



## 2022 Annual Report

**PHARMACEUTICAL INSPECTION CONVENTION  
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME**

**Our vision is to enable one inspection per site that is fit for all regulatory authorities in the benefit of public health.**



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PS/W 4/2023  
11 May 2023

## 2022 Annual Report

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) was established in 1995 as an extension to the Pharmaceutical Inspection Convention (PIC) of 1970 (see Annex 1). PIC/S is a non-binding co-operative arrangement between Regulatory Authorities in the field of Good Manufacturing Practice (GMP) of medicinal products for human or veterinary use. It is open to any Authority having a comparable GMP inspection system. On 31 December 2022, PIC/S comprised 54 Participating Authorities (PAs) from all continents. For the list of PIC/S PAs, see Annex 2.

PIC/S' vision is to enable one inspection per site that is fit for all regulatory authorities in the benefit of public health.

PIC/S' mission is to strive to improve public health by leading development and implementation of inspection frameworks for human and veterinary medicines through harmonisation of standards and offering world class training to regulatory inspectors around the globe.

A Committee of the PA representatives (the PIC/S Committee) supervises the operation of the Scheme. All decisions are taken unanimously. The Committee is assisted in its task by (i) various Sub-Committees; (ii) an Executive Bureau, which steers the Organisation in-between meetings; and (iii) a Secretariat, which assists PIC/S bodies in their duties.

This is the Annual Report of PIC/S' activities in 2022.

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# ANNUAL REPORT 2022

## 1. MAIN FEATURES OF THE YEAR

### 1.1 New PIC/S Chairperson

On 1 January 2022, Mr Paul Gustafson from Health Canada / Regulatory Operations and Enforcement Branch (ROEB) became the twenty-fifth Chairperson of PIC/S for the period 2022-23. He succeeds to Ms Anne Hayes (Ireland / HPRA) and is the first PIC/S Chairperson from the American continent in PIC/S' history.



Mr Gustafson was the Deputy Chairperson of PIC/S in 2020-21. He has been an active member of the PIC/S Committee since 2013 and served as a PIC/S Executive Bureau member since 2014, in particular as Chair of the Sub-Committee on the Harmonisation of GMDP, which is one of the largest PIC/S Sub-Committees.

Photo: Mr Paul Gustafson, PIC/S Chairperson

### 1.2 50<sup>th</sup> Anniversary

Covid-19 related travel restrictions continued to impact on PIC/S activities in the first half of 2022 with meetings and training events taking place virtually. The first in-person event was PIC/S' 50<sup>th</sup> Anniversary, which took place in Dublin (Ireland) on 4 October 2022, back-to-back with a PIC/S Committee meeting (on 3 October) and an annual training seminar (on 5-7 October). All events were hosted by Ireland's Health Products Regulatory Authority (HPRA).

PIC/S' 50<sup>th</sup> Anniversary was originally scheduled in June 2021 to coincide with the entry into force of the Pharmaceutical Inspection Convention in 1971, but was postponed to October 2022 due to the pandemic. It consisted of a special symposium entitled "Thriving at 50 and Striving Forward", which highlighted PIC/S' contribution to past and future international co-operation in the field of pharmaceutical inspections. The symposium was opened by HPRA's Chief Executive, Ms Lorraine Nolan. The PIC/S Chairperson, Mr Paul Gustafson (Health Canada), presented on PIC/S new strategic plan for 2023-2027 while the PIC/S Deputy Chairperson, Ms Susan Laska (US FDA), outlined the evolution of pharma industry and PIC/S. The keynote speaker, Ms. Emer Cooke, Executive Director of the European Medicines Agency (EMA), addressed how to strive for better international relationships and collaboration. The programme comprised a wide range of presentations and panel discussions on inspection-related topics, which included participation from Heads of Medicines Agencies, Heads of GMDP Inspectorates and official PIC/S representatives.

Close to 200 participants from all continents participated in the event, including most of PIC/S 54 Participating Authorities and 7 (Pre-)Applicant Authorities, PIC/S Associated Partner Organisations (European Commission, EDQM, EMA, UNICEF, WHO and

WOAH) as well as a number of non-PIC/S Competent Authorities. The anniversary also provided a unique opportunity to meet and engage with a range of invited stakeholders present for the occasion and to reconnect with the wider PIC/S network after the pandemic.



50<sup>th</sup> Anniversary Group Photo

### 1.3 Ukraine

In relation with the war in Ukraine, PIC/S issued the following public statement on 25 March 2022:

*"PIC/S is a non-binding, informal co-operative arrangement among Regulatory Authorities in the field of Good Manufacturing Practice (GMP) of medicinal products for human or veterinary use. It has the legal status of an Association under the Swiss law. PIC/S presently comprises 54 Members, which includes the State Service of Ukraine on Medicines and Drugs Control (SMDC).*

*Given the ongoing tragic events in Ukraine, PIC/S wishes to express its sympathy with all those affected by the war, in particular the most vulnerable: the wounded and the sick. More than ever, patients, whether civilian or military, must be granted indiscriminate access to medicines and medical treatment, irrespective of the circumstances.*

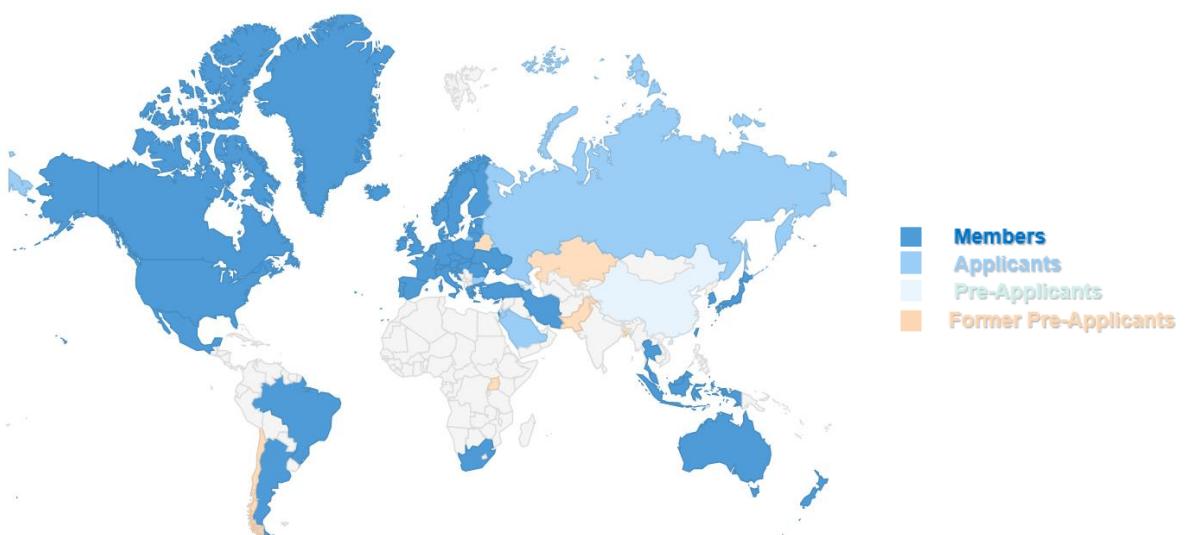
*As any organisation around the world, PIC/S stands by its Members. PIC/S appeals for a peaceful resolution to the crisis to enable all its Members to continue their important work in protecting patient safety, including the inspection of medicinal products. Violence against staff of any PIC/S Member, who are working to ensure the access of patients to medicine, is unacceptable.*

*Peaceful co-operation among Regulatory Authorities is at the very heart of PIC/S. PIC/S wishes to reaffirm that as a technical, non-political organisation, it is more important than ever to promote co-operation between Regulatory Authorities in the field of public health. PIC/S is not an agreement among States. While waiting for peace to return to Europe, PIC/S will continue to work untiringly to protect patient safety."*

## 1.4 Potential new Members

PIC/S' 50<sup>th</sup> anniversary was a welcome opportunity to reach out to potential new members. Several Non-Member Regulatory Authorities were invited to attend the PIC/S Committee meeting in Dublin. The Philippines Food and Drug Administration (PFDA) announced that it intended to re-apply for membership after becoming the 5<sup>th</sup> ASEAN Listed Authority in 2020. Pakistan's Drug Regulatory Authority (DRAP), which went through pre-accession in 2017, also indicated that it would submit a membership application.

The continuous expansion of PIC/S (see map below) shows that the organisation is viewed as a key organisation by more and more Medicines Regulatory Authorities worldwide.



## 1.5 A mix of virtual and in-person training events

With the progressive end of Covid-19 travel and other sanitary restrictions, PIC/S slowly resumed face in-person training events while continuing to organise virtual or hybrid training events in 2022. The following training events were organised:

- A webinar was organised by the Expert Circle on Quality Risk Management (QRM) and hosted by UK / MHRA on 2 March 2022. It was attended by over 250 participants (for more information, see section 21.5).
- The 2022 PIC/S annual seminar was hosted by Ireland / HPRA in Dublin on 5-7 October 2022. The topic was the “Inspection of the Pharmaceutical Quality System (PQS)”. Approximately 200 inspectors from 56 Regulatory Authorities around the world participated in this first post-Covid-19 in-person event (for more information, see section 15.1).
- The Expert Circle on Quality Risk Management (QRM) organised an Advanced Training Event and Meeting in São Paulo (Brazil) on 29 November – 2 December 2022, which was hosted by Brazil / ANVISA. The hybrid meeting was attended by over 177 inspectors from 25 jurisdictions, of which 64 attended in person and 113 remotely (for more information, see section 21.5)

## **1.6 Revision of Annex 1 “Sterile Manufacturing”**

PIC/S continued to contribute to expert discussions and to consult its stakeholders on contemporary GMP issues such as the manufacture of sterile products (Annex 1 of PIC/S-EU GMP Guide). The joint PIC/S-EMA Working Group on Annex 1 successfully completed the revision process, which was tabled for parallel adoption by PIC/S, the European Union, and the World Health Organization (WHO) in 2022.

## **1.7 First pilot training modules are developed by the PIC/S Inspectorates’ Academy (PIA)**

The PIC/S Inspectorates’ Academy (PIA) is a PIC/S training initiative to set up a web-based educational centre in order to provide harmonised and standardised GMP training to inspectors as well as to set up a standardised qualification process of inspectors. PIA continued to unfold in 2022 and a PIA Project Manager was recruited in September 2022.

Following the successful establishment of a PIA Learning Management System (LMS), four e-learning modules were developed:

- The first on Quality Risk Management (QRM) based on ICH Q9 and PIC/S GMP Annex 20;
- The second on auditors training based on the joint EU – PIC/S Auditors Training, which took place on 22-23 March 2022 and recorded by EMA.
- The third on ICH Q12 (basic introduction to inspectors); and
- The fourth on soft skills (supported by the Support Group on Soft Skills).

The first two modules were successfully launched at the end of 2022; the last two modules will be posted on the PIA website in 2023.

In parallel with the development of training modules, new training materials are published on a continual basis on PIA. To facilitate the financing of PIA and in parallel to regular calls for voluntary contributions from PAs, other sources of financing have been explored. In February 2022, a presentation on PIA was delivered to EU Heads of Medicines Agencies (HMA) by the SCT Chairman, Jacques Morénas (France/ ANSM), followed by a meeting with the EU Network Training Centre (NTC).

## **1.8 PIC/S strategic plan (2023-2027)**

PIC/S successfully adopted a Strategic Plan for the period 2023-27 (PS/W 15/2022), which includes a new vision and revised mission for PIC/S:

- PIC/S’ vision is to enable one inspection per site that is fit for all regulatory authorities in the benefit of public health.
- PIC/S’ mission is to strive to improve public health by leading development and implementation of inspection frameworks for human and veterinary medicines through harmonisation of standards and offering world class training to regulatory inspectors around the globe.

The Strategic Plan was published on the PIC/S website and officially presented at PIC/S' 50<sup>th</sup> anniversary in Dublin on 4 October 2022.

## 1.9 Executive Bureau

The Executive Bureau (EB) met in Dublin (Ireland) on 2 October 2022 to discuss objectives, work plan and resource allocation for 2023; PIA operation & funding; and staff issues. This was the in-person meeting of the EB since November 2019.

