Setting the scene on ICH and where it is headed

11th ARC, Oct 2022

Dr. NAKASHIMA Nobumasa

Vice-Chair, Management Committee, ICH
Associate Executive Director for International Programs, PMDA
ICH Regulators in 1990 / ICH Assembly and MC in 2019

ICH at 30 - What Will Come the Next 30 Years?
Dr. F. Sauer, DIA EURO 2020
ICH achievements 1; Growing Membership

ICH directly involves 1091 persons:
- 106 Representatives of Members/Observers in the ICH Assembly, the ICH MC and the MedDRA MC
- 708 Experts in WGs
- 284 Persons serving in support roles

Number of experts in ICH WGs

- Founding/Standing member; 408; 58%
- Standing Observer; 30; 4%
- Observer; 57; 8%
- Member; 208; 29%
- Other; 5; 1%

New Members

Patients Academia

20 members, 35 observers

Collaboration with Other Organizations such as WHO, ICMRA, IPRP, PIC/S etc
ICH achievements 2; Increasing guidelines

**Close to 70 Guidelines on technical requirements on:**

- **Safety** – 15 Guidelines
- **Quality** - 24 Guidelines
- **Efficacy** – 21 Guidelines
- **Multidisciplinary** - 8 Guidelines

<table>
<thead>
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<th>Safety</th>
<th>Quality</th>
<th>Efficacy</th>
<th>Multidisciplinary</th>
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<tr>
<td>▪ S1A – S1C: Carcinogenicity studies (3)</td>
<td>▪ Q1A – Q1E: Stability (5)</td>
<td>▪ E1: Clinical safety (1)</td>
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<td>▪ S2: Genotoxicity studies (1)</td>
<td>▪ Q2: Analytical validation (1)</td>
<td>▪ E2A – E2F: Pharmacovigilance (6)</td>
<td>▪ M4, M4Q, M4S, M4E: CTD (4)</td>
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<td>▪ S3A – S3B: Toxicokinetics and Pharmacokinetics (2)</td>
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<td>▪ M7: Genotoxic impurities (1)</td>
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<td>▪ S4: Toxicity Testing (1)</td>
<td>▪ Q4 – Q4B: Pharmacopoeias (1)</td>
<td>▪ E4: Dose-response studies (1)</td>
<td>▪ M9: Biopharmaceutics Classification System-based Biowaivers (1)</td>
</tr>
<tr>
<td>▪ S5: Reproductive toxicology (1)</td>
<td>▪ Q5A – Q5E: Quality of biotechnology products (5)</td>
<td>▪ E5: Ethnic factors (1)</td>
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<td>▪ S6: Biotechnology products (1)</td>
<td>▪ Q6A – Q6B: Specifications (2)</td>
<td>▪ E6: Good Clinical Practice (1)</td>
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<td>▪ E7, E8, E9, E10, E11-E11A: Clinical Trials (5)</td>
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<td></td>
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<td>▪ E14: Clinical evaluation (1)</td>
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<td>▪ S8: Immunotoxicology studies (1)</td>
<td>▪ E15: Definitions in Pharmacogenomics (1)</td>
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<td>▪ S9: Nonclinical evaluation for anticancer pharmaceuticals (1)</td>
<td>▪ E16: Qualification of Genomic Biomarkers (1)</td>
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<td>▪ S10: Photosafety evaluation (1)</td>
<td>▪ E17: Multi-Regional Clinical Trials (1)</td>
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<td></td>
<td>▪ S11: Nonclinical Paediatric Safety (1)</td>
<td>▪ E18: Genomic Sampling (1)</td>
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</table>
ICH achievements 3; Spread of MedDRA

Over 6,600 MedDRA Subscribing Organisations in more than 125 Countries
ICH 30th Anniversary

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ICH – the global platform for harmonisation

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmacokinetics and develop ICH Guidelines.

