Current Status of ICH Efficacy Topics

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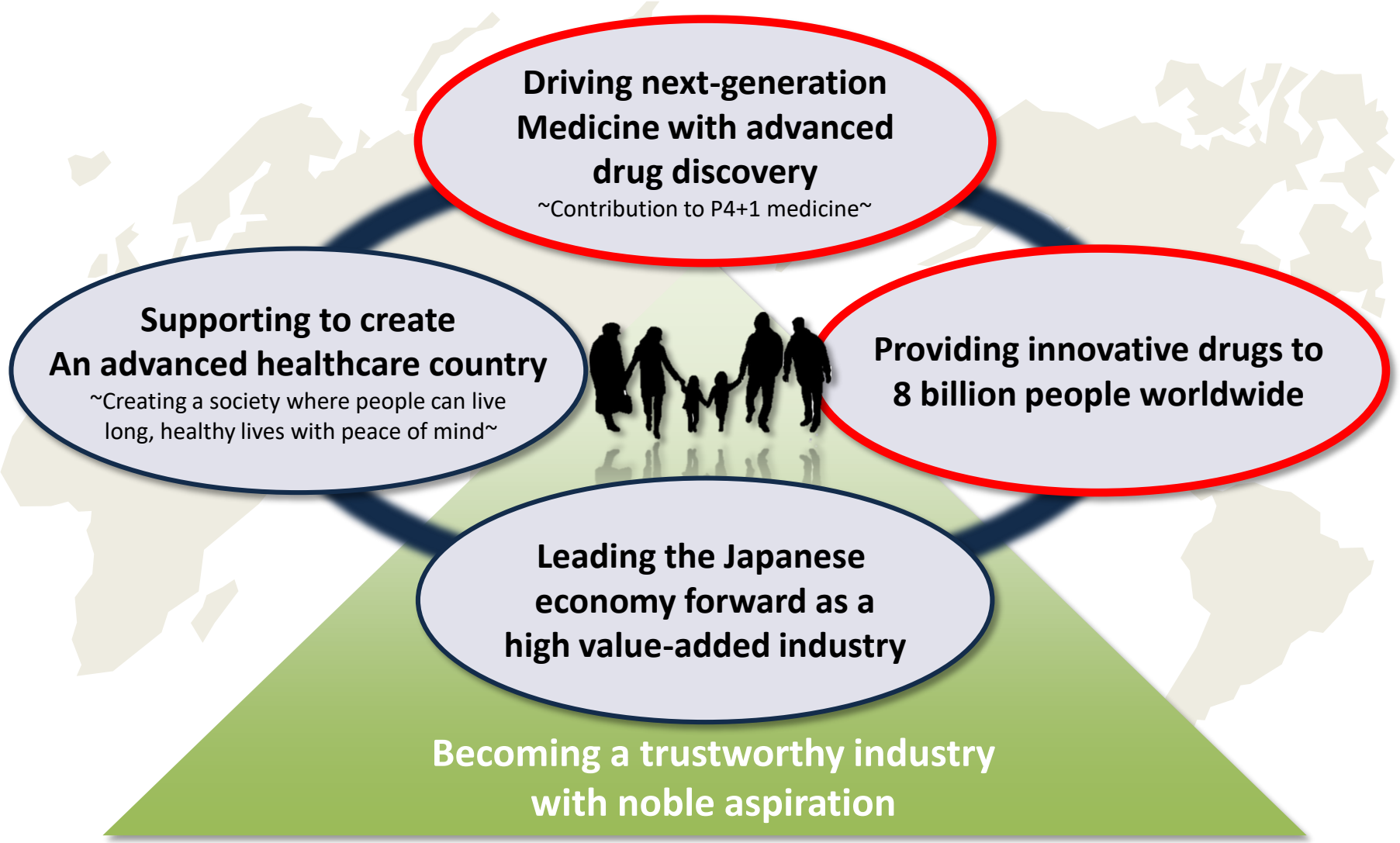
Outline

1. JPMA Industry Vision 2025
2. Background – Evolving ICH
3. Challenges in Harmonization of Technical Topics
   - Enhancing Training Activities
   - Overarching “Strategic Discussion” and “New Topics” Process
4. Recent Topics and the Future

JPMA's Industry Vision 2025

- The vision represents JPMA' aspiration in ICH activities as well.



JPMA's Business Plan in FY2019

- In FY2019, JPMA is working on 4 major activities, aiming for the 2025 vision.

I. **Improve quality of medical care through fostering innovation (R&D for innovative new medicines) and promoting proper use of medicines. Contribute to economic growth with multifaceted assessment of the value of medicines.**

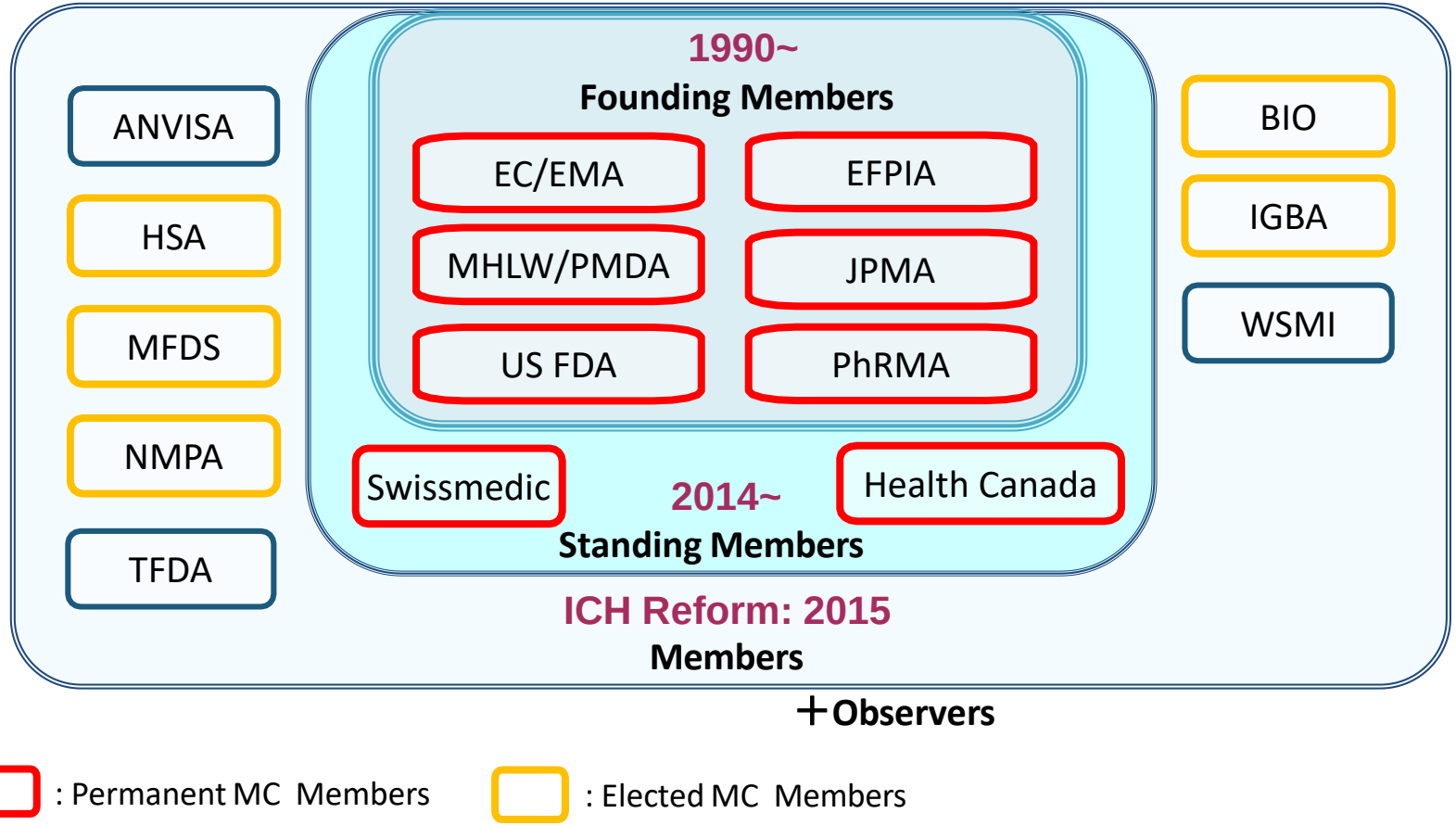
II. **Drive international activities and cooperation. Contribute to global health.**
   1. Contribution to ICH as one of the founding industry associations
   2. Further collaboration in Asia (APAC, etc.)