The EB consists of:

- Mr Paul Gustafson (Canada / ROEB), PIC/S Chairperson;
- Ms Susan Laska (US FDA), PIC/S Deputy Chairperson and Chair of the Sub-Committee on Strategic Development (SCSD).
- Ms Anne Hayes (Ireland / HPRA), immediate past PIC/S Chairperson;
- Mr Jacques Morénas (France / ANSM), Chair of the Sub-Committee on Training (SCT);
- Dr Andreas Krassnigg (Austria / AGES), Chair of the Sub-Committee on Expert Circles (SCEC);
- Mr Ger Jan van Ringen (Netherlands / IGJ), Chair of the Sub-Committee on Budget, Risk and Audit (SCB);
- Mr Ian Jackson (UK / MHRA), Chair of the Sub-Committee on GM(D)P Harmonisation (SCH);
- Dr Kentaro Hara (Japan / PMDA), Chair of the Sub-Committee on Communication (SC COM); and
- Mr Henning Willads Petersen (Denmark / DKMA), Chair of the Sub-Committee on Compliance (SCC).



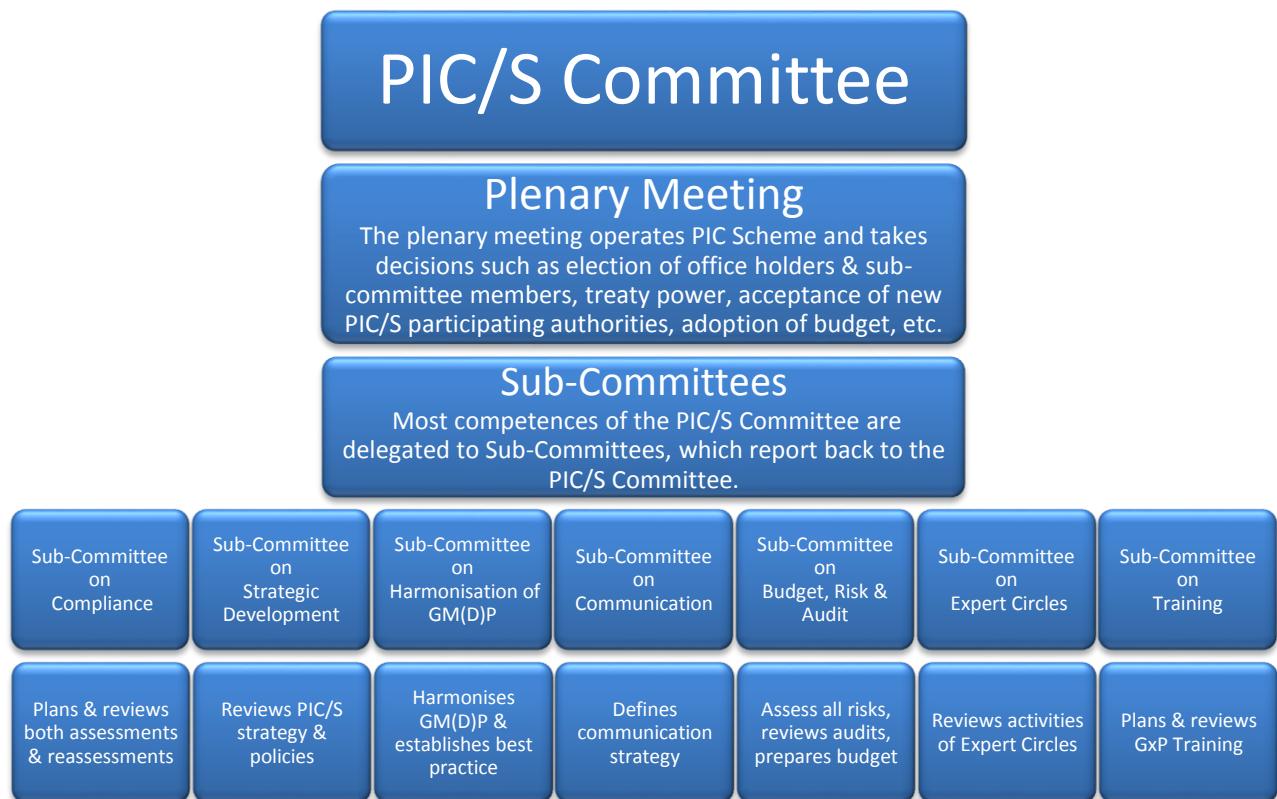
PIC/S Chairperson and PIC/S Deputy Chairperson  
Mr Paul Gustafson (Canada / ROEB) and Ms Susan Laska (US FDA)

## 2. PIC/S SUB-COMMITTEE STRUCTURE

PIC/S has established seven Sub-Committees (SC) in the following fields: Training (SCT); Expert Circles (SCEC); Strategic Development (SCSD); Compliance (SCC); GM(D)P Harmonisation (SCH); Budget, Risk and Audit (SCB) and Communication (SC COM). See also organisational chart below.

The activities of the PIC/S Committee and the seven Sub-Committees are summarised in this Annual Report.

### Overview of PIC/S Sub-Committee Structure



### 3. COMPLIANCE

One of the essential requirements to join PIC/S is that Competent Authorities must have “*the arrangements necessary to apply an inspection system comparable to that referred to in this Scheme and whose requirements and procedures could ensure the proper implementation of the Scheme and contribute to its effective operation*”, as stipulated in the PIC Scheme. Being equivalent is not only required for accession but all the time and duly verified during reassessments. This is why the compliance to the PIC Scheme is one of PIC/S’ most important and critical activities.

This task has been entrusted to the Sub-Committee on Compliance (SCC). For the complete mandate, see box below.

The mandate of the SCC is to:

1. Co-ordinate, plan and monitor all assessments, pre-assessments, re-assessments, etc.
2. Co-operate with the Secretariat on the validation (i.e. completeness) of (pre)applications
3. Plan and review (i) the assessment of Applicants and Pre-Applicants; and (ii) the re-assessment of Participating Authorities (PA)
4. Review and assess communications from Inspectorates, which could trigger a reassessment
5. Pre-select Rapporteur / Team Leader and auditors who are appointed by the CO
6. Review reports and recommendations by Rapporteur / Team Leader
7. Monitor and review corrective actions by Applicants and Re-Assessed PA and ensure that they are followed up and fully implemented
8. Ensure consistency of assessments and re-assessments (and between them)
9. Ensure that Accession, Pre-Accession & Re-Assessment Guidelines (including Questionnaire and Checklist) are implemented / adhered to and make proposals for their amendment
10. Define and review the tools used for assessment and re-assessment of PA (e.g. the audit checklist) in close co-operation with interested parties such as the EMA Compliance Group and EU MRA Partners (in particular Health Canada)
11. Co-operate with EU Joint Audit Programme, the European Heads of Medicines Agency network and other similar initiatives in order to avoid duplication of work
12. Report back to the PIC/S Committee, as provided for in the Terms of References, and summarises discussions on on-going applications
13. Make proposals / recommendations

The Chair of the SCC is Henning Willads Petersen (Denmark / DKMA); the Deputy Chair is Virginie Waysbaum (France / ANSM). The SCC held four virtual meetings in 2022: on 24 February, 19 May, 2 September and 29 November 2022. During these meetings, it discussed membership applications, pre-accession applications, assessment and reassessment procedures as well as contacts with non-Members, as detailed below. Due to Covid-19 related travel restrictions, planned on-site visits had to be rescheduled, as

the year before, with one exception: the distant reassessment of New Zealand / Medsafe was conducted virtually (see section 7.2 below). It also discussed the organisation of a training course for new auditors jointly with the European Commission (EC) and the European Medicines Agency (EMA) (see following section).

## 4. Evaluation and Re-evaluation Procedures

Following the entry into force in 2020 of the PIC/S Guidelines for the Pre-Accession Procedure as well as the Interpretation Guide on the PIC/S Audit Checklist, the SCC revised the PIC/S Guidelines for Accession and a number of other related procedures such as the questionnaire for assessment, the report template, and other documents used either for the assessment of Applicants or for the reassessment of Members under the PIC/S Joint Reassessment Programme (JRP). All these procedures were finalised, adopted by the PIC/S Committee and entered into force on 19 April 2022.

An EC – EMA – PIC/S Auditors Training course, hosted by the EC, took place virtually on 22-23 March 2022. Over 180 participants from 40 different countries participated. The course was recorded and uploaded on PIA.

## 5. Membership Applications

In 2022, PIC/S continued the assessment of the 4 membership applications (see below in alphabetical order). The membership application by the Russian Competent Authorities was frozen – see section 5.4 below.

### 5.1 Armenia / SCDMTE

Armenia's Scientific Center of Drug and Medical Technologies Expertise (SCDMTE) applied for PIC/S membership on 8 September 2017. The application was formally completed on 13 April 2018. However, due to various changes, notably in the legislation, SCDMTE was asked to update its documentation. In 2021, the Rapporteur, Michel Keller (formerly Switzerland / Swissmedic), and the Co-Rapporteur, Mark Cilia (Malta / MAM), were able to finalise their review of the updated documentation. In 2022, a high-level report, prepared by the Rapporteur, was tabled to the SCC for discussion.

### 5.2 Bulgaria / BDA

The Bulgarian Drug Agency (BDA) submitted a complete membership application on 27 August 2018. As BDA went through an audit under the EU Joint Audit Programme (JAP) in 2017 and the report was shared with PIC/S, the application process will be abridged and consist of a partial assessment taking into account the EU JAP audit. The PIC/S audit will also be combined with an MRA assessment by Health Canada.

The appointed Rapporteur, Jacques Morénas (France / ANSM), and the Co-Rapporteur, Ana Rita Martins (Portugal / INFARMED I.P.), have reviewed the JAP report as well as updated documentation submitted by BDA with the support of Esther Ing (Health Canada) as well as Kathleen Sinninger (US FDA). Due to the Covid-19 pandemic and

related travel restrictions, the on-site assessment visit has been put on hold. It is scheduled to take place in early 2023.

### **5.3 Jordan / JFDA**

Following the closure of the pre-accession process on 31 December 2020, the Jordan Food and Drug Administration (JFDA) lodged a membership application on 20 January 2021. The audit team was appointed by written procedure on 10 September 2021 and comprises a Rapporteur, Henning Willads Petersen (Denmark / DKMA), a Co-Rapporteur, Ferenc Lukács (Hungary / NIPN) and a Team Member, Patricia Serpa (Brazil / ANVISA). The on-site assessment visit to JFDA is scheduled to take place in Q3 2023.

### **5.4 Russian Federation / Minpromtorg, Roszdravnadzor, FSI “SID & GP” and FSBI "SCEMD"**

The Competent Authorities of the Russian Federation, as listed below, jointly submitted a complete membership application to PIC/S on 22 December 2020:

- Ministry of Industry and Trade of the Russian Federation (Minpromtorg Russia);
- Federal Service for Surveillance in Healthcare (Roszdravnadzor), including Federal State Budgetary Institution “Information and Methodological Center for Expertise, Accounting and Analysis of Circulation of Medical Products” (FGBU “IMCEUAOSMP” of Roszdravnadzor);
- Federal State Institution “State Institute of Drugs and Good Practices” (FSI “SID & GP”);
- Federal State Budgetary Institution "Scientific Center for Examination of Medical Devices" of the Ministry of Health of the Russian Federation (FSBI "SCEMD").

Due to security and travel restrictions to Russia in relation with the war in Ukraine, the Committee decided in early 2022 to freeze the membership application until conditions allow for an on-site assessment visit.

### **5.5 Saudi Arabia / SFDA**

The Saudi Food & Drug Authority (SFDA) applied for PIC/S membership on 17 February 2020. The Rapporteur, Jacques Morénas (France / ANSM), the Co-Rapporteur, Ferenc Lukács (Hungary / NIPN), and a Team Member, Gülsen Yilmaz (Turkey / TMMDA), were appointed on 26 March 2021. The Rapporteur completed the paper review in the course of the year and a report was shared with the SCC in November 2022. The on-site assessment is scheduled to take place in early 2023.