The purpose of ICH is the promotion of public health through international harmonisation that contributes to:
- Reduction of unnecessary animal research
- Improvement of the safety and effectiveness accomplished through technical guidelines implemented by the regulatory authorities

ICH has grown over the years in terms of Members, Observers and experts. The ICH Members include regulatory authorities as well as global organisations representing the generics industry and the over the counter industry known as CIHC. This reflects the global dimension, diversity and complexity of drug regulation and the importance of broad engagement to achieving its mission – considerations central to the ICH Reform in 2019.
- Prevention of unnecessary duplication of clinical trials and post-marketing clinical evaluations
- Development and manufacturing
- Registration and supervision of new medicines
- Post-authorisation safety reporting and pharmacovigilance

Some specifics:
- Over 1000 individuals are involved in ICH work.
- Membership spans all six populated continents

An inconspicuous yet vital…

ICH has developed over 60 technical guidelines since its establishment.

Not only above…

✓ Constructs the systematic regulation among world regulators

✓ Spread the awareness that guideline should be developed based on regulatory science without any involvement of politics

✓ Gives experts opportunities to work hard and encourage their skills each other

✓ Builds the network of experts
Recent notable achievements in each area and expectations for the future

① Quality Guidelines;
   • Post-Approval Change Management Protocol [PACMP]; Newly established Article 14-7-2 of the Pharmaceutical and Medical Device Act (Q12)
   • Promotion of stable supply by establishing **continuous manufacturing guideline** (Q13)
   • **Targeted revisions of the ICH Stability Guidelines Series (Q1/Q5C)**

② Safety Guidelines;
   • Improved efficiency of animal tests; **about a quarter** of 2-year rat carcinogenicity study can be omitted (S1B(R1))
   • First application of **iPS technology** to guidelines; including iPS-cell derived cardiomyocytes to regulatory guidelines → Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) (E14/S7B)
   • Developing ICH guidelines in gene therapy field(S12)
Recent notable achievements in each area and expectations for the future

③ Efficacy Guidelines;
  • **Optimization of safety data collection** (E19); reduce the cost of clinical trials by focusing on the essential parts
  • **GCP renovation**; considering the latest technology, reducing clinical trial cost and improving efficiency of GCP inspection by fit-for-purpose quality design (E6(R3))
  • **Model-Informed Drug Development** General Principles Guideline (M15)
  • **Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials** (E21); based on experience of Covid-19 pandemic

④ Multidisciplinary Guidelines;
  • First guideline on how to utilize **real world data** (M14)
  • **Bioanalytical Method Validation** (M10)
  • Biopahrmaceutics Classification System-based Biowaivers (M9); standardization of guidelines including **generics**
ICH recent activities and Challenges 1;
Collaboration with new stakeholders

ICH has promoted the collaboration with new stakeholders. It will increase the efficiency of ICH activity and build the confidence and trust with stakeholders.

① **Other regulatory bodies; ICMRA, IPRP and PIC/S**
   ICMRA-ICH-PIC/S-IPRP Joint Reflection Paper on PQ KMS Capability

② **Patient and Academia**
   ICH has traditionally worked with regulators and industry to develop science-based guidelines. In recent years, stakeholder involvement, especially patient involvement, has become an issue.

③ Other organization (DIA etc.,..)
Joint Reflection Paper on PQ KMS Capability

1. Introduction
2. Proposed Areas of Harmonization Work
   • ICH – Data Elements and Standards
   • IPRP – Alignment of Regulatory Assessment and Expectations
   • PIC/S – Inspections
   • Cross-Organizational Collaboration – Unique Identifiers
3. Coordination of PQ KMS-Related Work Streams
4. Future Considerations and Challenges
   • Supporting Technology Platform for Virtual Repository
   • Legal and Regulatory Considerations
5. Capability-Piloting Strategy
6. Stakeholder outreach and engagement strategy
   • Conclusion
   • References
Joint Reflection Paper on PQ KMS Capability

• ICH Role

2. Proposed Areas of Harmonization Work

• ICH – Data Elements and Standards
  ➢ The work proposed for ICH is primarily focused on further specification or clarification of harmonization of required data elements and data standards submitted in the quality modules of the common technical document.
  ➢ The work currently under way in the ICH M4Q(R2) Expert Working Group (EWG) as “structured product quality submissions”
  ➢ ICH could further advance PQ KM capabilities and support PQS assessments for PACs through harmonization of data elements and data standards to be submitted in the quality modules of the CTD
Global Movement for Patient First

• ICH

Stakeholder Engagement on E6(R3)

Objectives
• Supporting development of a responsive guideline with stakeholders’ perspectives and advances in technology and clinical trial design
• Improving understanding and implementation of ICH-E6(R3) supporting smoother adoption by stakeholders
• Providing transparency and responsiveness to stakeholders’ needs for further involvement during medicines development

Approach for patients
• Regional public engagement (e.g. surveys, workshops)

Patient Focused Drug Development (PFDD)

• Reflection Paper on Patient Focused Drug Development (PFDD) was endorsed on Sep. 21th, 2020 and ICH held a public consultation until Mar. 7th, 2021.

