on the revision

https://www.ich.org/news/ich-reflection-gcp-renovation-modernization-ich-e8-and-subsequent-renovation-ich-e6

Revision of E8 Guideline

- Provide guidance on the clinical development lifecycle
  - Considering the broad range of clinical study designs and data sources used
  - Designing quality into clinical studies
- Consider ‘quality of a clinical study’ as ‘fitness for purpose’
- Introduce ‘quality by design’ in clinical study
  - Quality by design: prospective attention to the design of all components of the study protocol, procedures, associated operational plans and training
  - Focusing on critical to quality factors
  - Management of risks for critical to quality factors using a risk-proportionate approach

Purpose of E6 Revision

- Modernization of ICH E8 and subsequent renovation of ICH E6(R2) to address the increasing diversity of clinical trial designs and data sources

ICH Reflection on “GCP Renovation” (endorsed 2017, revised 2021)

1: Revision to ICH E8

- Address broader concerns about the principles of study design and planning for an appropriate level of data quality
- Provides comprehensive cross-referencing to the family of ICH guidance documents

2: Renovation of ICH E6 GCP

- Address flexibility concerns with respect to a broader range of study types and data sources
- Retains the current focus on good clinical investigative site practices

https://www.ich.org/news/ich-reflection-gcp-renovation-modernization-ich-e8-and-subsequent-renovation-ich-e6

Structure of ICH E6(R3) Guideline -from the Original Concept Paper-

- Overarching Principles and Objectives
- Annex 1 - Interventional clinical trials

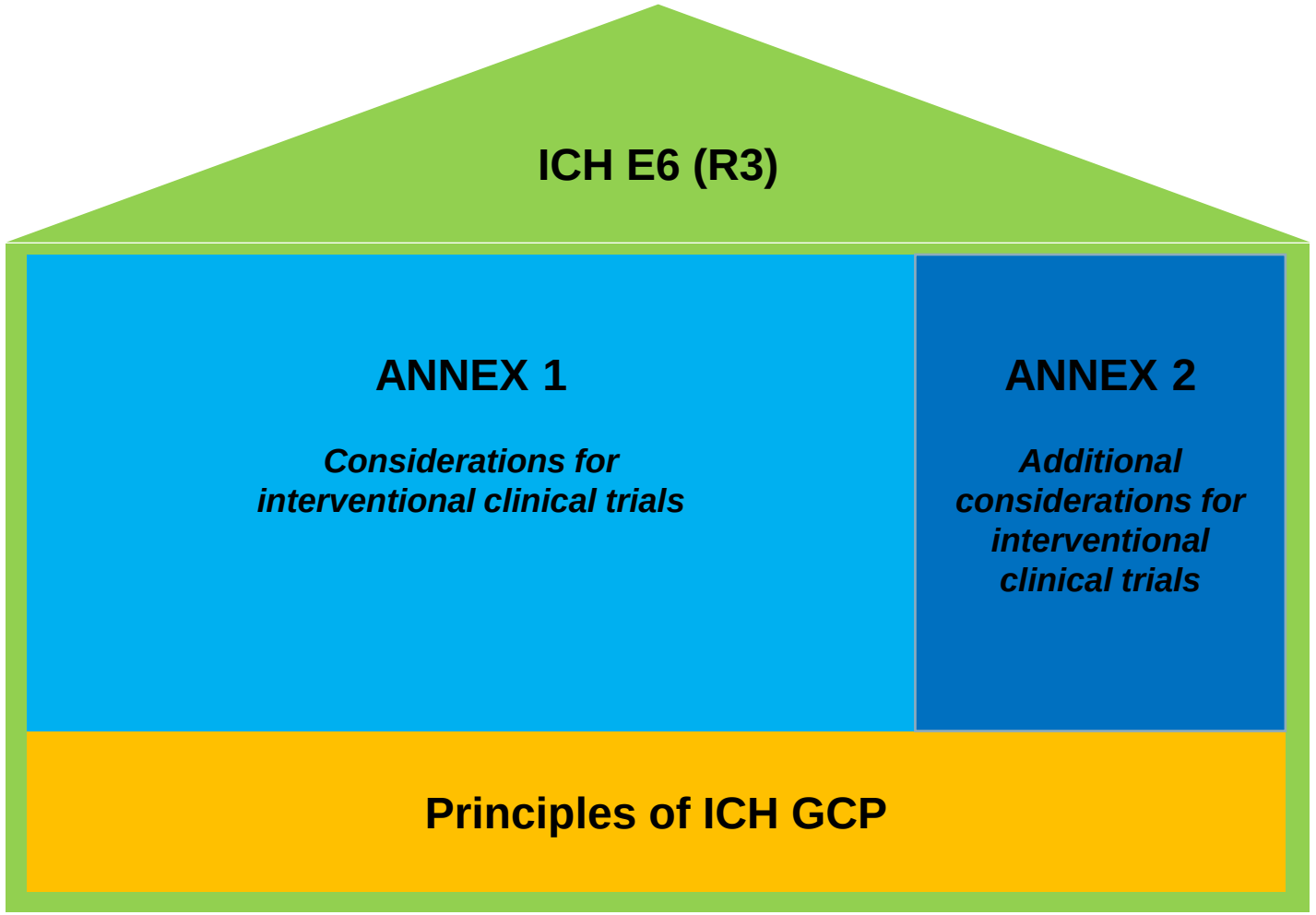
This will include the use of unapproved or approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data. This Annex will be developed simultaneously with the principles and objectives document to ensure consistency and to provide stakeholders with a complete package that can replace E6(R2); and