## **6. Pre-Accession Applications**

In 2022, the following two pre-accession applications were under review (in alphabetical order):

## **6.1 Azerbaijan / AEC**

The Analytical Expertise Center (AEC) of the Ministry of Health of Azerbaijan applied for PIC/S pre-accession on 18 August 2020. The Rapporteur, Nataliya Takhtaulova (Ukraine / SMDC), was appointed on 12 March 2021 and started with the review of the pre-accession application. Ms Takhtaulova left SMDC at the end of 2021 but continued the review at the request of PIC/S. Several videoconferences were organised in the course of the year and the draft report by the Rapporteur was shared with the SCC in November 2022.

## **6.2 China / NMPA**

China's National Medical Products Administration (NMPA) applied for PIC/S pre-accession on 24 September 2021. The Audit Team was appointed by written procedure on 10 December 2021 and consists of a Rapporteur, Jacques Morénas (France / ANSM), a Co-Rapporteur, Raphael Yeung (Hong Kong SAR, China / PPBHK) and a trainee Co-Rapporteur, Kathleen Sinninger (US FDA).

Four videoconferences were organised in the course of 2022 in order for the Team and NMPA to review the indicators of the PIC/S audit checklist. The related high-level report by the Rapporteur was endorsed by the SCC in 2022 and will be formally submitted to the Committee for approval in early 2023.

# **7. Reassessment of Participating Authorities**

In order to ensure that both new members and existing members of PIC/S fulfil the same requirements, high quality standards are maintained and GMP Inspectorates remain equivalent, a Joint Reassessment Programme (JRP) was introduced in 2000 under which existing PIC/S members are reassessed for equivalence on a regular basis. The JRP is run in parallel with the EU's Joint Audit Programme (JAP) and uses the same tools. JAP assessments and JRP reassessments are deemed equivalent. The JRP assessments and reassessments are sometimes combined with the MRA maintenance program of Health Canada, which is following a similar approach, thus contributing to saving resources for regulators and reducing the burden for the audited party.

The reassessment process usually stretches over several years starting with a decision by the Committee to reassess a PA and finishing with the endorsement of the reassessment report.

In 2022, the Committee reviewed the following reassessment processes (in alphabetical order):

## **7.1 Reassessment of Indonesia / NADFC**

The reassessment of Indonesia / NADFC was due to take place in 2020 and then put on hold due to the pandemic. A Rapporteur, a Co-Rapporteur, and a Team Member have been identified. The reassessment process should start in 2023 following their appointment by the Committee.

## **7.2 Reassessment of New Zealand / Medsafe**

In 2019, the Committee appointed the Audit Team, which consists of the Team Leader, Jacques Morénas (France / ANSM), in charge of the on-site assessment visit, and an auditor from Ireland / HPRA, who observed an inspection of an aseptic manufacturer in December 2019.

Due to the pandemic, the on-site visit by the Rapporteur, planned in 2020, was postponed. It was eventually replaced with a desktop assessment, as described in the recently revised JRP procedures. Medsafe was invited to submit all requested documents for its reassessment by 31 December 2021.

The Rapporteur, Jacques Morénas (France / ANSM), and New Zealand / Medsafe organised several videoconferences in 2022 in order to review the documentation. The outcome of the reassessment was positive and a report will be tabled to the Committee for approval.

## **7.3 Reassessment of South Africa / SAHPRA**

The reassessment of South Africa / SAHPRA has been postponed several times since 2019, partly at the request of SAHPRA and partly due to the pandemic. In 2020, SAHPRA and PIC/S agreed to start the reassessment process remotely. Following contacts between SAPHRA and the Rapporteur, Jacques Morénas (France / ANSM), SAHPRA submitted all reassessment documents on 30 September 2021. However, due to other conflicting engagements, the Rapporteur stepped down from his position in 2022 and following a call made to replace him, a new Rapporteur has been identified.

## **7.4 Corrective Action / Update by recently acceded PAs or PAs under Reassessment**

The SCC continued to monitor corrective actions by recently acceded PIC/S PAs or PIC/S PAs under reassessment.

# **8. Non-Members**

Several Non-Member Regulatory Authorities were invited to attend the PIC/S Committee meeting in Dublin in relation with PIC/S' 50<sup>th</sup> anniversary. This was notably the case of Moldova's Medicinal and Medical Devices Agency (MMDA), Pakistan's Drug Regulatory Authority (DRAP), and the Philippines Food and Drug Administration (PFDA).

# **9. GMDP**

The harmonisation of Good Manufacturing Practice (GMP) is at the very heart of PIC/S. More recently, good practices were also harmonised in other fields such as Good Distribution Practice (GDP) or Good Practices for Blood Establishments. The main reasons for adopting common standards are:

- ◆ to maintain high standards of quality in the development, manufacture and control of medicinal products;
- ◆ to promote uniformity in licensing decisions;
- ◆ to promote consistency and uniformity of inspections; and
- ◆ to facilitate the removal of barriers to trade in medicinal products.

The main instrument for harmonisation has been the PIC/S GMP Guide, which PIC/S is striving to keep equivalent in terms of GMP requirements with the EU GMP Guide. Close co-operation with the EMA is thus essential.

The mandate of the Sub-Committee on the Harmonisation of GM(D)P (SCH) is to harmonise GMP, establish best inspection practices, and harmonise the interpretation of GMP to ensure consistency in inspection / audit practices. For the complete mandate, see box below.

The mandate of the SCH is to:

1. Harmonise GM(D)P and establish best inspection practices
2. Ensure the harmonisation and the equivalence of the PIC/S GMP Guide with the EU GMP Guide
3. Encourage the uniform interpretation and application of GM(D)P
4. Co-operate and work closely together with the EC, EMA (GMDP IWG), EDQM and WHO in the field of GM(D)P harmonisation and best practices
5. Co-ordinate with the PIC/S – EMA Liaison Officer and the EMA representative the involvement of PIC/S Experts in EMA GMDP IWG on revision of the GMP Guide, Annexes, Q&A and other relevant guidance documents
6. Make proposals for the drafting of new guidance documents (Aide-Memoire, recommendations, etc.) on the basis of best inspection practices and co-ordinate their revision
7. Review activities, mandates, etc. of Working / Drafting Groups dealing with the harmonisation of GM(D)P – in particular Joint Drafting Groups working on the revision of the EU-PIC/S GMP Guide
8. Harmonise the interpretation of GMP to ensure consistency in inspection / audit practices
9. Supervise the finalisation of guidance documents arising from PIC/S Seminars
10. Identify possibilities for promoting international harmonisation in the field of GM(D)P
11. If the Chair of the SCH is not attending EMA GMDP WG meetings, appoint a Liaison Officer
12. Report back to the PIC/S Committee, as provided for in the Terms of References, and make proposals / recommendations

The SCH is chaired by Ian Jackson (UK / MHRA), who is assisted by Jennifer Maguire (US FDA), Deputy Chair. In the course of 2022, the SCH held four virtual meetings: on 7 April, 29 June, 29 September and 1 December 2022. During these meetings, it discussed various revisions to the PIC/S GMP Guide as well as new or revised guidance documents. The drafting (or revision) of all guidance documents normally follows the same, 3-step process (see box below).

#### **Adoption Process of PIC/S guidance documents**

Step 1: PIC/S internal consultation of Members on a draft guidance, which has been prepared by a dedicated PIC/S Working Group, with the aim of reaching a consensus amongst all PIC/S PAs. In a few exceptional cases, the draft guidance can also be applied on a trial basis by PAs.

Step 2: external public consultation of stakeholders, mainly industry and other associations located in the jurisdictions of PAs as well international professional or industry associations. The consultation may be limited in some cases, either in terms of stakeholders or scope. There is no public consultation for guidance documents, which are intended for inspectors only.

Step 3: adoption by PIC/S of the guidance document, followed by its publication and entry into force.

The SCH also monitored and reviewed the work carried out by a number of Working Groups, operating under the SCH, as detailed below.

## **10. Working Groups under the SCH**

Eight Working Groups are operating under the SCH but not all are active.

### **10.1 Working Group on Annex 1**

The PIC/S Working Group on Annex 1 (manufacture of sterile products) was established at the Rome meeting on 15-16 May 2014. It was then merged with the EMA IWG Drafting Group with a view to jointly revise Annex 1. The joint PIC/S-EMA Working Group includes representatives of the Competent / Participating Authorities of PIC/S and EEA as well as WHO. From 2014 to 2019, the Working Group was led by Andrew Hopkins (UK / MHRA). Since 2019, it has been chaired by Abdelaali Sarakha (France / ANSM).

Following two written consultations of PIC/S PAs and EU/EEA Competent Authorities, the revision of Annex 1 was advanced to Step 2 in December 2017 for a joint public consultation. Over 6,300 comments were received during the 3-month consultation and then reviewed by the Working Group in 2018-19.

This resulted into a new draft of the revised Annex 1, which was submitted to a second joint PIC/S-EMA-WHO public consultation from 3 February to 20 July 2020. Approximately 2,000 comments were received, which were reviewed by the Working Group in 2020-21.

Despite some differences on a number of technical issues, the WG has been able to find compromises thanks to a best-in-class model of international collaboration between EMA, WHO, and PIC/S PAs. The revised Annex 1 to the PIC/S GMP Guide was formally adopted by PIC/S by written procedure on 29 April 2022 and published with a transitional period prior to its entry into force on 25 August 2023 in line with EU Annex 1.

At its meeting in Dublin, the Committee discussed the need to promote Annex 1 and train both industry and inspectors. The Working Group was mandated to develop training material in priority for inspectors focusing on the main differences introduced by the revision with the aim of achieving a uniform interpretation of the revised Annex 1. The latter will also be useful for industry. In addition, inspection skills needed for the successful implementation of the revised Annex 1 will be developed to enable inspectors to inspect in line with the new requirements.

## **10.2 Working Group on the revision of Annex 2**

Following the adoption by the European Commission of the EU Guidelines on GMP for Advanced Therapies Medicinal Products (ATMPs) and the revision of Annex 2 to the EU GMP Guide, a PIC/S Working Group was established in 2018 on the revision of Annex 2 of the PIC/S GMP Guide (manufacture of biological medicinal substances and products for human use).

The Working Group, first chaired by Francesco Cicirello (Australia / TGA) until 2020 and then by Christina Meissner (Austria / AGES), prepared two documents: (i) a new Annex 2A for the Manufacture of ATMP for Human Use based on the requirements of the EU Guidelines on ATMP, and (ii) an Annex 2B for the Manufacture of Biological Medicinal Substances and Products for Human Use based on the revised EU Annex 2 for biologics.

Following a PIC/S-internal consultation and a public consultation, Annexes 2A and 2B were successfully adopted on 1 April 2021 with an entry into force on 1 May 2021.

In 2022, the Working Group and the Expert Circle on Human Blood, Tissues, Cells & ATMP discussed the need to train inspectors on the new Annex 2A on ATMP. See Section 21.4.

## **10.3 Working Group on Data Integrity**

The PIC/S Working Group on Data Integrity was established in 2015 and was co-chaired by Matthew Davis (Australia / TGA) and David Churchward (UK / MHRA) until 2021. Since 2022, it is chaired by Matthew Davis. The Working Group has developed a PIC/S data integrity guidance document to provide inspectors with the basic skills for performing data integrity inspections.

The PIC/S Guidance on Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments (PI 041-1) was adopted by the Committee on 1 June 2021 and entered into force on 1 July 2021 along with a restricted Aide Memoire on inspection of data management and integrity (PI 049), which was also developed by the Working Group and made available to inspectors on the password-protected Members Area.

#### **10.4 Working Group on Harmonisation of the Classification of Deficiencies**

The Working Group on Harmonisation of the Classification of Deficiencies, led by Jenny Hantzinkikolas (Australia / TGA), has drafted a PIC/S Guidance on Classification of Deficiencies (PI 040-1), which was successfully adopted on 25 September 2018 and entered into force on 1 January 2019.