III. Secure thorough compliance, build further trust with the public.

IV. Enhance PR activities to foster further understanding of the industry.

ICH – Unique Venue for Regulatory Harmonization

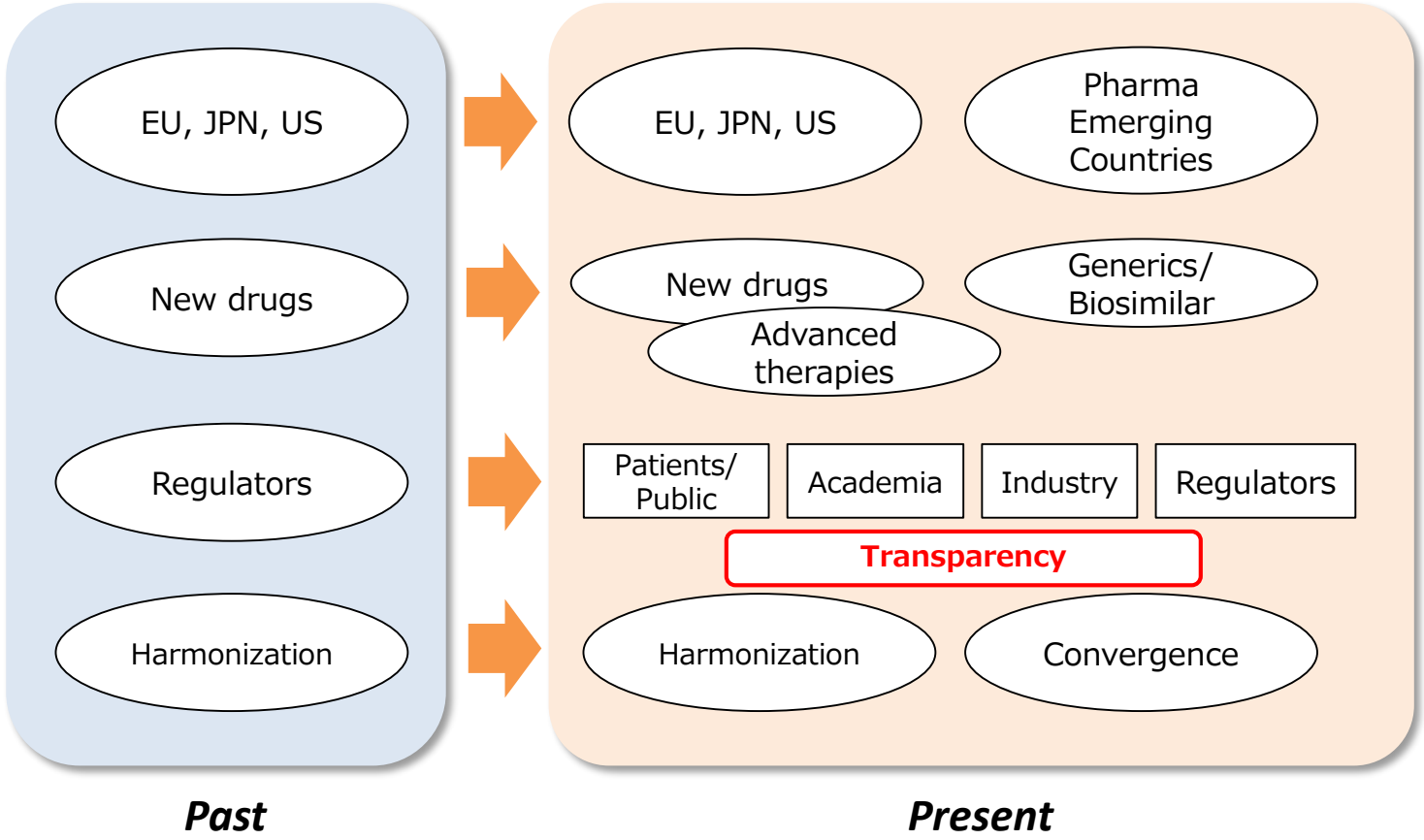
- ICH is a unique harmonization project, involving the Regulators and Industries across the globe.