- Annex 2 - Additional considerations for non-traditional interventional clinical trials

This will include designs such as pragmatic clinical trials and decentralized clinical trials, as well as those trials that incorporate real world data sources. Before the drafting of Annex 2, its scope will be further clarified, to define the nature of trials involved, in an update to this concept paper.

https://database.ich.org/sites/default/files/E6-R3_FinalConceptPaper_2019_1117.pdf

OVERVIEW OF ICH E6 (R3)



E6 (R3) Development Process

- **Engagement** with academic stakeholders in a series of joint meetings with the Expert Working Group.

  Summary of Stakeholder Engagement to Support the Development of ICH E6(R3), 21 April 2020
  https://database.ich.org/sites/default/files/E6-R3_PublicEngagemenSummary_2020_0421.pdf

- New approaches to **enhance transparency** (published draft principles in April 2021 and held public web conferences (2 days) in May 2021).

- Extensive training materials are planned to be developed (with use-cases) that clarify or provide supplementary explanation to the application of GCP guidelines.

Current Status of ICH E6(R3)

- Principles & Annex 1
  - May 2023 Step1 sign off, reached Step2a/2b
  - May-Nov 2023 ICH public consultation
  - Close to finalising the document

- Annex 2
  - Nov 2024 Step1 sign off, reached Step2a/2b
  - until Mar 2025 ICH public consultation

- Training Materials
  - Nov 2024- Under development

What is new about E6(R3) structure and content?

- **New structure** to provide clarity and better readability.
  - Principles to remain relevant as technology, methods and trial design evolve.
  - Annexes and appendices
- **Provide additional clarity on the scope.**
- **Language to facilitate innovations in clinical trial design, technology and operational approaches.**
  - Facilitate innovative clinical trial designs, for example, clinical trials utilising decentralised elements and pragmatic elements, reflecting trials that closely resemble routine clinical practice.
  - Facilitate the use of Digital Health Technologies (DHTs), healthcare infrastructure, and other tools to facilitate enrollment and retention, capture data, monitor, and to analyse results.
- **Set a foundation for practical/feasible expectations around the responsibilities of sponsor and investigator in a digital ecosystem.**

What is new about E6(R3) structure and content? (2)

- Encourage **fit-for-purpose** approaches.
  - Proportionality and risk-based approaches with a focus on the clinical trial's critical-to-quality factors whose integrity is fundamental to safety of participants and the reliability of trial results;
  - Thoughtfulness in the design and conduct
- **Incorporate learning** from innovative clinical trial designs and lessons from public health emergencies/pandemics.
- Encourage transparency by clinical trial registration and result reporting.
- Provide additional language to enhance the informed consent process.

Revised Structure

E6 (R3) Draft Guideline

E6 (R3) draft guideline subject to public consultation consists of parts I, II, III (composed of 4 sections), glossary, and appendices.