#### **10.5 Working Group on Controlling Cross-Contamination in Shared Facilities (CCCISF)**

The Working Group on Controlling Cross-Contamination in Shared Facilities has prepared an Aide Memoire, which aims at harmonising and standardising terminology used in relation with the control of cross-contamination in shared facilities while addressing questions which inspectors should ask themselves during inspections – in particular in relation with risk management. The Aide-Memoire on Cross-Contamination in Shared Facilities (PI 043-1) was adopted on 17 April 2018 and entered into force on 1 July 2018.

At its meeting in Toyama in November 2019, the Committee mandated a new Working Group on Controlling Cross-Contamination in Shared Facilities (CCCISF) to update the Aide-Memoire PI 043-1. Members of the Working Group were tacitly appointed by written procedure in June 2020. The Working Group, chaired by Simone Pitts (US FDA), operates along with the Expert Circle on CCCISF.

#### **10.6 Working Group on the Revision of PIC/S Guidance Documents for Blood**

The Working Group on the Revision of PIC/S Guidance Documents for Blood, chaired by Christian Schärer (Switzerland / Swissmedic), has been established in order to revise the PIC/S GMP Guide for Blood Establishments (PE 005-3) and the PIC/S Guide to Inspections of Source Plasma Establishment and Plasma Warehouses (PI 008-3) with a view to harmonise them with the EDQM-EC Good Practices Guidelines (GPG) for Blood Establishments.

The Working Group revised PE 005-3, which was renamed “PIC/S Good Practice Guidelines for Blood Establishments and Hospital Blood Banks” (PE 005-4), and converted PI 008-3 into an Aide-Memoire to Inspections of Blood Establishments and Plasma Warehouses (PI 008-4). Both documents were adopted on 9 April 2021 and entered into force on 1 June 2021.

The Working Group is now working on the revision of “PI 019: PIC/S Site Master File for Source Plasma Establishments” and “PI 020: PIC/S Site Master File for Plasma Warehouses”.

#### **10.7 Working Group on the revision of PI 006**

A full revision of the PIC/S Recommendations on Validation Master Plan; Installation and Operational Qualification; Non-Sterile Process Validation; and Cleaning Validation (PI 006-3) has been initiated by a Working Group, led until 2022 by Norman Gray (UK /

MHRA). The aim is to delete repetition with Annex 15 and provide an updated interpretation.

Step 1 (consultation of PAs) was launched on 24 August 2020 and ended on 27 November 2020. The Committee was then consulted on whether to advance the revised recommendations to Step 2 (public consultation). At this occasion, additional comments were received and integrated.

In 2021, the Committee agreed on a focused stakeholder consultation with selected industry and professional organisations. Due to other commitments, notably the organisation of the 50<sup>th</sup> anniversary, this consultation has been put on hold.

## **10.8 Working Group on the Aide Memoire on Tissues and Cellular Therapy Products Inspections**

Following a call to Members in 2019, a Working Group on an Aide Memoire on Tissues and Cellular Therapy Products Inspections has been established with the aim of developing an Aide Memoire. Members were successfully appointed by written procedure on 14 May 2020. The Working Group, chaired by Alyce Maksoud (Australia / TGA), has started its work and is developing an Aide Memoire.

# **11. Revision of the PIC/S and EU GMP Guides and Annexes**

One of the main duties of the SCH is to harmonise GM(D)P guidance documents with the EU, in particular the PIC/S GMP Guide and Annexes, and to transpose EU (proposed) revisions for PIC/S purpose. PIC/S experts are also involved in EMA Drafting Groups on the revision of Chapters and Annexes of the PIC/S-EU GMP Guide in line with the PIC/S-EMA Joint Consultation Procedure.

The following Chapters and Annexes of the PIC/S-EU GMP Guide are in the process of being drafted / revised:

## **11.1 Chapter 1 (Pharmaceutical Quality System) of PIC/S-EU GMP Guide**

The revision of Chapter 1 has been put on hold since 2019 following EMA's business continuity planning. PIC/S will be represented by an Expert in this Drafting Group.

## **11.2 Chapter 4 (Documentation) and Annex 11 (Computerised Systems) of PIC/S-EU GMP Guide**

PIC/S is represented in the EMA IWG Drafting Group on the revision of Chapter 4 and Annex 11 by experts from Australia / TGA and Canada / ROEB. A concept paper was jointly issued by EMA and PIC/S for public consultation on 16 November 2022 for a 2-month period.

### **11.3 Annexes 4 & 5 (Veterinary Medicinal Products)**

The PIC/S Working Group on Veterinary Medicinal Product (VMP), chaired by Grégory Verdier (France / ANSES-ANMV), has temporarily merged with the EMA Drafting Group on the revision of Annexes 4 & 5 of the EU-PIC/S GMP Guide (manufacture of veterinary medicinal products other immunological veterinary medicinal products, and manufacture of immunological veterinary medicinal products).

Following the adoption of the concept papers, the Working Group has started with the revision process and is preparing an outline (skeleton) of the revised Annexes.

### **11.4 Annex 13 (Investigational Medicinal Products) of PIC/S-EU GMP Guide**

The SCH has transposed a revision of EU Annex 13 (Investigational Medicinal Products) for PIC/S purposes. Step 1 (internal consultation of PIC/S PAs) was concluded on 10 February 2019. Step 2 (consultation of non-EEA PA of their national industry associations) ended on 15 November 2019.

The revised Annex 13 was formally adopted by the PIC/S Committee by written procedure on 26 January 2022 with an entry into force on 1 February 2022, which coincides with the entry into force of EC Regulation No. 536/2014 on Clinical Trials. From the date of entry into application of this Regulation, EU Annex 13 has been replaced by 'Detailed Commission Guidelines on good manufacturing practice for investigational medicinal products for human use', pursuant to the second subparagraph of Article 63(1) of Regulation (EU) No 536/2014.

### **11.5 Annex 16 (Certification by an Authorised Person & Batch Release) of PIC/S-EU GMP Guide**

The SCH has discussed a proposal to adapt EU Annex 16 (Certification by the Qualified Person and Batch Release) for PIC/S purposes. As neither the PIC Scheme nor the PIC/S GMP Guide deal with import or import controls, the SCH has recommended that the implementation for import-related requirements, contained in Annex 16, be voluntary for non-EU/EEA PAs of PIC/S.

Following an internal consultation of PIC/S PAs (Step 1), which ended on 10 February 2019, Annex 16 was advanced to public consultation (step 2) on 15 June 2021 for a 3-month period. Comments were reviewed by the SCH and the revised Annex 16 (Certification by the Authorised Person and Batch Release) was formally adopted by the PIC/S Committee by written procedure on 26 January 2022 with an entry into force on 1 February 2022.

### **11.6 Annex 21 (GMP Obligations for Importation to the EU) of EU GMP Guide:**

PIC/S was represented by Switzerland / Swissmedic in this Drafting Group on Annex 21 of the EU GMP Guide, which entered into force on 21 August 2022. Following a review of draft Annex 21, the SCH recommended to the PIC/S Committee to not transpose it for PIC/S purposes.

## 12. Other Harmonisation Activities

### PIC/S Inspection Report Format

In order to align the PIC/S SOP on Inspection Report Format (PI 013-3) with the PIC/S Guidance on the Classification of Deficiencies (PI 040-1), in particular with regard to the definitions of critical, major, and other deficiencies, the SCH started a revision of PI 013-3. A first draft was advanced to Step 1 on 4 April 2019 with a deadline for comments until 31 May 2019. In 2020, the revision of the SOP was put on hold due to other priorities.

In 2021, the SCH reviewed and integrated comments received during Step 1. A revised draft SOP (PI 013-4, Draft 2) was advanced to Step 3 (adoption) on 8 December 2021, with possible comments or objections due by 15 January 2022.

In 2022, the revision was put on hold due to parallel discussions by the Committee on the ‘Joint Reflection Paper on Pharmaceutical Quality Knowledge Management System’ (PQ KMS) – see section 24 – and the need to fully harmonise the PIC/S Inspection Report format with the inspection report format used in the EU (as per Compilation of Community Procedures).

### WHO Initiative on Environmental Control Measures

At its meeting in Dublin, the Committee agreed to support an initiative by WHO to draft a guideline to address environmental control measures at sites where antimicrobials are manufactured as finished products or APIs for human or veterinary use. Antimicrobial resistance is also mentioned in the PIC/S Strategic Plan for 2023-27.

### Planned revisions

GMP guidance documents are periodically revised to comply with updated GMP requirements and technological progress. A number of guidance documents are due for revision or undergoing revision. This is notably the case of:

- PI 011-3 “Good Practices for Computerised Systems in Regulated “GXP” Environments”;
- PI 023-2: “PIC/S Aide-Memoire on the Inspection of Pharmaceutical Quality Control Laboratories”;
- PI 030-1: “PIC/S Aide-Memoire on the Inspection of APIs”; and
- PE 010-4: “PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments (in order to include an EMA / EU Parenteral Nutrition guidance as an appendix).

All PIC/S guidance documents are available on the PIC/S website <https://www.picscheme.org/en/publications>.

## 13. PIC/S Library

The PIC/S library is a project to establish a list of all available documents related to GM(D)P inspection drafted by Members and Partner Organisations. A first, partial compilation has been available to PIC/S inspectors on the password-protected website.

In conjunction with the PIC/S library, ECA, ISPE and PDA have continued to share GMP-related guidance documents with PIC/S, which are also made available to inspectors on the password-protected website. These guidance documents contain very useful technical information.

## 14. TRAINING

Harmonising GMP requirements through the PIC/S GMP Guide is not sufficient to ensure a uniform interpretation and application of GMP. Notably, the training of GMP inspectors is an essential tool to achieve this goal. This is why the training of GMP inspectors is a core activity, essential in terms of PIC/S meeting its goals. PIC/S has also opened its training programme to inspectors active in other areas such as Good Practices for Human Blood, Tissues, Cells & ATMPs, Good Distribution Practice (GDP), Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP).

The Sub-Committee on Training (SCT) is the oldest Sub-Committee and was initially established as a Working Group under the PIC/S Committee. Its mandate has remained by and large the same over the past decades – see box below.

The mandate of the SCT is to:

1. Identify training needs
2. Co-ordinate and monitor PIC/S training activities
3. Review the planning and organisation of annual training seminars, in particular:
  - propose and validate the seminar topic,
  - review the seminar programme,
  - assess the seminar report,
  - make recommendations for future seminars,
  - propose amendment to the Aide Memoire on the Organisation of Seminars (PI 003).
4. Monitor the Joint Visits Programme and the Coached Inspection Programme and carry out a review of reports in order to identify divergences on GMP interpretation and inspection practices
5. Ensure the rotation of training between the various regions, taking into consideration the expansion of PIC/S
6. Consider proposals for co-operation with professional organisations (e.g. ISPE, PDA) in the field of training
7. Report back to the PIC/S Committee, as provided for in the Terms of References, and make proposals / recommendations

The SCT is chaired by Jacques Morénas (France / ANSM); the SCT Deputy Chair is Y-H (Ellen) Chen (Chinese Taipei / TFDA). The SCT met four times by videoconference in 2022: on 11 April, 21 June, 19 October and 22 November 2022. It discussed the

development of the PIC/S Inspectorates' Academy (PIA) as well as the planning and organisation of PIC/S training events.

The following training events were successfully organised by PIC/S in 2022 (in chronological order):

Date	Place	Activity	Organised by
2 March 2022	Virtually in London (UK)	Webinar on Quality Risk Management (QRM)	UK / MHRA & PIC/S Expert Circle on QRM
5-7 October 2022	Dublin (Ireland)	PIC/S 2022 Seminar on the "Inspection of the Pharmaceutical Quality System (PQS)"	Ireland / HPRA
29 November – 2 December 2022	São Paulo (Brazil)	Advanced Training Event and Expert Circle Meeting on QRM	Brazil / ANVISA & PIC/S Expert Circle on QRM

## 15. Annual Training Seminar

PIC/S arranges an annual Training Seminar for inspectors, with each Seminar dealing with a specific topic and hosted by a different PIC/S PA. The SCT, jointly with the PIC/S Committee, reviews the organisation and outcome of annual seminars in line with the PIC/S Aide Memoire on the Organisation of Seminars.