Environmental Change surrounding ICH

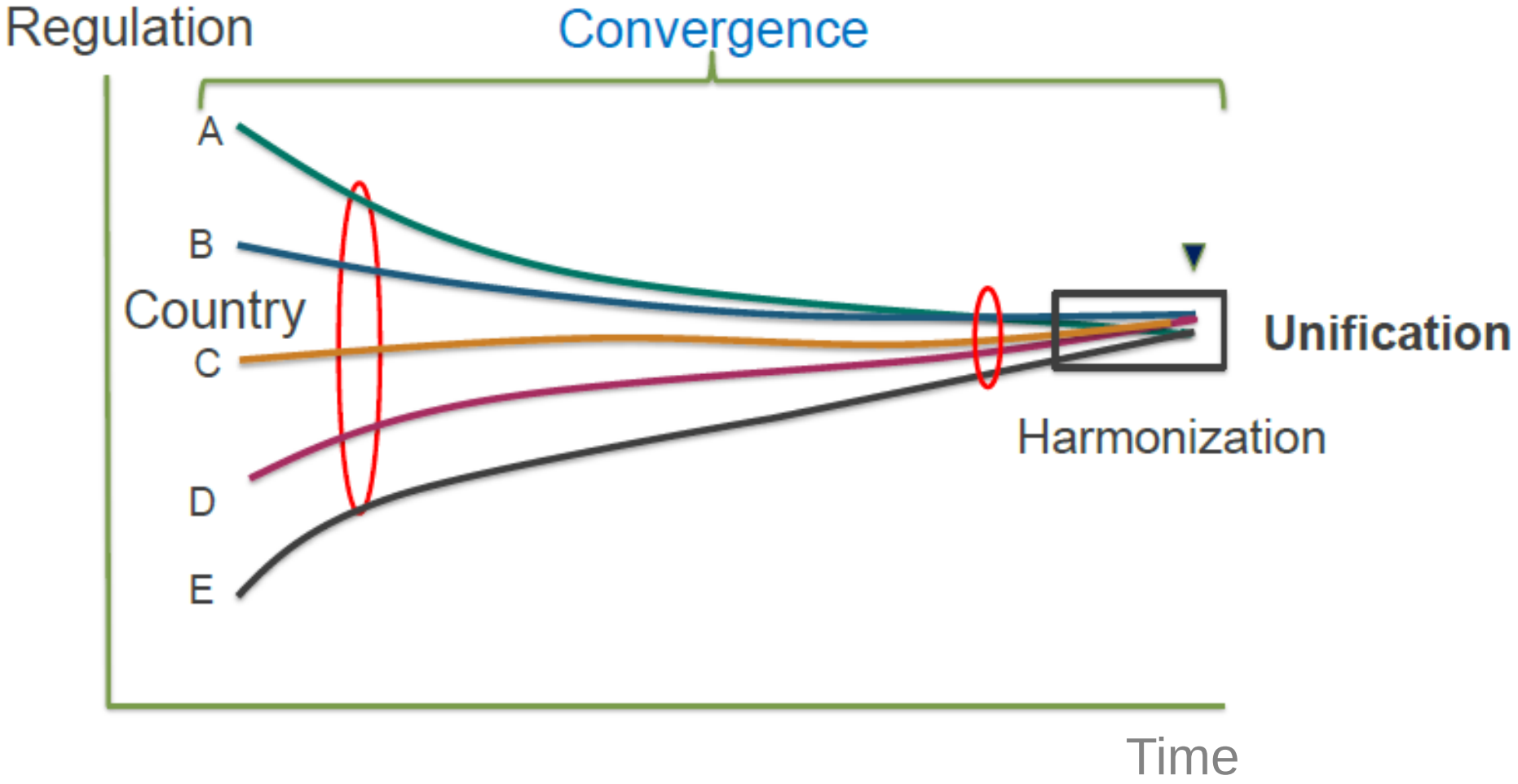
- With the momentum of the ICH reform in 2015, ICH is evolving to adapt to the paradigm shift in pharmaceutical regulatory field.

Paradigm Shift in Pharmaceutical Regulatory Field



“Convergence” and “Harmonization”

- The expanding ICH includes various ICH Regulatory Members with a wide range of convergence status.



Improving Management of the ICH Process

- For further improvements in its productivity and effectiveness, ICH is working on several initiatives:

✓ Visualizing status of ICH GL implementation

Enhancing training activities

✓ Managing the size of WGs

✓ Further engagement of relevant stakeholders

Overarching "Strategic Discussion" and "New Topics" process

Advancing Training Activities in ICH

- To address the increasing needs of training for ICH guidelines, a wide range of initiatives were launched by the ICH:

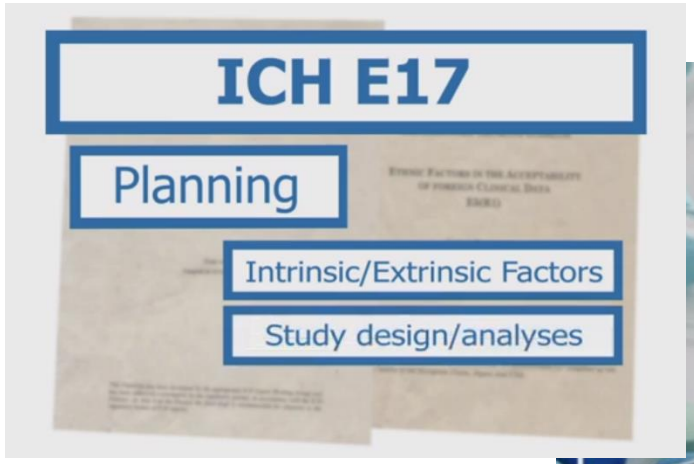
Enrichment of Public Meetings
- ✓ For Step2 & Step4 guidelines
- ✓ Multiple locations
- ✓ Engagements of stakeholders

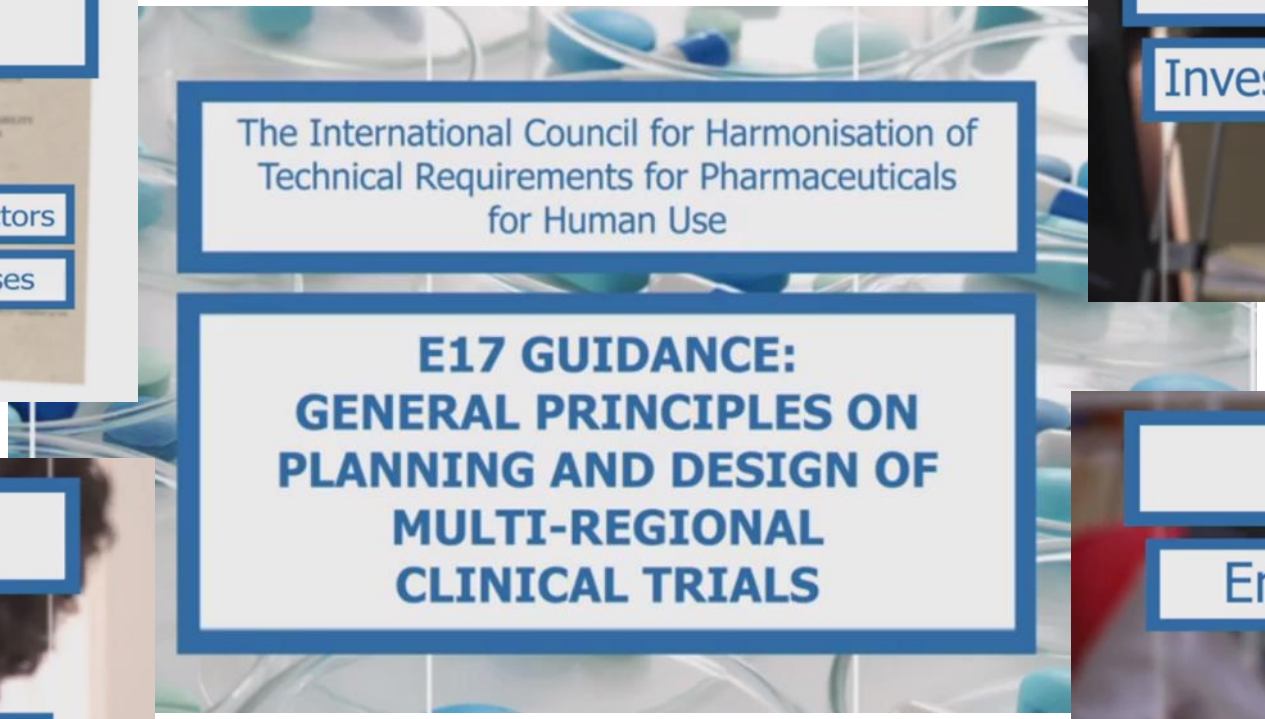
Diversified Training Tools
- ✓ Online training videos - YouTube
- ✓ Case studies
- ✓ Supported by Training SubCom