• PMDA

ICH recent activities and Challenges 2; Dissemination of Guideline

Since the ICH reform in 2015, the number of ICH members and observers has been increasing dramatically.
To disseminate the ICH guidelines and to address the training needs, a wide range of initiatives were (are) launched.

① To publish Q&As and training materials ---- EWG initiative
② To provide diversified training activities ------ Training sub-com initiative
③ To establish expert network among regulators --- IPRP initiative
④ To facilitate the collaboration among regulators --- Japan and APEC initiative
Diversified training activities in ICH

To address the increasing needs of training for ICH guidelines, a wide range of initiatives were launched in ICH, led by ICH Training SubCom.

**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
- ✓ **Training Library (multi-languages)**

**New - Training Associates**
- ✓ Collaborating with non-profit institutions selected by ICH; already partnered with 2 institutions
- ✓ Expanding work with ICH Training Associates to **develop online training under multi-year contracts**

Mr. Yanagisawa, ICH forum in 2021
Utilization of ICH’(IPRP’)s Experts Network

Network of experts

Promotion of regulatory science research for emerging technologies

Experts converge to agree on a common direction for the emerging technology

Earlier development of ICH Guideline
IPRP Paper Publication Promotion Project (proposal from Japan)

**Purpose**
- Strengthening the network of IPRP member experts
- Publicity of IPRP activities to academia, etc.
- Effective use of surplus

**Overview**
- Subsidizing the fees for professional editing, paper publishing and electronic reprint required for IPRP working groups and drafting groups to submit their activity results to scientific journals.
- Proposal by Japan. Conducting a pilot and determine whether to continue based on the results

**Current status**
- Currently drafted and submitted a paper to a journal using the results of the [e-labeling drafting group (experts from 8 regulatory authorities)] led by Japan.

**Paper Title:** Electronic product information for human medicines: The current situation and future projection based on a cross-sectional survey
IPRP Paper on e-labelling

Currently submitted to a journal for publication

Electronic product information for human medicines: The current situation and future projections based on a cross-sectional survey

Rosaline de Aquino Silva¹, Juan Garcia Burgos², F.A. Sayed Tabatabaei³, Teruyoshi Ebara⁴, Tomoko Osawa⁴, Mai Okamoto⁴, Yousef S. Al-Armi⁵, Bashayer K. Albaikhi⁶, Stephan Jaermann⁷, Irmgard Schmitt-Koopmann⁷, Chyn-Liang Huang⁸, Po-Wen Yang⁸, Lih-Jia Huang⁸, Miao-Ju Chien⁸, Yu-Ting Chiu⁸, Tony Manderson⁹

1. ANVISA, Brazil
2. EC, Europe
3. CBG–MEB, The Netherlands
4. POMA, Japan
5. SFDA, Saudi Arabia
6. Swissmedic, Switzerland
7. TFDA, Chinese Taipei
8. TGA, Australia

The authors contributed to this paper equally.

This manuscript represents personal opinions of the authors and does not necessarily represent the views or policies of their corresponding regulatory agencies.

• Survey result of 21 IPRP authorities
• Current status of e-labelling (electronic product information)
  ➢ Up-to-date and reliable information
  ➢ Environmental friendly; less paper
  ➢ open access, easily accessible, preferably Interoperable
• Best practices and future projection
-Capacity Building Activities at PMDA-

Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC)

• Established in April, 2016.
• Endorsed as Centers of Excellence (CoE) of APEC-LSIF-RHSC.
• Promote capacity building and human resource development through training seminars for Asian regulators.

Action Policy of PMDA-ATC
Contribute to universal health coverage in Asia through developing a foundation for regulatory harmonization in the Asian region.