### 15.1 2022 Seminar

The 2022 seminar was hosted by Ireland / HPRA on the "Inspection of the Pharmaceutical Quality System (PQS)". This seminar took place in Dublin (Ireland) on 5-7 October 2022 and was attended by around 200 inspectors from 56 Agencies. All continents were represented.



The seminar consisted in presentations, case studies, panel discussions and workshops. Presentations focused on what a PQS is and how its effectiveness is assessed through the inspection of product quality reviews (PQRs), annual product reviews (APRs), deviations & CAPA management, change management, and management of out of specification (OOS) investigations. There were also discussions on risk-based inspections in the assessment of the PQS as well as on strategies to manage and reduce quality related drug shortages.

The parallel workshops were run on the same topics, presented earlier during the seminar, but focused on case studies and interactive discussions between inspectors.

The workshops were on the following 4 topics:

- The inspection of PQRs/APRs;
- The inspection of deviations & CAPA;
- Change management; and
- The inspection of the management of OOS investigations.

The last day consisted in presentations from both industry and regulators on the “forward vision of pharmaceutical quality systems in the context of product lifecycles aligned to ICH Q10 and ICH Q12 principles” as well as a feedback on the workshops’ outcome.



Dublin Seminar Group Photo

## 15.2 Past and Future Seminars

In 2022, the SCT and the Committee reviewed:

- The evaluation report on the 2021 Seminar on “GMP Assessment Approaches in Post COVID-19 Era”, which was virtually hosted the Ministry Food and Drug Safety (MFDS), Republic of Korea on 9-11 November 2021.
- The preparations of the 2023 Seminar on “Soft skills that make a good GMP/GDP inspector in 2023” to be hosted by Thailand / Thai FDA in Bangkok on 8-10 November 2023.

At its meeting in Dublin, the Committee accepted an invitation by Brazil / ANVISA to host the 2024 Seminar in Brazil while Hong Kong SAR, China / PPBHK signalled its interest to host the 2025 Seminar.

## 16. Joint Visits Programme / Coached Inspection Programme

The PIC/S Joint Visits Programme (JVP) and Coached Inspections Programme (CIP) continued to be suspended in 2022, partly due to COVID-19 related travel restrictions in the first half of 2022 and partly because the JVP needs to be completely restarted after an interruption of almost three years.

The JVP is open to PIC/S inspectors specialised in specific fields (for the functioning, see box below). The participation in the JVP has been progressively extended from GMP inspectors to GDP, GCP and GVP inspectors. Joint Visits Groups for GCP/GVP are co-ordinated by the PIC/S Working Group on GCP/GVP.

In order to participate in the JVP, inspectors must be employed by PIC/S PAs. Non-Member inspectors cannot join joint visits groups with the exception of GCP/GVP inspectors from either PIC/S Applicant Authorities or PIC/S jurisdictions, where the competence for GCP/GVP is not with the PA.

The SCT has started working on a revision of the JVP Guidelines in order to clarify and improve the operation of the programme. The revision has been put on hold.

#### **PIC/S Joint Visit Groups**

*Another means of training inspectors of the PIC/S countries has been devised in the form of joint visits to manufacturers by inspectors of different countries. Groups of three inspectors are set up on the basis of applications sent to the PIC/S Secretariat. Each inspector is assigned within his/her group to act in turn as host for one year and guest for the other two years.*

*Visits are carried out in English or in a language commonly agreed by inspectors. Joint reports are drafted after each visit and sent to the Committee for evaluation.*

*The organisation of the joint visits has proved an excellent means for the further training of inspectors through mutual exchange of experience and a useful contribution to the maintenance of mutual confidence between competent authorities. Participants have also the possibility to discuss and compare their inspection methods and their interpretation of GMP rules.*

## **17. PIC/S New Inspector Training Course**

From 2011 to 2019, Ireland / HPRA has run, on behalf of PIC/S, a “New Inspectors Training Course” (NITC) in Dublin (Ireland). This course is essentially designed for newly recruited inspectors. It is very popular amongst PIC/S inspectors and always well attended. A “Train the Trainer” course was also organised back in 2014 in order to complement the NITC. Following a request by the SCT, Ireland / HPRA has agreed to conduct the NITC on a regular basis every 18 months with the support of trainers of other PIC/S PAs. NITCs have been put on hold due to the pandemic and related travel restrictions.

## **18. PIC/S Inspectorates’ Academy (PIA)**

The PIC/S Inspectorates’ Academy (PIA) is the most prominent project under development in PIC/S. It is a global capacity building initiative in the field of training, developed by PIC/S PAs, which aims at delivering harmonised and standardised training to GMDP inspectors and establishing a uniformed qualification process of inspectors in order to ensure that high quality standards for medicinal products are met worldwide in

the interest of public health (see box below). The PIA motto is “Inspection Excellence through Harmonised Training”.



## THE PIC/S INSPECTORATES' ACADEMY (PIA)

PIA aims at delivering:

- Training to improve inspection expertise in the manufacturing of medicines and of their distribution
- for regulators by regulators, developed on the basis of PIC/S recognised GMP training experience and expertise since 1971
- supported by 54 PIC/S Participating Authorities from all continents
- for close to 2,000 inspectors worldwide
- offering currently over 1,100 training materials and 350 training videos
- webinars, on-line learning tools, forum which are in development
- a library of relevant GMP references.

This web-based educational centre, placed under the PIC/S umbrella, will not only deliver general or advanced training but also serve as a platform for discussion and sharing among regulators thus contributing to global harmonisation and interpretation of GMP. It offers a single point of access to all PIC/S training activities. The initiative already benefits from a strong support from Head of Agencies, PIC/S Members (and non-Members) as well as interested Partner Organisations and Third Parties. It is an ambitious project which will span several years and be implemented in stages. It is run and monitored by the Sub-Committee on Training.

The idea to establish a professional “Inspectors’ Academy” delivering a variety of courses ranging from general training to highly specialised training for inspectors was presented for the very first time at PIC/S’ 40th Anniversary in 2011. The harmonisation and calibration of training as well as the standardised qualification of GMP Inspectors are key to a consistent interpretation and uniformed application of GMP by inspectors worldwide. This is key to mutual trust, which in turn will allow for mutual reliance between Competent Authorities (in line with the PIC/S Guidance on GMP Inspection Reliance). This will allow not only to maximize inspectional resources but also to strengthen the protection of public health by ensuring effective, high-quality and comparable GMP inspections for the quality of regulated pharmaceutical products.

PIA will also help pool together training resources for PIC/S PAs and thus contribute to cost savings for Agencies while strengthening co-operation, harmonisation and resource sharing in the field of training.

PIA was officially established at the PIC/S Committee meeting in Paris (France) on 20-21 October 2014 and followed a 3-stage development model. Stage 1 of the Academy consisted in successfully launching the PIA website and incorporate all existing PIC/S training. Stages 2 & 3 are in progress and will encompass a fully integrated learning management system extending the current training resources available, on the basis of a harmonised training curriculum. The latter provides for 3 levels: basic, specialised and

ongoing. Delivery and monitoring are to be optimised and the training curriculum steps to result in recognised certification.

Over the past few years, thanks to a generous grant by Chinese Taipei / TFDA, a Learning Management System (LMS) has been successfully developed to include e-learning modules. The LMS is the backbone for the management of PIA's training tools and content.

In parallel, a harmonised PIA Training Programme has been developed, including a training curricula and cycle (see chart below) as well as a qualification process. The PIA Training Programme aims to define harmonised minimum requirements for the training of inspectors in specific fields (e.g. API, sterile, biologicals, etc.). Training is based on high quality training materials focusing on GMP requirements and inspection skills, to be delivered through various formats. The formats are provided either through training tools offered by PIA or by the PIC/S PAs or both. While PIC/S establishes a PIA Training Programme, PAs remain responsible for the training and is exclusively responsible to determine the training for each inspector.



Outline of PIA Training Cycle

In 2022, with the assistance of the Expert Circle on QRM, the PIC/S Secretariat developed a pilot e-learning module on Quality Risk Management (QRM) based on ICH Q9 and PIC/S GMP Annex 20. A curriculum on QRM for GMP Inspectorates has also been published on the password-protected part of the PIA website. The Secretariat also developed, with the assistance of the PIC/S Working Group on ICH Q12 Training Material, a training module on ICH Q12 (basic introduction to inspectors).

Two other modules were developed in the course of 2022 and will be posted on the PIA website in 2023:

- A training module on soft skills (supported by the Support Group on Soft Skills);
- A training module on auditors training based on the joint EU – PIC/S Auditors Training, which took place on 22-23 March 2022 and which was recorded by EMA.

In parallel with the development of training modules, new training materials are published on a continual basis on PIA. As of 31 December 2022, over 1,100 PIC/S training materials and videos were available on PIA of which a large number have been rated according to their relevance and level (e.g. for new inspectors) with respect to a future training curriculum.

The increase of human and financial resources to ensure the successful development of PIA remains a constant priority for PIC/S. A PIA Project Manager was recruited in September 2022. A project plan on PIA has been developed to ensure the adequate and timely planning of the project alongside a 5-year Budget Plan (2020-2024). Calls for voluntary contributions from PAs are made on an annual basis. Other sources of financing are explored. In February 2022, a presentation on PIA was delivered to EU Heads of Medicines Agencies (HMA) by the SCT Chairman followed by a meeting with the EU Network Training Centre (NTC).

## 19. Co-operation with other Agencies & Organisations

The annual GMP Training Course, organised by Japan / PMDA and the Asia Training Center (ATC), was held virtually on 25-26 October 2022 on Data Integrity with the support of PIC/S. The seminar was opened by the PIC/S Chairperson and a presentation provided by the Chairman of the PIC/S Working Group on Data Integrity, Matt Davis (Australia / TGA).

Following the signing of a Memorandum of Understanding (MoU) with ISPE on 8 June 2021, a trial review of ISPE's e-learning offer has been performed in relation with the development of the e-learning QRM Training module for PIA. A draft content license agreement has also been proposed by ISPE, which is under consultation.

## 20. EXPERT CIRCLES

PIC/S Expert Circles have been set up by the PIC/S Committee to facilitate the discussions and the exchange of information among inspectors specialised in a specific area of GMP such as blood, computerised systems, active pharmaceutical ingredients, quality risk management, etc. Expert Circles meet regularly to develop draft guidance, recommendations, etc. and offer training in their respective fields of specialisation.

The main task of the Sub-Committee on Expert Circles (SCEC) is to review the composition and functioning as well as the various mandates of the Expert Circles. The mandate of the SCEC is detailed in the box below.

The mandate of the SCEC is to:

1. Identify the need to create / terminate Expert Circles
2. Co-ordinate and monitor activities and meetings of Expert Circles
3. Ensure that activities of Expert Circles are in line with their respective mandates, as approved by the PIC/S Committee, as well as with the Guidelines for PIC/S Expert Circles (PI 022)

4. Review the planning and organisation of Expert Circles meetings, in particular:
  - validate the yearly objectives as well as meetings' objectives
  - review the programme
  - assess the meeting report
  - make recommendations for future meetings
  - ensure that Guidelines on Expert Circles are implemented / adhered to
  - propose amendment to the Guidelines on Expert Circles
5. Report back to the PIC/S Committee, as provided for in the Terms of References and make proposals / recommendations

The SCEC is chaired by Andreas Krassnigg (Austria / AGES), who is assisted by Marisa Delbò (Italy / AIFA), Deputy Chair. The SCEC met once during the year on 27 April 2022. Five Expert Circles and three Working Groups operate under the SCEC – their activities (in the alphabetical order of the Expert Circle) are described below.

### **20.1 Expert Circle on API**

The Expert Circle on Active Pharmaceutical Ingredients (APIs) was established by PIC/S in 2005. It meets on average every two years. The Expert Circle last met in Madrid on 7-9 October 2019. There are plans to revive the Expert Circle.

### **20.2 Expert Circle on Controlling Cross Contamination in Shared Facilities**

The Expert Circle on Controlling Cross Contamination in Shared Facilities (CCCSIF) was established in 2017. First led by Graeme McKilligan (UK / MHRA), it is chaired by Vimal Sachdeva (WHO) since 2020.