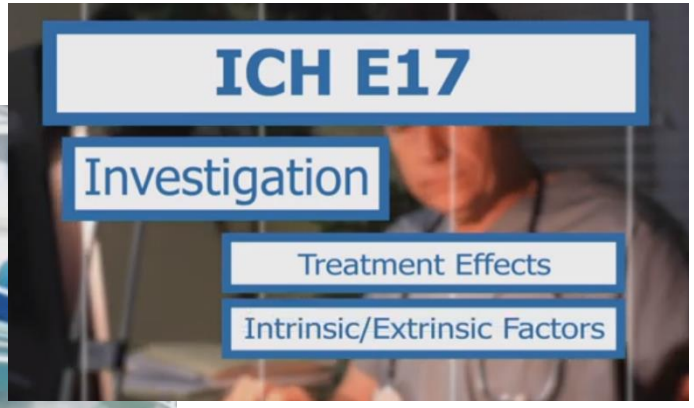
***New* - Training Associates**
- ✓ Accredited non-profit training organizations/institutions funded by ICH
- ✓ Collaborate with ICH to address in a strategic manner the training needs

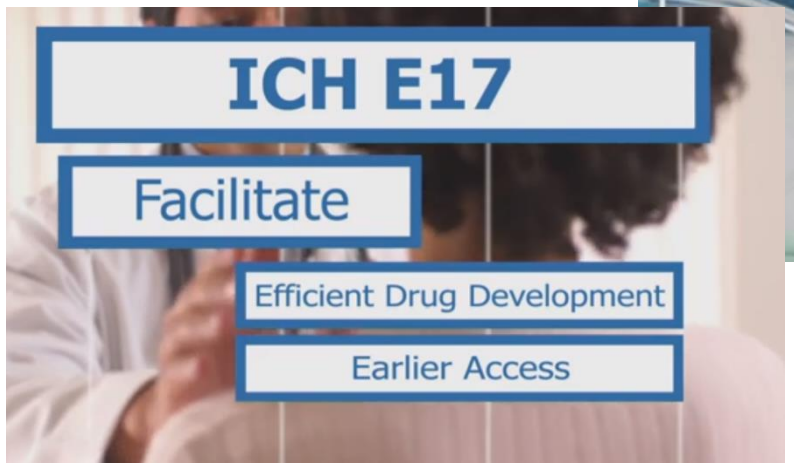
Recent Example – E17 Training Video

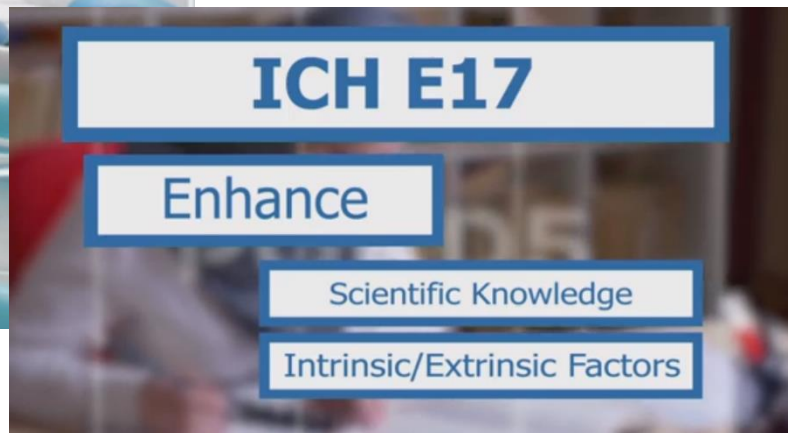
- This video highlights "**what is E17 guideline**" for wide ranging stakeholders involving in MRCTs.











Strategic Theme vs New Topic

- Since reforms in 2015 ICH has established the practice of developing "**Reflection Papers**" to describe proposed guideline work under ***Strategic Themes***.

➡ These RPs support more productive discussion and convergence on topic priorities as ICH Membership grows larger and more diverse.

New Topic

- Single topic proposal
- Bottom-up approach driven by interests of each ICH Member
- Not necessarily assure total optimization

Strategic Theme

- Comprehensive proposal on multiple GL revisions/new GL creations
- More top-down approach
- Based on cross-disciplinary discussions

Recent ICH Reflection Papers

- Several initiatives are ongoing: "**GCP renovation**" firstly went ahead, followed by "**Pharmaceutical Quality**".

1. GCP Renovation

- Modernize ICH **E8** to address broader considerations of study quality and data quality – ***now underway***
- Further revise ICH **E6** to anticipate and address a broader range of study types retaining focus on clinical investigator site practices – ***to be initiated as E6(R3)***

2. Pharmaceutical Quality

- Develop a series of quality guidelines including ICH Q11, Q12, **Q13** (continuous manufacturing), and **Q14** (analytical procedures)
- Informal Quality Discussion Group (IQDG) – ***now underway***

Emerging ICH Reflection Papers

- And more initiatives are emerging in the ICH:

3. Generic Drugs

- Develop a series of guidelines for generic drug development
- Informal Generic Drug Discussion Group (IGDDG) – ***now underway***

4. Pharmacoepidemiological Study

- Harmonize technical requirements for pharmacoepidemiological studies submitted to regulators to advance more effective utilization of **Real-World Data**
- Informal Discussion Group – ***to be established***

5. Model Informed Drug Development (MIDD)

- Under discussion in ICH Management Committee

Overview of Pharmacoepidemiology Reflection Paper

- The RP aims to harmonize the technical scientific requirements related to pharmacoepidemiological studies submitted to regulatory agencies, which facilitates utilization of Real-World Data.