Visits sites and conducts lectures, case studies and practical trainings.

Provides trainings tailored to local needs for more people.

Invites Asian regulatory representatives and offers training seminars.

Shares Japanese knowledge and experiences in the regulation of pharmaceuticals and medical devices with Asian countries.
# PMDA’s Contribution on APEC LSIF RHSC

## As a PWA champion
- PMDA takes a lead in the following 3 PWAs.

<table>
<thead>
<tr>
<th>Priority Work Areas (PWAs)</th>
<th>Champion Economies</th>
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<tbody>
<tr>
<td>MRCT/GCP inspection</td>
<td>Japan, Thailand</td>
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<tr>
<td>Pharmacovigilance</td>
<td>Republic of Korea</td>
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<tr>
<td>Biotherapeutics</td>
<td>the United States</td>
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<td>Sub-champion:</td>
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<tr>
<td></td>
<td>Biotechnological Innovation Organization (BIO)</td>
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<tr>
<td>Advanced Therapies</td>
<td>Singapore, the United States</td>
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<td>Sub-champion:</td>
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<td>Biotechnological Innovation Organization (BIO)</td>
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<tr>
<td>Good Registration Management</td>
<td>Chinese Taipei, Japan</td>
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<tr>
<td>Global Supply Chain Integrity</td>
<td>the United States</td>
</tr>
<tr>
<td>Medical Device</td>
<td>Japan, the United States, Republic of Korea</td>
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<td>Sub-champions:</td>
</tr>
<tr>
<td></td>
<td>Japan Medical Imaging and Radiological Systems Industries Association (JIRA), Advanced Medical Technology Association (AdvaMed)</td>
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## As a CoE host institute
- PMDA is formal CoE for the following 3 PWAs.
- PMDA provides seminars (webinars*¹) every year in each areas.

<table>
<thead>
<tr>
<th>PWAs</th>
<th>Endorsed</th>
<th>Trainings provided *³</th>
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<tbody>
<tr>
<td>MRCT &amp; GCP *²</td>
<td>February 2017</td>
<td>6</td>
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<tr>
<td>Pharmacovigilance</td>
<td>February 2017</td>
<td>6</td>
</tr>
<tr>
<td>Medical Device</td>
<td>June 2020</td>
<td>3</td>
</tr>
</tbody>
</table>

*¹ Since FY2020, the seminars are provided online.
*² Since FY2020, The webinar is offered with the collaboration of the National Cancer Center Japan (NCC).
*³ including pilot CoE trainings

(As of Oct 3, 2022)
## Training Seminars provided by ATC

### Seminars held in FY2021 (open to all regulators)

<table>
<thead>
<tr>
<th>Contents</th>
<th>Date</th>
<th>Location</th>
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<tbody>
<tr>
<td>Quality Control (Herbal Medicine)</td>
<td>June 22-24, 2021</td>
<td>Online</td>
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<tr>
<td>Good Registration Management (GRM)</td>
<td>September 14-16, 2021</td>
<td>Online</td>
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<tr>
<td>Pediatric Review*1</td>
<td>September 21-24, 2021</td>
<td>Online</td>
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<tr>
<td>Medical Devices Review*2</td>
<td>November 15-17, 2021</td>
<td>Online</td>
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<tr>
<td>Good Manufacturing Practice (GMP)</td>
<td>November 25-26, 2021</td>
<td>Online</td>
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<tr>
<td>Pharmaceuticals Review</td>
<td>December 6-8, 2021</td>
<td>Online</td>
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<tr>
<td>Multi-Regional Clinical Trial (MRCT)*2,*3</td>
<td>January 18-21, 2022</td>
<td>Online</td>
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<tr>
<td>Pharmacovigilance*2</td>
<td>January 31, February 2-4, 2022</td>
<td>Online</td>
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*1 Joint Seminar with U.S.FDA, *2 APEC-LSIF-RHSC CoE Workshop, *3 Collaboration with National Cancer Center Japan