The 1<sup>st</sup> Expert Circle meeting was hosted by Chinese Taipei / TFDA in Taipei on 19-21 June 2019. The 2<sup>nd</sup> Expert Circle meeting was virtually hosted by WHO on 14-15 December 2021 and the related report was reviewed by the SCEC and the Committee in 2022. The Expert Circle's mandate is currently under revision.

### **20.3 Expert Circle on GDP**

The Expert Circle on Good Distribution Practice (GDP) was established in 2013 and is chaired by Karen Ford (South Africa / SAHPRA). The Expert Circle organised five meetings between 2013 and 2018. It was supposed to meet Kyiv (Ukraine) in May 2020 but the meeting was cancelled due to the pandemic. A virtual meeting is likely to take place in 2023.

The Co-ordinating Committee of the Expert Circle on GDP has developed a new mandate, which was reviewed by the SCEC in 2022. The Co-ordinating Committee also successfully completed the adoption process of (i) the PIC/S Aide-Memoire on the Inspection of Good Distribution Practice for Medicinal Products in the Supply Chain; and (ii) Questions & Answers regarding the PIC/S GDP Guide. Both documents, which were initiated in 2017, will enter into force in 2023.

## **20.4 Expert Circle on Human Blood, Tissues, Cells & ATMPs**

The Expert Circle on Human Blood, Tissues and Cells is the oldest Expert Circle in PIC/S. In 2015, the Expert Circle expanded the scope of its mandate to include Advanced Therapies Medicinal Products (ATMPs). A revised mandate was adopted by the Committee in 2021. The Expert Circle is led by Marisa Delbò (formerly Italy / AIFA).

The Expert Circle last met in Jakarta on 8-10 October 2019 and was supposed to reconvene in 2021. However, due to the pandemic, this did not materialise. The Co-ordinating Committee of the Expert Circle investigated alternative activities in co-operation with other organisations such as the EU Commission Expert Sub-Group on Inspections in the Blood, Tissues and Cells Sectors (IES) and PDA (see 2021 Annual Report).

In 2022, the PIC/S Committee agreed on an offer by Austria / AGES to host a joint virtual Expert Circle meeting and a training webinar on Annex 2A, which will take place in March 2023. The Co-ordinating Committee of the Expert Circle met virtually to prepare the events and discuss the related programmes.

The Chair of the Expert Circle on Human Blood, Tissues, Cells and ATMPs (BTCA), Marisa Delbò (Italy / AIFA), also prepared three PIA draft training curricula for inspectors, which were circulated for comments to the Co-ordinating Committee and IES (in order to avoid any duplications). These are:

- Draft training curriculum for inspector for Advanced Therapies Medicinal Products (ATMPs);
- Draft training curriculum for inspector for Blood Establishments, hospital blood banks and plasma warehouses (BE);
- Draft training curriculum for inspector for Tissues & Cells Establishments (T&CE).

## **20.5 Expert Circle on QRM**

The Expert Circle on Quality Risk Management (QRM) was initially established in 2007 and has since organised a series of Advanced QRM Training Courses in line with its mandate, which was revised in 2017 and 2021.

The Expert Circle was very productive in 2022 and organised two events:

- A QRM training webinar was hosted virtually on 2 March 2022 by UK / MHRA. The webinar consisted in a 0.5-day event and was attended by over 250 participants. Three topics were discussed: QRM, the effectiveness of Pharmaceutical Quality Systems (PQS), and the revision of the Aide-Memoire on QRM.
- An Expert Meeting and Advanced Training on QRM was organised by Brazil / ANVISA in São Paulo (Brazil) on 29 November – 2 December 2022. This event in Brazil was the 5<sup>th</sup> such training event, and addressed topics not covered previously, including the ongoing revision of ICH Q9 and the ongoing revision of the PIC/S Aide Memoire on QRM Implementation. The hybrid event was conducted both in-person and remotely: it took place physically in the city of São Paulo with virtual remote transmission by videoconference. In terms of remote participation, 113 inspectors successfully took part representing 25 different jurisdictions. Physically, 64 inspectors participated in person representing authorities from 13 different jurisdictions and 2 international organisations.

An ad-hoc Working Group under the Expert Circle, led by Rick Friedman (US FDA), is working on a revision of the PIC/S Aide Memoire on QRM Implementation (PI 038-1).

## **20.6 Working Group on GCP / GVP**

The Working Group on Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP) was established in July 2014 with the aim to facilitate technical co-operation and harmonisation of practices (including the development of guidance and training material), capacity building and information sharing. From 2014 to 2019, the Working Group was led by Mandeep Rai (UK / MHRA). Since 2019, it is chaired by Mandy Budwal-Jagait (UK / MHRA).

The Working Group is very active in the field of training through the PIC/S Joint Visits Programme (JVP), allowing 3 inspectors from 3 different countries to team up in order to observe inspections in each country with a view to comparing inspections procedures and techniques. It has prepared JVP specific guidelines for conducting GCP and GVP Inspections. Due to the pandemic, all Joint Visit Groups have been put on hold and not restarted yet.

In 2021, the Committee endorsed a proposal by the Working Group to establish two distinct Expert Circles: one on GCP and one on GVP. Both will promote the Joint Visits Programme. The Expert Circle on GCP will have a Working Group on ICH M10 (multidisciplinary) as well as a Working Group for computerised systems. The Expert Circle on GVP will have WG on artificial intelligence and machine learning.

In 2022, a call was issued by the Secretariat to identify possible volunteers who could establish the future Expert Circles on GCP and GVP. As a next step, the Co-ordinating Committees will be established.

## **20.7 Working Group on Medicinal Products for Veterinary Use (VMP)**

In 2016, the Committee established an ad hoc group in order to assess the need to have a specific platform in PIC/S on Veterinary Medicinal Products (VMP). It was succeeded by a Working Group on VMP, which was formally established in April 2019. It is chaired by Grégory Verdier (France / ANSES-ANMV) with Jason Todd (UK / VMD) acting as Deputy Chairman.

In 2020-21, the Working Group prepared two concept papers on the revision of veterinary specific GMP guidelines (Annex 4 on Manufacture of Veterinary Medicinal Products other than Immunological Veterinary Medicinal Products and Annex 5 on Manufacture of Immunological Veterinary Medicinal Products) through a joint EMA-PICS drafting group.

The concept papers were published by both PIC/S and EMA for public consultation and comments reviewed by the Working Group in the course of 2022. For the next step, see section 11.3.

## **20.8 Working Group on Computerised Systems**

The Working Group on Computerised Systems, chaired by Ib Alstrup (Denmark / DKMA), has been mandated to revise the PIC/S Good Practices for Computerised Systems (PI 011), which is partially outdated. The Working Group has been put on hold following

the launching of the revision of Annex 11 (Computerised Systems) of the EU-PIC/S GMP Guide, which will impact on the PIC/S guidance. The revision process started in 2022.

## 21. STRATEGIC DEVELOPMENT & CO-OPERATION

The Sub-Committee on Strategic Development was set up in 2009 in order to discuss, the outcome of a survey on how to improve the operation of PIC/S. It proposed to establish a sub-committee structure under the PIC/S Committee, which was implemented in 2014.

The mandate of the SCSD has since then been widened to define PIC/S' strategies and future policies and to make proposals on how to improve the structure and the operation of PIC/S as well as co-operation with PIC/S Associated Partner Organisations. For the full mandate, see box below.

The mandate of the SCSD is to:

1. Define and review PIC/S strategy and (future) policy
2. Make proposals / recommendations on how to improve the structure and the operation of PIC/S
3. Ensure the implementation of strategical policies (e.g. roadmaps such as the Blueprint) as well as strategical decisions
4. Discuss new projects for PIC/S and make proposals on the possible "expansion" of PIC/S' mandate to other areas
5. Address implementation of new projects and resource management – in particular funding (e.g. external) – in consultation with PIC/S PA and Heads of Agencies
6. Review co-operation with Partners and make proposals / recommendations for the possible improvement of the co-operation
7. Promote the participation of authorities interested in the PIC Scheme
8. Report back to the PIC/S Committee, as provided for in the Terms of References and make proposals / recommendations

The SCSD has taken a number of initiatives aiming at strengthening international regulatory co-operation in the field of GMP. The objective of these initiatives is to improve the sharing of GMP information between PIC/S PAs as well as to facilitate mutual reliance on a voluntary basis.

The SCSD is chaired by Susan Laska (US FDA). Tracy Moore (UK / MHRA) was the Deputy Chair until November 2021. The SCSD met virtually on 23 February 2022. Five Working Groups operate under the SCSD, as listed below. The setting up of a 6<sup>th</sup> Working Group to review a proposed PIC/S pilot on the management of borderline compliance cases has been put on hold.

## **22. Policy to remain non-political & non-discriminatory**

At the virtual PIC/S Committee meeting in October 2021, the SCSD Chair presented a draft policy paper which aims at ensuring that “*PIC/S remains at all times a scientific, technical organisation, which is non-political, non-discriminatory and egalitarian*”. The policy is mainly codifying past practices and clarifying them where necessary. A mechanism to enforce the policy is also foreseen.

PAs were duly consulted on the paper on 14 December 2021 with a deadline until 28 January 2022 to provide their feedback. Following the positive feedback of PAs, the SCSD prepared several documents, which – following another consultation of PAs during the summer (30 June – 31 July 2022) – were successfully adopted on 14 September 2022. These documents are:

- Policy to maintain PIC/S as a non-political, non-discriminatory organization (PS/W 12/2021);
- Amendment of the Committee’s Rules of Procedure (PH/PS 9/97 (Rev. 5));
- Procedure on the suspension / exclusion of representatives and Participating Authorities (PS/W 10/2022).

16. The documents were included in the Compilation of PIC/S Documents with an entry into force on 1 October 2022.

## **23. Working Groups operating under the SCSD**

### **23.1 Unique Facility Identifiers (UFI)**

The PIC/S Working Group on the Unique Facility Identifiers (UFI) for drug establishments was established in 2016 following a survey by US FDA showing that PIC/S PAs use different systems to identify the location of a drug manufacturing site. The purpose of the Working Group is to create a harmonised and consistent system in order to localise a manufacturing site. The Working Group consists of representatives of Canada / ROEB, EDQM, EMA, Spain / AEMPS, UK / MHRA and US FDA. It is co-chaired by Susan Laska (US FDA) and Jennifer Maguire (US FDA),

In January 2022, the Committee endorsed a proposal by the WG to collect, verify, and use WGS84 geographic coordinates (geocoordinates) in a specific format, along with name and address of a facility, as well as the existing national identifier, to aide in the identification of global pharmaceutical manufacturing facilities, for both national and third country inspections. The proposal was revised in May 2022 in order to include geocode precision fields. In order to implement the proposal, other steps will be taken, amongst others, a survey to ensure that the geocodes can be included in the databases of all inspectorates; a revision of the PIC/S inspection report format as well as the Site Master File (SMF). Through the SMF, companies will provide geocodes, which will then be verified and validated by inspectors during on-site inspections.

## **23.2 Inspector Safety**

The Inspector (Travel) Safety Working Group (ISWG) was established following the 2016 Seminar in Manchester. Its mandate was approved at the Committee meeting in Chicago in September 2018. The Working Group was led by Tracy Moore (UK / MHRA) until November 2021. It comprises representatives from Australia / TGA, Brazil / ANVISA, Canada / ROEB, EDQM, Indonesia / NADFC, Ireland / HPRA, Netherlands / IGJ, Sweden / MPA, Thailand / Thai FDA, UK / MHRA, and US FDA.

The aim of the Working Group is to consider means to mitigate health, security or site-related risks affecting inspectors. In 2020, the Working Group drafted a guidance document related to “COVID-19 risk assessment for routine on-site inspections” (PI 055-1), which – following adoption by the Committee – entered into force on 15 July 2021.

The Working Group did not meet in 2022, pending the appointment of a new Chair.

## **23.3 Informants**

The Working Group on Informants, co-led by UK / MHRA and US FDA, was set up in 2019 following the adoption of a mandate focusing on three priorities: the definition and distinction between “informants” and “whistle blowers”; the limitations regarding inspectors’ involvement; and how to handle intelligence from informants.