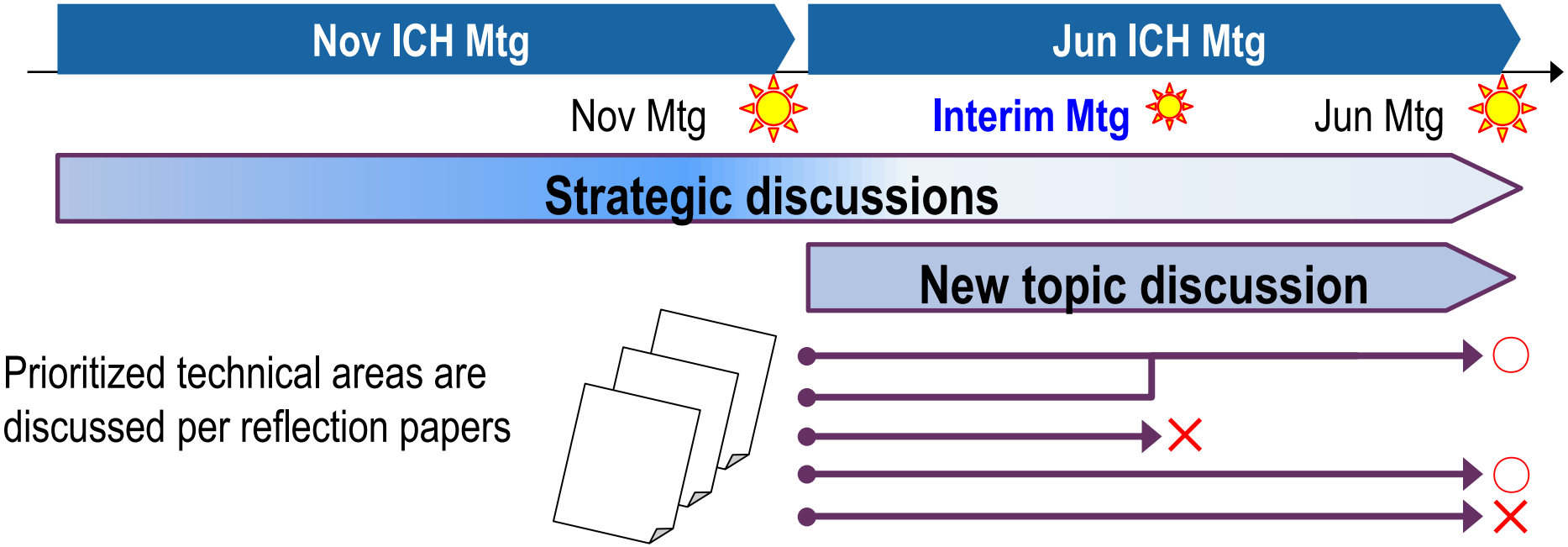
	1st Stage 2019.Q4 -2020.Q2	2nd Stage 2020.Q3 -2021.Q1	3rd Stage 2021.Q2 -2021.Q3	4th Stage 2021.Q4 -20XX.QX
Tasks	• Considering the specific areas and opportunities for international harmonization	• Prioritizing harmonization area as ICH guidelines • Creating overall structure of these guidelines	• Creating opportunity proposal for high priority topics to propose a form of expert working group	• Following regular ICH process; New Topic proposal, adoption and Steps 1-4
Deliverables	**List of harmonizable areas in ICH**	**Priority list and overall structure of all guidelines**	**Opportunity proposal**	**ICH Guideline**

➡ ICH MC will consider the final recommendation from the Discussion Group to determine the next steps.

Process for Strategic Discussion & New Topics

- In general, Nov ICH Mtg focuses on strategic discussion while Jun ICH Mtg mainly deals with New topic selection.

Typical Scheme



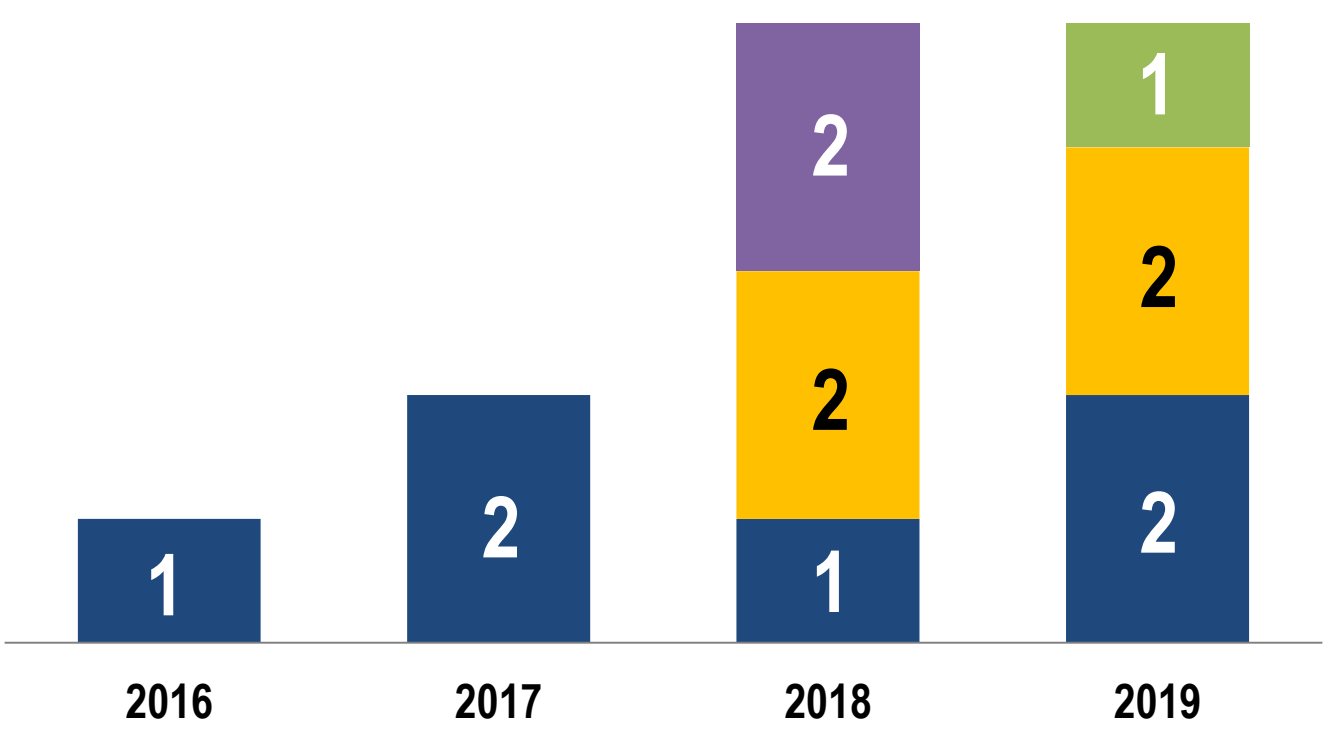
a. Prioritized technical areas are discussed per reflection papers

b. According to the priorities, each party submits New Topic proposals
→ discussed in MC

Trend of New Topics after ICH Reform in 2015

- After ICH Reform and Strategic discussion process implemented, the productivity of new topic creations has maintained high level.