### Seminars held in FY2021 (for specific members)

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<tr>
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<tr>
<td>Pharmaceuticals Review etc. (for SFDA, Saudi Arabia)</td>
<td>May, 2021 - March, 2022</td>
<td>Online</td>
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<tr>
<td>Regenerative Medicinal Products Review (for CDSCO, India)</td>
<td>June 3, 2021</td>
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<tr>
<td>Medical Devices Review (Reprocessed Single-Use Medical Devices (R-SUD)) (for Thai FDA)</td>
<td>July 16, 2021</td>
<td>Online</td>
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<tr>
<td>Good Manufacturing Practice (GMP) (for FDA Philippines)</td>
<td>July 27, 2021</td>
<td>Online</td>
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<tr>
<td>Medical Devices Review (for AMDC member states)</td>
<td>August 25-26, 2021</td>
<td>Online</td>
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<tr>
<td>Medical Devices Review (Reprocessed Single-Use Medical Devices (R-SUD)) (for MDA, Malaysia)</td>
<td>September 1, 2021</td>
<td>Online</td>
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<tr>
<td>Good Clinical Practice (GCP) (for FDA Philippines)</td>
<td>September 8, 2021</td>
<td>Online</td>
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<tr>
<td>Pharmacovigilance (for NPRA, Malaysia)</td>
<td>October 4, 2021</td>
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<tr>
<td>COVID-19 related In Vitro Diagnostics (IVDs) Review (for MDA, Malaysia)</td>
<td>February 8, 2022</td>
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<tr>
<td>COVID-19 related Medical Products Review (for DAV, Vietnam)</td>
<td>March 30, 2022</td>
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PMDA-ATC Seminars in this fiscal year are offered as “Webinars” given the global impact of COVID-19
### ATC Planned Trainings Courses in FY2022

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<td>1     Quality Control (Herbal Medicine)</td>
<td>August 23-25, 2022</td>
<td>Online</td>
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<td>2     Pediatric Review*¹</td>
<td>September 12-15, 2022</td>
<td>Online</td>
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<tr>
<td>3     Good Manufacturing Practice (GMP)</td>
<td>October 25-26, 2022</td>
<td>Online</td>
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<td>4     Medical Devices Review I*²</td>
<td>November 14-16, 2022</td>
<td>Online</td>
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<td>5     Medical Devices Review II</td>
<td>November 28-30, 2022</td>
<td>Online</td>
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<tr>
<td>6     Pharmaceuticals Review</td>
<td>December 6-10, 2022</td>
<td>Online</td>
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<tr>
<td>7     Multi-Regional Clinical Trial (MRCT)*²</td>
<td>January 16-19, 2023</td>
<td>Online</td>
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<tr>
<td>8     Pharmacovigilance*²</td>
<td>February 6-9, 2023</td>
<td>Online</td>
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**Those seminars are open to all regulators**

Please access to the following website for more information including completed trainings.
https://www.pmda.go.jp/english/int-activities/training-center/0004.html

*1 Joint Seminar with U.S.FDA
*2 APEC-LSIF-RHSC CoE Workshop
*3 Collaboration with National Cancer Center Japan

PMDA-ATC & U.S. FDA Pediatric Review Webinar 2022

[Image of webinar participants]
PMDA-ATC E-learning Contents

• PMDA-ATC offers videos on
  - current topics
  - main services of PMDA
  - what PMDA do to promote international regulatory harmonization.


Over 40 contents

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<tr>
<th>Category</th>
<th>Last updated</th>
<th>Note</th>
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<tbody>
<tr>
<td>1. Review New!</td>
<td>2022.8.1</td>
<td>added Review of OTC Drugs content</td>
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<tr>
<td>2. Safety</td>
<td>2020.10.31</td>
<td>added post-marketing safety content</td>
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<tr>
<td>3. Relief</td>
<td>2020.10.31</td>
<td>added &quot;relief system for ADRs&quot; content</td>
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<tr>
<td>4. Medical Device</td>
<td>2022.1.5</td>
<td>added COVID-19 test kit content</td>
</tr>
<tr>
<td>5. GxP</td>
<td>2022.5.2</td>
<td>added Remote GMP Inspection content</td>
</tr>
<tr>
<td>6. PMDA Efforts</td>
<td>2022.4.1</td>
<td>added CRS content, renewed International Activities content</td>
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‘Coming together is a **beginning**
Keeping together is **progress**
Working together is **success**’

By Henry Ford (ICH 30\textsuperscript{th} Anniversary Publication)

Thank you for your attention!