- **I. INTRODUCTION**
- **II. PRINCIPLES OF ICH GCP**
- **III. ANNEX 1**
  1. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
  2. Investigator
  3. Sponsor
  4. Data Governance – Investigator and Sponsor [New]
- **GLOSSARY**
- **APPENDICES**
  - Appendix A. Investigator's Brochure
  - Appendix B. Clinical Trial Protocol and Protocol Amendment(s)
  - Appendix C. Essential Records for the Conduct of a Clinical Trial

ICH E6 (R3) Principles

ICH E6 (R3) PRINCIPLE	TOPIC	ICH E6 (R2) REF
1	**Ethical Principles**	2.1, 2.2, 2.3, 2.7, 2.11
2	**Informed Consent**	2.9
3	**IRB/IEC Review**	2.6
4	**Science**	2.4, 2.5
5	**Qualified Individuals**	2.8
6	**Quality**	2.13
7	**Risk Proportionality**	N/A
8	**Protocol**	2.5
9	**Reliable Results**	2.10
10	**Roles and Responsibilities**	N/A
11	**Investigational Product**	2.12

OVERVIEW OF CHANGES

Substantial changes

- **Principles of GCP**
- **Annex 1**
  - Investigator
  - Sponsor
  - Data Governance – Investigator and Sponsor **[NEW]**
- **Glossary**
- **Appendices**
  - Essential Records for the Conduct of a Clinical Trial

Other changes

- **Annex 1**
  - Institutional Review Board (IRB)/ Independent Ethics Committee (IEC)
- **Appendices**
  - Investigator's Brochure
  - Clinical Trial Protocol and Protocol Amendments

ICH E6 (R3) Annex 2 - Background

- Addresses the GCP considerations that arise from the increased use of a wider range of design elements and data sources. It has its foundations in the key concepts of quality-by-design, fitness for purpose and risk proportionality
- The scope remains to be interventional clinical trial
- Should be read in conjunction with the ICH E6(R3) Principles and Annex 1 document
- Annex 2 provides considerations that focus on examples of trials that incorporate: **1) decentralised elements, 2) pragmatic elements, 3) real world data (RWD) sources**

ICH E6 (R3) Annex 2 - Structure

Introduction

1. Institutional Review Board/ Independent Ethics Committee (IRB/IEC)

2. Investigator

- Communication with IRB/IEC
- Informed Consent Considerations
- Investigational Product Management
- Investigator Oversight
- Safety Assessment and Reporting

3. Sponsor

- Engagement and Communication
- Protocol and Trial Design
- Communication with IRB / IEC
- Consent or Permission Considerations for RWD
- Data Considerations
- Investigational Product Management
- Privacy and Confidentiality Considerations
- Sponsor Oversight
- Safety Assessment and Reporting

Emphasis on practical considerations for the use of various design elements and data sources

Training Materials

- Provide clarity and supplementary information on application of E6(R3)
- Work closely with ICH Training Associate, the Multi-Regional Clinical Trials (MRCT) Center of Brigham and Women’s Hospital and Harvard
- Use case-based
- Develop in parallel with the discussion of Annex2 (discussion already started)

What is introduced by ICH E6 (R3)

Fundamentals remain unchanged:

- The basic principle of GCP is to ensure the safety of trial participants and reliability of trial results

Updates:

- Encourage fit-for-purpose approaches and take appropriate measures depending on the risks
- Instead of taking an uniformed approach, thorough consideration on what is important and where resources should be allocated

Future Plan

- Principles & Annex 1
  - Dec 2024 Step 3 sign-off, reach Step 4
- Annex 2
  - Mar 2025 End of ICH public consultation
  - Mid-2025 Step 3 sign-off, reach Step 4
- Training Materials
  - May 2025 Madrid meeting

Thank you

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PANEL DISCUSSION

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QUESTIONS AND ANSWERS

We encourage you to use the Q&A box to raise questions to the speakers.

If a question you would like to ask has already been raised, you can also “like” that question.

KEY TAKEAWAYS AND INSIGHTS

- **Consistent Understanding of E6(R3)**

A unified understanding of the revisions is essential for implementing this **Tier 1 guideline**. It is critical to understand the “why” behind the changes, as outlined in the ICH Reflection Paper and Concept Paper.

- **Fit-for-Purpose, Risk-Proportionate Approach with Unchanged Core Principles**

E6(R3) introduces a fit-for-purpose, risk-proportionate framework focusing on the factors critical to quality - what matters most for participant protection and trial reliability. While the guideline introduces flexibility, the fundamental principles of ensuring participant safety and the reliability of trial results remain unchanged.

- **Stakeholder Mindset and Behavior Shift**

A shift in mindset and behavior among all stakeholders is essential for successful implementation. **Training, education, and proactive communication** will help drive this cultural change and ensure alignment with E6(R3).

- **Real-World Data (RWD) Integration**

It's crucial to ensure that RWD is fit for purpose by managing control over data collection, securing access agreements, ensuring accurate data linkage, and prioritizing cybersecurity and privacy in remote trials.

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03-06 December 2024

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