Number of Adopted New Topics after ICH Reform



E	6 New Topics
Q	4 New Topics
M	2 New Topics
S	1 New Topics

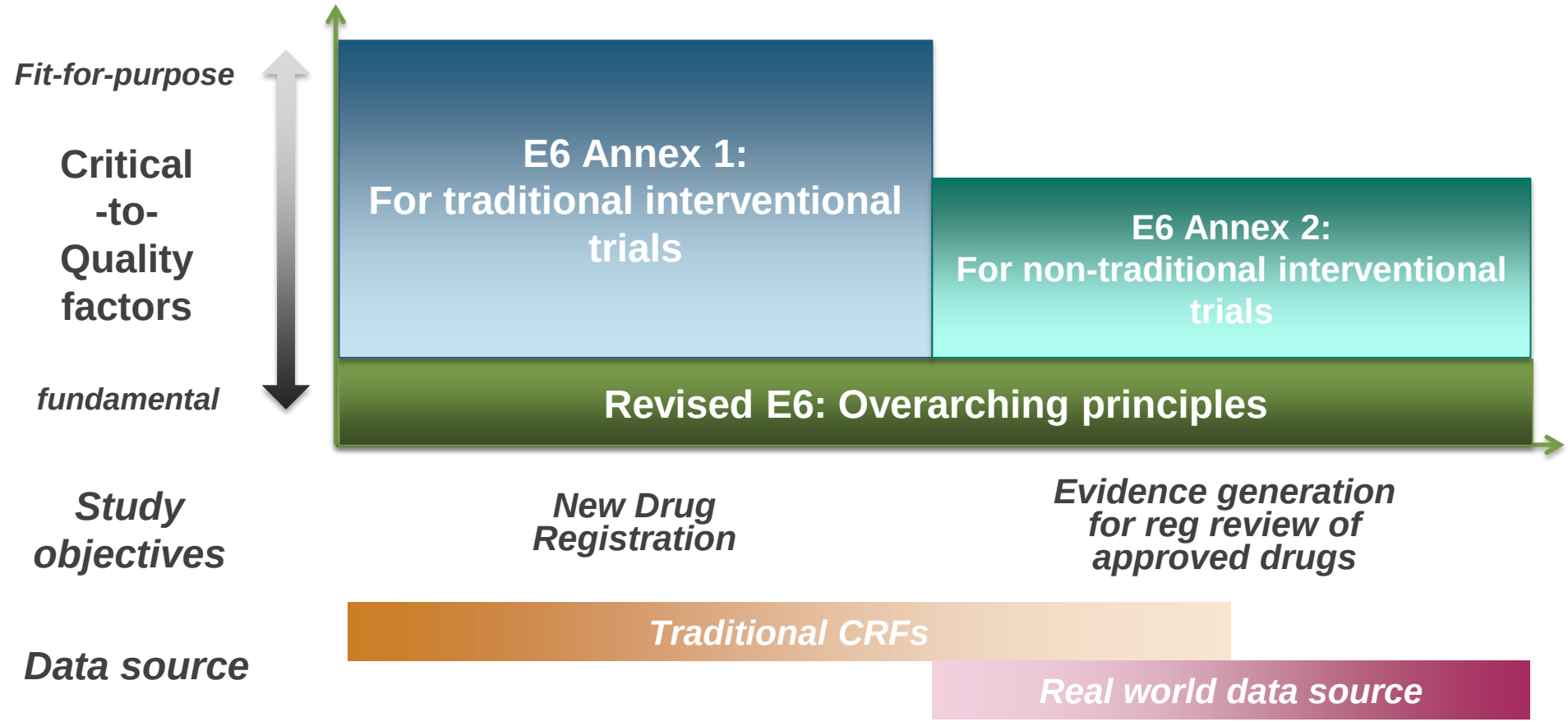
in 4 years

Adopted Five New Topics in 2019

- New topics endorsed at ICH Amsterdam mtg in Jun 2019 and informal Working Groups are going to be established for Q5A(R1), E6(R3), E2D(R1) and Gene Therapy Biodistribution:
  - **Q5A(R2)**: Revision of ICH Q5A Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
  - **E6(R3)**: Revision of ICH E6 Good Clinical Practice
  - **E2D(R1)**: Revision of ICH E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting
  - **S12**: Biodistribution Studies for Gene Therapy Products
- Also, one more New topic was endorsed with a delayed start:
  - **Q3E**: Guideline on Impurity: Assessment and Control of Extractables and Leachables (E&L) for Pharmaceuticals and Biologics

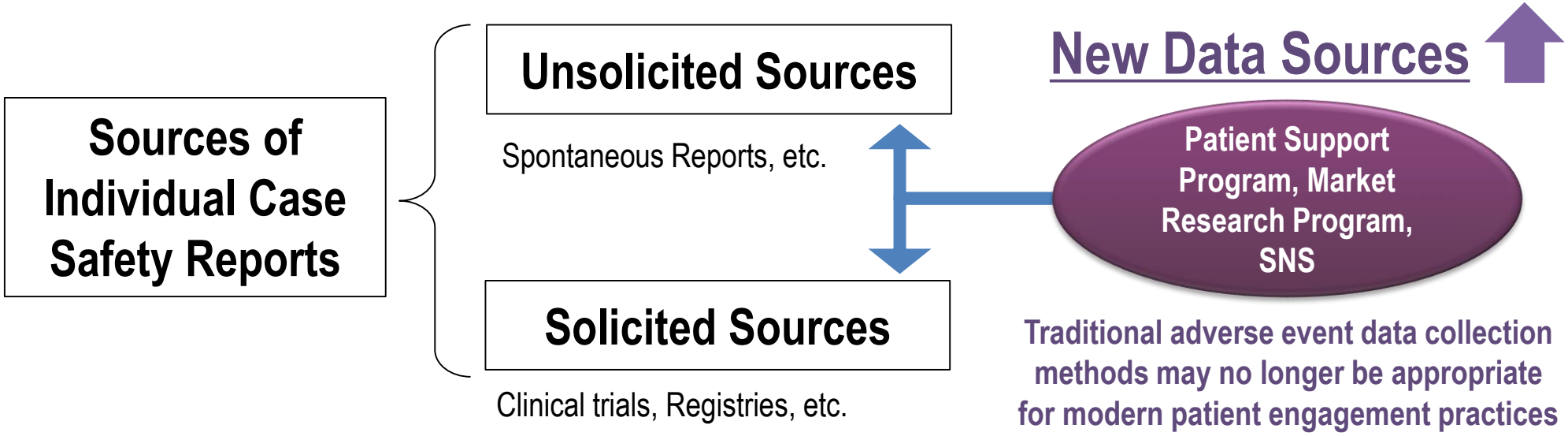
E6(R3) – Reconstruction of GCP

- The revised E6 and annexes to be blocks of the GCP; Critical-to-Quality factors addressed/focused would be different depending on the components.