Due to the pandemic and other priorities of the SCSD, the Working Group has been put on hold.

## **23.4 Inspection Reliance**

Although the Working Group on PIC/S Inspection Reliance was only established in 2020, inspection reliance has a long history in PIC/S.

In the context of increased foreign inspections, PIC/S adopted in 2009 a procedure for team inspections (PI 031-1). In 2012, it established an annual list of planned foreign inspections to be carried out by PIC/S PAs and Partner Organisations with the aim of reducing duplicate foreign inspections. In 2015, PIC/S adopted a “Procedure to inform Foreign Regulatory Agencies of Foreign Inspections to be conducted in their Jurisdiction” (PI 039-1). The same year, a survey was conducted on how PAs addressed the issue of “same scope inspections”, i.e. GMP inspections, which have the same scope and which are thus redundant. The outcome of the survey identified similarities and differences between PAs in accepting (or refusing) information on GMP inspections from other PAs.

In 2017, the Committee accepted an offer from the International Coalition of Medicines Regulatory Authorities (ICMRA) to adapt an ICMRA draft Guidance on Inspection Reliance for PIC/S purpose. The aim of this guidance is to maximise inspection resources by relying on other trusted Regulatory Authorities for the GMP compliance of overseas facilities. The PIC/S network provides a strong foundation for this process by ensuring the capability of PAs via the PIC/S accession process and Joint Reassessment Programme. The PIC/S Guidance on Inspection Reliance (PI 048-1) was adopted by the Committee in April 2018 with an entry into force on 1 June 2018.

In order to measure the efforts made by PIC/S PAs to rely on each other in line with the inspection reliance initiative, PIC/S PAs were invited in 2019 and 2020 to collect statistics on the number of desk-top assessments made by PAs. These assessments are made on the basis of an already existing GMP certificate or GMP inspection report and allow agencies to waive a foreign inspection. The survey showed that over 7,000 inspections are waved annually by PIC/S PAs. It also showed that some PAs do not rely on PIC/S inspection reports from other PAs.

In order to identify barriers that prevent PAs to rely on already existing inspection reports, the Committee, based on a proposal by the SCDC, established a Working Group on Inspection Reliance on 6 October 2020. The Working Group, led by Stephen Farrell (Australia / TGA), comprises 7 Agencies, namely Australia / TGA, Canada / ROEB, EMA, Switzerland / Swissmedic, UK / MHRA, UK / VMD and US FDA.

The Working Group has prepared a survey to identify barriers to inspection reliance. The survey was circulated to PAs in 2022. The deadline to complete the survey has been extended to early 2023 to allow all PAs to respond. As a next step, the WG will review the data and prepare a report.

### **23.5 Remote Assessment**

Following the PIC/S Seminar on "Distant Assessment of GMP Compliance", organised by Finland / FIMEA on 8-10 December 2020, the PIC/S Committee agreed to establish a Working Group on Remote Assessment. The Working Group was formally established on 1 October 2021. It is chaired by Jenny Hantzinkikolas (Australia / TGA) and comprises 25 WG Members from 16 PAs and 2 Partner Organisations (EDQM and EMA).

The WG first discussed its mandate, which was adopted by the PIC/S Committee on 4 February 2022. On the basis of this mandate, the WG will develop a guidance document that covers both remote assessments as well as hybrid assessments. A very first draft was completed in the course of 2022. It includes definitions as well as specific guidance, including on risk management. The WG is also working on an Aide Memoire covering the preparation and conduct of remote / hybrid assessments as well as post-inspection activities.

## **24. ICMRA PQ KMS Joint Reflection Paper**

PIC/S has co-operated on the drafting of a 'Joint Reflection Paper on Pharmaceutical Quality Knowledge Management System' (PQ KMS), which was published by the International Coalition of Medicines Regulatory Authorities (ICMRA) on 19 August 2022 on its website. The aim of the PQKMS project is to provide greater regulatory reliance by allowing the use of common documents (e.g. marketing authorisation, inspection report) through a secure remote cloud environment. PIC/S will be involved in the project, which stretches over a period of 5 to 10 years, and share its experience regarding the inspection report format, the Unique Facility Identifier (UFI), PQS assessment, risk assessment of companies, inspection reliance and training through PIA. The related PIC/S Working Groups (e.g. WGs on UFI, on Q12 Training Materials, on Remote Assessment, on Reliance, etc.) will be actively involved.

At its meeting in Dublin, the Committee unanimously supported PIC/S' involvement in the PQ KMS project.

## **25. Co-operation with Associated Partners and other Organisations**

### **25.1 Associated Partners (EC, EDQM, EMA, OIE, UNICEF and WHO)**

In 2022, PIC/S continued to co-operate closely with Associated Partner Organisations, namely:

- European Directorate for the Quality of Medicines & HealthCare (EDQM),
- European Medicines Agency (EMA),
- United Nations International Children's Emergency Fund (UNICEF),
- World Health Organization (WHO), and
- World Organisation for Animal Health (OIE).

In 19 July 2022, following the successful signing of a bilateral arrangement, the European Commission (EC) became a new PIC/S Associated Partner Organisation. The EC's participation through the Directorate General Health and Food Safety (DG SANTE) will be complementary to that of EMA. It will allow the EU network to be more active and leverage more resources for PIC/S training, the international harmonisation of GMP as well as the assessment of regulatory authorities under the EEA HMA Joint Audit Programme (JAP) and PIC/S Joint Reassessment Programme (JRP).

Co-operation with Associated Partner Organisations normally covers fields such as the harmonisation of GMP guides and guidance documents, the exchange of audit reports on the (re)assessment of Competent Authorities, the sharing of information on foreign GMP inspections, and the participation in training events and expert discussions.

### **25.2 Other organisations**

#### **ASEAN**

In 2019, an exchange of letters was signed between PIC/S and the ASEAN Pharmaceutical Product Working Group (PPWG) related to co-operation on GMP related matters. Based on a recommendation by the SCSD, the PIC/S Committee also agreed to initiate a similar exchange of letters with the ASEAN Traditional Medicines Health Supplements Product Working Group (TMHS PWG). Due to the pandemic, the project has been put on hold.

#### **DIA**

A remote presentation on PIC/S and the revision of Annex 1 was given at the DIA China Annual Meeting.

#### **Heads of EEA Medicines' Agencies**

Under the framework of a letter of agreement between PIC/S and EU/EEA Heads of Medicines Agencies (HMA), which entered into force on 15 August 2016, PIC/S and HMA co-operate in exchanging information in the context of the EEA Joint Audit Programme (JAP) of GMP Inspectorates and the PIC/S Joint Reassessment Programme (JRP) of PAs, which ensures that both new and current PIC/S PAs meet the same requirements. PIC/S and HMA also recognise that in the EEA context the EEA JAP and the PIC/S JRP

are deemed equivalent. Audit schedules are also exchanged between the two parties with a view to avoid any duplication and foster mutual acceptance and recognition of audits as well as maintain equivalent auditing tools and programmes, including joint training of auditors. In 2022, PIC/S and EMA continued to share audit reports as well as information on upcoming (re)assessments. The HMA network has also provided resources for EU GMP inspectors to participate in PIC/S training events such as the annual training seminar in Dublin.

### **ICMRA**

PIC/S regularly exchanges with the International Coalition of Medicines Regulatory Authorities (ICMRA) on regulatory collaboration. In 2022, exchanges focused on the drafting of the ‘Joint Reflection Paper on Pharmaceutical Quality Knowledge Management System’ (PQ KMS) – see preceding section.

### **ISPE**

The PIC/S Chairperson attended several ISPE meetings and presented, in particular on the revision of Annex 1.

Further to the signing of a Memorandum of Understanding (MoU) with ISPE on 8 June 2021, a trial review of ISPE’s e-learning offer has been performed by the PIA Technical Advisor and the SCT Chairman in relation to the development of the e-learning QRM Training module for PIA. Following subsequent exchanges with ISPE, a draft content license agreement has been proposed by ISPE, for which the SCT and PIC/S Executive Bureau will be consulted.

### **PDA**

The PIC/S Chairperson and Deputy Chairperson presented at several PDA meetings, in particular on the revised Annex 1 as well as on PIC/S efforts to harmonise remote assessment.

## **26. BUDGET, RISK & AUDIT**

The Sub-Committee on Budget (SCB) was established back in 2004. Its mandate was widened to encompass issues related to risk and audit in 2014. For the full mandate, see box below.

The mandate of the SCB is to:

1. In line with good governance:
  - 1.1 Assess regulatory risk, financial risk, reputational risk and risk management and make proposals / recommendation to minimise such risk
  - 1.2 Appraise the performance, efficiency, effectiveness and adequacy of internal and external controls
  - 1.3 Evaluate internal and external audits and the implementation of their recommendations

- |     |   |
|-----|---|
| 1.4 | Ensure that PIC/S adheres to good governance practices  |
| 2.  | In line with PIC/S' Financial Rules (PS/W 1/2004):  |
| 2.1 | Establish a budget proposal to the PIC/S Committee  |
| 2.2 | Propose updates and amendments of the Financial Rules to ensure effective financial administration, the exercise of economy and consistency in financial reporting  |
| 2.3 | Maintain an internal financial control and examine financial transactions in order to ensure:<br>(i) the regularity of the receipt, custody and disposal of all funds and other financial resources of PIC/S;<br>(ii) the conformity of commitments and expenditures with the budget voted by the PIC/S Committee;<br>(iii) the efficient and economic use of the resources of PIC/S. |
| 2.4 | Avoid any duplication with the external auditor   |
| 3.  | Report back to the PIC/S Committee, as provided for in the Terms of References and the Financial Rules, and make proposals / recommendations  |

The SCB is chaired by Ger Jan van Ringen (Netherlands / IGJ); the Deputy Chair is Kathleen Sinninger (US FDA). The SCB held three virtual meetings: on 31 March; 2 June; and 30 November 2022. During these meetings, it reviewed the 2021 financial report, monitored the 2022 accounts, prepared the separate PIC/S and PIA budgets for 2023, and discussed the financing of PIC/S as well as that of PIA, as detailed below.

## 27. 2021 Accounts

The SCB reviewed the report on the 2021 accounts by the external auditor, Moore Stephens Refidar S.A. as well as the 2021 financial report ('Statement of Accounts for the Financial Year 2021'). In line with the SCB's recommendation, the Committee approved by written procedure the 2021 financial report. It also agreed to transfer the 2021 balance and the bank interests for a total of CHF 47,703.54 to the PIC/S Reserve Fund and to discharge the Secretary of his responsibility for the 2021 accounts.

The SCB also reviewed the following reports:

- The financial report on the 2021 annual seminar virtually hosted by Korea (Republic of) / MFDS, which resulted in a surplus of US\$ 81,136.61. MFDS generously donated this surplus to PIC/S.
- A Note on "PIA Activities & Accounts for the Financial Year 2021", which was circulated to the Committee for information.

## **28. 2022 Accounts**

The SCB reviewed the status of income and expenditures of the 2022 accounts (including those of PIA) during the year while the Committee appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2022 accounts, which will take place in early 2023.

## **29. 2023 Budget**

As recommended by the SCB, the Committee approved by written procedure, which was successfully completed on 21 December 2022, the 2023 PIC/S Budget for an amount of CHF 1,366,798 (compared with CHF 1,331,265 the year before). It also approved in the same written procedure the 2023 PIA Budget.

## **30. Future Financing of PIC/S and PIA**

In the course of 2022, the SCB discussed the future financing of both PIC/S and PIA.

With regard to PIC/S, the SCB considered the possible introducing of long-term financial measures in order to address future financial gaps and ensure balanced accounts. At the same time, these measures should enable to maintain the operational capacity of the Secretariat and the related increase of its human resources to support the growth of PIC/S activities.

With regard to PIA, the SCB was updated on the status of voluntary contributions to PIA and discussed how to secure the further development of PIA in line with the PIA Business Case and the 5-year Budget Plan.