E2D(R1) – Modernization of Pharmacovigilance

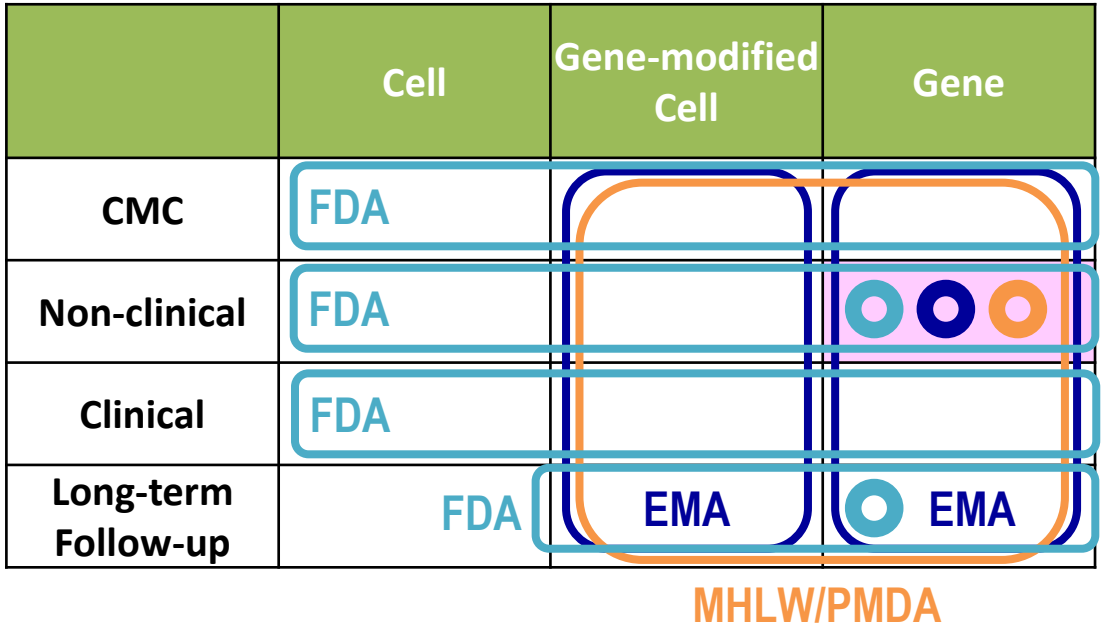
- E2D(R1) will update the existing E2D GL
  - to incorporate pragmatic potentially risk-based approaches of the management of information from existing and any **new data sources**,
  - to enable a greater focus on the data sources that will optimize signal detection activities and public health.



S12 – Biodistribution Studies for Gene Therapy

- Based on the outcome from the IPRP discussion, ICH will initiate new ICH guideline preparation for Non-clinical BD studies for gene therapy products.

Current guideline for Gene Therapy Products in the Founding Regions



- Scope of Guideline
- Timing and design of BD study to support early human clinical trials
- Design of BD studies and collection of BD data, etc.

○ : where BD consideration is described in each guideline

➡ Streamlined development of the gene therapy products with higher scientific rigor while minimizing the unnecessary use of animals.

Other New Topics to be initiated

JPMA

M12 – **to start mid 2019**

- New guideline to harmonize approaches in designing, conducting, and interpreting Drug-Drug Interaction Studies

E20 – **to start mid 2019**

- Harmonize regulatory perspective on the planning, conduct, and regulatory review of adaptive clinical trial designs
- Define set of principles (much like ICH-E9) to guide all aspects of design, conduct, analysis and interpretation
- Clarify study design changes that are not considered adaptive design
- Avoid disharmonized approaches to adaptive clinical programs that can further complicate simultaneous global drug development

New Topic Issues to be considered at ICH

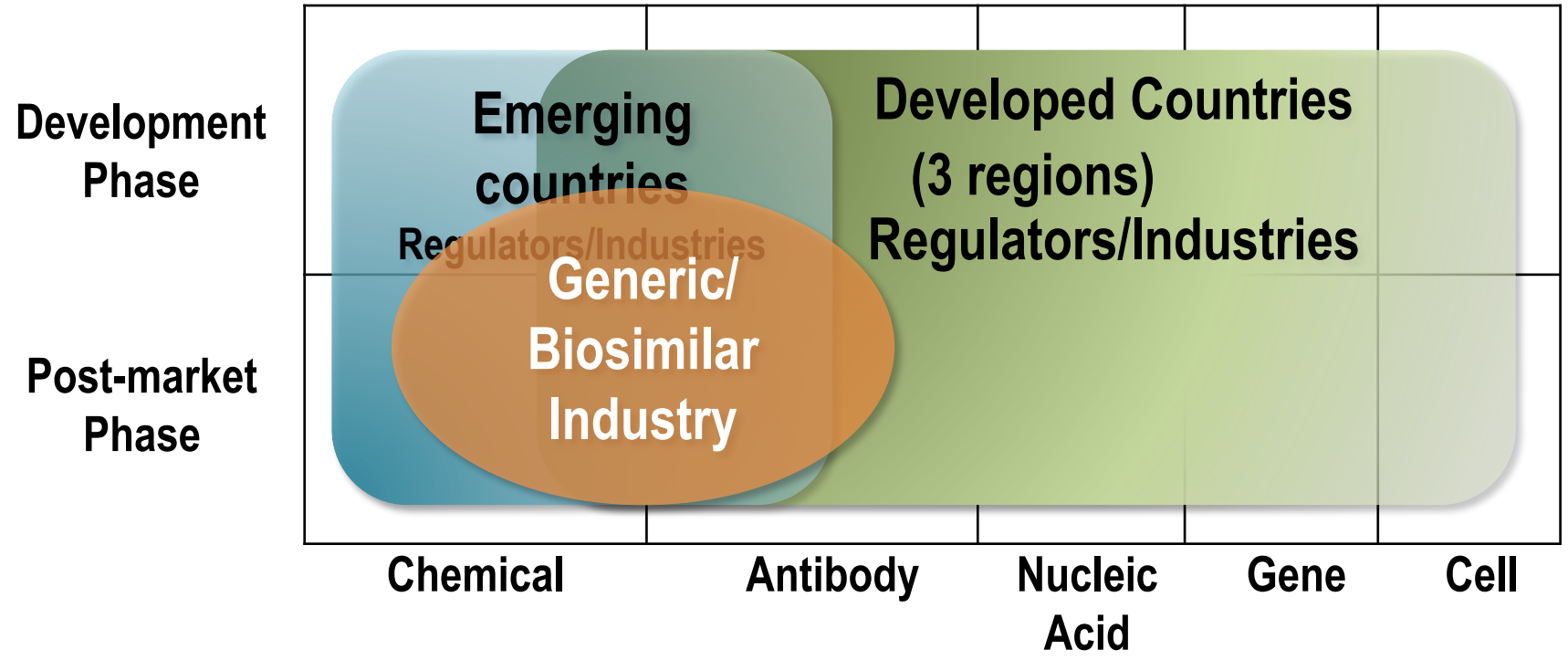
JPMA

- Numerous new topic proposals are necessary to maintain the ICH's operation rate, given the anticipated Step 4 achievements by 2020.
- However, ICH needs to wisely select ***right*** opportunities.
  - Discern: what we want to do; what we can do; what we should do
    → Do numerous GLs really make everyone happy?
  - **In general, difficulty of GL preparation is increasing**
    - Almost no low-hanging fruits
    - Need high-profile experts with multiple expertise: e.g., stats & safety
  - **Diversity of needs in the expanding ICH**
    - For example, how many common interests on new ICH GLs can be identified between 1) EU/JPN/US and Emerging Countries; 2) R&D oriented industry organizations and Generic industry organizations?

Diversity of Guideline Needs in Expanding ICH

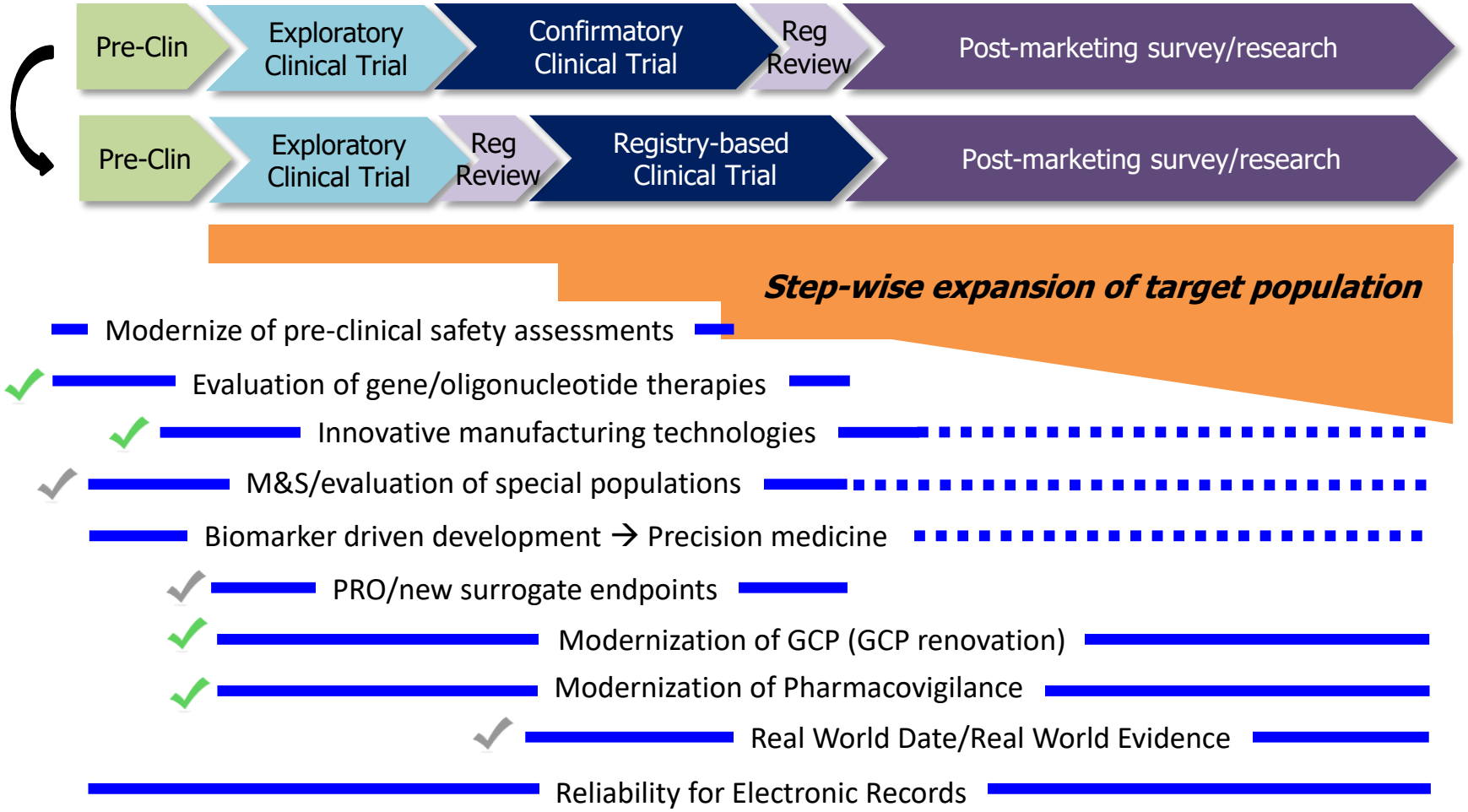
- ICH would need to consider some mechanism to deal with a broad range of needs in ICH, assuming the future ICH Membership.
  → May fit some portfolio mgmt. (**under discussion in MC**)

ICH Members and Needs for ICH Guidelines (just for illustrative purpose)



Potential Topics of Interest for JPMA

- JPMA would prioritize useful technical opportunities to accelerate patient access for innovative new drugs.



Future Strategic Discussion and New Topics

- Given the diversified ICH membership, two types of approaches would be anticipated:

- Modern tools to enhance quality and efficiency of new drug development
- Modernized safety assessment
- RWE/Medical Big Data
- New manufacturing technologies
- Oligonucleotide, Gene therapy, Regenerative medicine?

Points to Consider

- ✓ **Maturity of science/technology?**
- ✓ **Urgency/timeliness?**
- ✓ **Feasibility in terms of the scope of ICH? (e.g., medical device)**
- ✓ **Legal compatibility?**

- Generic/Biosimilar
- Vaccine
- Combating communicable diseases

- ✓ **Tangible benefits for stakeholders?**
- ✓ **Urgency/timeliness?**
- ✓ **Clear rationale for ICH?**

Summary – Take-home Points

- At the evolving and expanding ICH, variety of new technical opportunities can be pursued; both challenges and opportunities exist.

- Almost no low-hanging fruits – ICH continues to select right opportunities in right time to maximize our productivity to create new GLs and renovate existing GLs, which improves the public health in the world.

- The more complex guidelines, the more engagement/training need. The benefit of the ICH GLs would be truly realized when those GLs address pragmatic issues and are fully implemented in our daily work.

Bringing Innovation in
Drug Discovery to the World

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