## **31. COMMUNICATION**

Good internal communication between PAs through PA representatives is one of PIC/S' recognised benefits, which derives from membership. External communication has also become an important tool to promote the organisation. PIC/S regularly communicates on its activities on the PIC/S website [www.picscheme.org](http://www.picscheme.org) by publishing news, press releases, annual reports and other information documents. Considering the growing importance of communication, the PIC/S Committee has decided to establish a specific Sub-Committee on Communication (SC COM).

The mandate of the SC COM is to (i) monitor PIC/S' public relations and the exchange of information; and (ii) to define a communication strategy in order to better promote PIC/S and its key role in the field of inspections. In 2020, the scope of the mandate was expanded in order to cover the overall co-ordination with ICH. For the amended mandate, see box below.

The mandate of the SC COM is to:

1. Monitor PIC/S' public relations and the exchange of information
2. Define a communication strategy to better promote PIC/S

- 3. Represent PIC/S in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Co-ordinate PIC/S relations with ICH in co-operation with other involved Sub-Committees and disseminate relevant ICH information and guidelines to PIC/S PAs.
- 4. Monitor and propose changes to the PIC/S web site
- 5. Work on improving communications with PA, in particular with Heads of Agencies, as well as PIC/S Partners
- 6. Identify the most suitable speakers for (regional or international) conferences where PIC/S has been invited to speak
- 7. Report back to the PIC/S Committee, as provided for in the Terms of References and make proposals / recommendations

The SC COM is chaired by Kentaro Hara (Japan / PMDA), who is assisted by H-Y (Rachel) Wang (Chinese Taipei / TFDA), SC COM Deputy Chair. The SC COM held one virtual meeting 10 March 2022 and then exchanged by e-mails. It discussed objectives for 2022-23, ICH matters as well as communication-related topics, as listed below.

## 32. Co-operation with ICH

Since June 2017, PIC/S enjoys an observer status with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). It normally attends ICH Assembly meetings and take parts in ICH Expert Working Groups (EWG), in particular E6(R3) (on GCP); M10 (Bioanalytical method validation), Q9(R1) (on QRM), Q12 (Pharmaceutical Product Lifecycle Management) and Q13 (Continuous Manufacturing).

Co-operation has intensified since 2020 with a pilot on closer co-operation between the two organisations covering co-operation on ICH Q Guidelines, in particular ICH Q9 and Q12.

The Committee was consulted in January 2022 on ICH Q9(R1) – Quality Risk Management – and consolidated comments compiled by the PIC/S Expert Circle on QRM and then transmitted to ICH in March 2022. Regarding Q12 – Pharmaceutical Product Lifecycle Management – the report on the PIC/S webinar organised in May 2021 for inspectors by the PIC/S Working Group on ICH Q12 Training Materials was shared with both the PIC/S Committee and the ICH Management Committee.

Following a first grant on ICH Q12 Training Materials obtained in 2021, PIC/S was granted a second grant in 2022 to be used to reimburse costs in relation with the development of PIC/S training modules for Q9 and Q12 under PIA. See also Section 18.

## **33. Foreign Inspections**

Due to the pandemic and related travel restrictions, foreign inspections resumed only in the second half of 2022. This was confirmed by a PIC/S survey in which PAs and Partner Organisations were asked to indicate their plans to resume foreign on-site inspections. Due to the accumulated backlog, there was an increase interest by all agencies and organisations to share information on foreign inspections. A call to PIC/S PAs and Partner Organisations to contribute to the confidential ‘List of Planned Foreign Inspections’ was made. This list comprises over 500 planned foreign inspections in 2022.

The SC COM was invited to review proposals by Members to improve the sharing of information on planned foreign inspections.

## **34. Other SC COM issues**

The SC COM was invited to review proposals by Members on the involvement of PIC/S in social media as well as the content to be shared on social media, once the position of “SC COM Officer” had been opened at the PIC/S Secretariat.

## **35. PIC/S Website**

The PIC/S website <https://www.picscheme.org> was regularly updated throughout the year. This was also the case of the password-protected Members’ Area as well as the PIA sub-site.

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## **FROM THE PHARMACEUTICAL INSPECTION CONVENTION TO THE PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME**

The Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmaceutical Products (Pharmaceutical Inspection Convention) entered into force in 1971.

The Convention applies to inspection of the manufacture of medicinal and related products intended for human use, which are subject to control under health legislation. It provides that the Contracting States will exchange, on the basis of inspections, such information as is necessary for the health authorities in an importing Contracting State to be able to recognise inspections carried out in the Contracting State of the manufacturer.

In 2000 the Convention was operating between eighteen countries, namely, Australia, Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Liechtenstein, Norway, Portugal, Romania, Sweden, Switzerland and the United Kingdom.

The Convention's Contracting States realised in the early 1990s that because of an incompatibility between the Convention and European law, it was not possible for new countries to be admitted as Members of PIC. Australia was the last country which was able to become a Member of the Convention in January 1993.

Consequently, a new arrangement called "Pharmaceutical Inspection Co-operation Scheme" (or PIC Scheme) was established on 2 November 1995. This is an arrangement between the inspectorates of the present Contracting States to the Convention but also open to the participation of the inspectorates of other countries.

The Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme are run concurrently by one joint Committee and one Secretariat. The common logo for both is PIC/S.

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**LIST OF PIC/S PARTICIPATING AUTHORITIES AND PARTNER ORGANISATIONS**  
 (as of 31 December 2022)

in the alphabetical order of the jurisdiction's name in English  
 in which they are located

	PARTICIPATING AUTHORITY	ACRONYM
Argentina	Instituto Nacional de Medicamentos ( <i>National Institute of Drugs</i> )	INAME
Australia	Therapeutic Goods Administration	TGA
Austria	Austrian Agency for Health and Food Safety	AGES
Belgium	Agence Fédérale des Médicaments et des Produits de Santé ( <i>Federal Agency for Medicines and Health Products</i> )	AFMPS
Brazil	Agência Nacional de Vigilância Sanitária <i>National Health Surveillance Agency</i>	ANVISA
Canada	Health Canada - Regulatory Operations and Enforcement Branch (ROEB) ( <i>Santé Canada - Direction générale des opérations réglementaires et de l'application de la loi (DGORAL)</i> )	ROEB
Chinese Taipei	Taiwan Food and Drug Administration	TFDA
Croatia	Agency for Medicinal Products and Medical Devices of Croatia ( <i>Agencija za lijekove i medicinske proizvode</i> )	HALMED
Cyprus	Pharmaceutical Services	CyPHS
Czech Republic <sup>1</sup>	Státní Ústav pro Kontrolu Léčiv ( <i>State Institute for Drug Control</i> )	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv ( <i>Czech Institute for State Control of Veterinary Biologicals and Medicines</i> )	ISCVBM
Denmark	Danish Medicines Agency	DKMA
Estonia	State Agency of Medicines	SAM
Finland	Finnish Medicines Agency	FIMEA
France <sup>2</sup>	Agence nationale de sécurité du médicament et des produits de santé ( <i>French National Agency for Medicines and Health Products Safety</i> )	ANSM
	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du	ANSES

<sup>1</sup> SÚKL and ÚSKVBL count as two distinct Participating Authorities.

<sup>2</sup> ANSM and ANSES count as two distinct Participating Authorities.

	<i>travail (French Agency for Food, Environmental &amp; Occupational Health Safety)</i>	
Germany <sup>3</sup>	Bundesministerium für Gesundheit ( <i>Federal Ministry of Health</i> )	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten ( <i>Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices</i> )	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων ( <i>National Organization for Medicines</i> )	EOF
Hong Kong SAR, China	Pharmacy and Poisons Board of Hong Kong	PPBHK
Hungary	National Institute of Pharmacy and Nutrition	NIPN
Iceland	The Icelandic Medicines Agency	IMA
Indonesia	Indonesian Food and Drug Authority	Badan POM
Iran	Iran Food and Drug Administration	IFDA
Ireland	Health Products Regulatory Authority	HPRA
Israel	Institute for the Standardization and Control of Pharmaceuticals	ISCP
Italy <sup>4</sup>	Agenzia Italiana del Farmaco	AIFA
	Direktorate General for Animal Health and Veterinary Medicinal Products (Direzione generale della sanità animale e dei farmaci veterinari)	DGSASF
Japan <sup>5</sup>	Ministry of Health, Labour and Welfare	MHLW
	Pharmaceuticals and Medical Devices Agency	PMDA
	Japanese Prefectures	-
Korea (Republic of)	Ministry of Food and Drug Safety	MFDS
Latvia	Zāļu Valsts Aģentūra ( <i>State Agency of Medicines</i> )	ZVA
Liechtenstein	Amt für Gesundheit ( <i>Office of Healthcare</i> )	AG
Lithuania	State Medicines Control Agency	SMCA
Malaysia	National Pharmaceutical Regulatory Agency	NPRA
Malta	Malta Medicines Authority	MMA
Mexico	Federal Commission for the Protection Against Sanitary Risks ( <i>Comisión Federal para la Protección contra Riesgos Sanitarios</i> )	COFEPRIS

<sup>3</sup> BMG and ZLG count as one Participating Authority. All German Medicinal Authorities, which are listed on the ZLG web site, are considered as PIC/S Participating Authorities and are represented in PIC/S by ZLG.

<sup>4</sup> AIFA and DGSASF count as two distinct Participating Authorities.

<sup>5</sup> MHLW, PMDA and the Japanese Prefectures count as one Participating Authority. The Japanese Prefectures are represented by MHLW.

Netherlands	Inspectie voor de Gezondheidszorg en Jeugd ( <i>Health and Youth Care Inspectorate</i> ) <sup>6</sup>	IGJ
New Zealand	Medicines and Medical Devices Safety Authority	Medsafe
Norway	Norwegian Medicines Agency	NOMA
Poland	Chief Pharmaceutical Inspectorate	CPI
Portugal	Autoridade Nacional do Medicamento e Produtos de Saúde IP ( <i>National Authority of Medicines and Health Products IP</i> )	INFARMED IP
Romania	National Agency for Medicines and Medical Devices of Romania	NAMMDR
Singapore	Health Sciences Authority	HSA
Slovak Republic	State Institute for Drug Control	SIDC
Slovenia	Agency for Medicinal Products and Medical Devices	JAZMP
South Africa	South African Health Products Regulatory Authority	SAHPRA
Spain	Agencia Española de Medicamentos y Productos Sanitarios ( <i>Spanish Agency for Medicines and Medical Devices</i> ) <sup>7</sup>	AEMPS
Sweden	Swedish Medical Products Agency	MPA
Switzerland	Swiss Agency for Therapeutic Products	Swissmedic
Thailand	Food and Drug Administration	Thai FDA
Turkey	Turkish Medicines and Medical Devices Agency	TMMDA
Ukraine	State Service of Ukraine on Medicines and Drugs Control	SMDC
United Kingdom <sup>8</sup>	Medicines and Healthcare Products Regulatory Agency	MHRA
	Veterinary Medicines Directorate	VMD
United States of America	United States Food and Drug Administration	US FDA

<sup>6</sup> The competence for GMP/GDP inspections in the Netherlands is allocated to the central authority, the Health and Youth Care Inspectorate (IGJ). IGJ is the PIC/S Participating Authority representing GMP/GDP for human as well as veterinary medicinal products. IGJ performs national and international GMP/GDP inspections representing the Health and Youth Care Inspectorate - Pharmaceutical Affairs as well as the Medicines Evaluation Board - Veterinary Medicinal Products Unit, which is mandated to issue GMP certificates on behalf of the Ministry of Economic Affairs.

<sup>7</sup> The competence for GMP/GDP inspections in Spain is shared between the central authority, Spanish Agency for Medicines and Medical Devices (AEMPS), and the Spanish regional authorities, which count as one PIC/S Participating Authority. All Spanish Medicinal Authorities, which are listed on AEMPS' web site, are considered as PIC/S Participating Authorities and are represented in PIC/S by AEMPS.

<sup>8</sup> MHRA and VMD count as two distinct Participating Authorities.

<b>PARTNER ORGANISATIONS</b>	<b>ACRONYM</b>
European Directorate for the Quality of Medicines & HealthCare	EDQM
European Medicines Agency	EMA
European Commission	EC
United Nations Children's Fund	UNICEF
World Health Organization	WHO
World Organisation for Animal Health	WOAH