



## 2021 Annual Report

**PHARMACEUTICAL INSPECTION CONVENTION**

**PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME**

Leading the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products



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PS/W 2/2022  
25 March 2022

## 2021 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 2021, PIC/S comprised 54 Participating Authorities (PAs) from all continents. For the list of PIC/S PAs, see Annex 2.

PIC/S' mission is "to lead the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products". This will be achieved by harmonising inspection procedures worldwide, by developing common standards in the field of GMP, by providing training opportunities to inspectors and by facilitating co-operation and networking between competent authorities, regional and international organisations, thus increasing mutual confidence.

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 2021.

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## *In Memoriam*

Marta Alicia Cicero  
Victorita Ivascu.



Rest in Peace

Marta Alicia Cicero  
Argentina / INAME  
Deputy Chairperson  
Sub-Committee on Budget  
Risk and Audit (SCB)

Victorita Ivascu  
Romania / NAMMDR  
PIC/S Committee representative

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# ANNUAL REPORT 2021

## 1. MAIN FEATURES OF THE YEAR

### 1.1 A virtual chairmanship

2021 was the second year of the chairmanship of Ms Anne Hayes from Ireland's Health Products Regulatory Authority (HPRA). It was also PIC/S's second year of operation in a pandemic situation. Under Ms Hayes' dynamic leadership, the PIC/S Committee was able to meet virtually twice: on 20-21 April and on 18-19 October 2021.



Photo: Ms Anne Hayes  
PIC/S Chairperson

The first meeting was also the 100<sup>th</sup> meeting of the Pharmaceutical Inspection Convention (PIC), established in 1971, while the second meeting was the 50<sup>th</sup> meeting since the establishment under the Pharmaceutical Inspection Co-operation Scheme in 1995.

Ms Hayes is the first “virtual” Chairperson in PIC/S' history: she has presided over PIC/S activities without face-to-face meetings or in-person training events during her entire chairmanship.

### 1.2 Impact of COVID-19 on PIC/S

The COVID-19 pandemic continued to impact on PIC/S activities throughout the year. Face-to-face meetings or training events had to be either rescheduled or held virtually in line with a new PIC/S policy on the organisation of events during the COVID-19 pandemic. This was notably the case of the following:

- The 50<sup>th</sup> Anniversary of PIC/S, scheduled in June 2021 in Dublin (Ireland), was postponed to 2022;
- The 2021 PIC/S annual seminar, originally foreseen to be held in Dublin in conjunction with PIC/S' 50<sup>th</sup> Anniversary, was rescheduled to be held virtually by Korea (Republic of) / MFDS on 9-11 November 2021.
- All meetings of PIC/S bodies (Committee, Executive Bureau, Sub-Committees, Expert Circles and Working Groups) were held by videoconference.

As the year before, all important decisions in 2021 were taken by written procedure, in particular on financial and organisational matters such as for the adoption of the annual report or the annual budget as well as the election of the PIC/S Executive Bureau and all PIC/S Sub-Committees.

During the pandemic, PIC/S continued to actively promote inspection reliance by encouraging Participating Authorities (PAs) to rely on each other's GMP information while a related Working Group on Inspection Reliance looked at ways to facilitate reliance.

PIC/S was also at the forefront to harmonise the practice of "distant assessment" following a successful seminar by Finland / FIMEA in 2020 on "Distant Assessment of GMP Compliance". A Working Group on Distant Assessment was established in 2021 while the annual seminar, organised by Korea (Republic of) / MFDS, focused on "GMP Assessment Approaches in Post COVID-19 Era". PIC/S also adopted a guidance on "COVID-19 risk assessment for routine on-site inspections" (PI 055-1), which was drafted by the Working Group on inspectors' travel safety.

### 1.3 PIC/S' expansion continues

PIC/S' membership continued to expand in 2021.



Brazil's Agência Nacional de Vigilância Sanitária (ANVISA) acceded to PIC/S on 1 January 2021 to become PIC/S' 54<sup>th</sup> PA. ANVISA applied in 2014. An on-site assessment visit took place on 9-21 October 2019 and the related report was approved in 2020. ANVISA is Latin America's 3<sup>rd</sup> Agency to join PIC/S. It is South America's largest market for medicinal products.



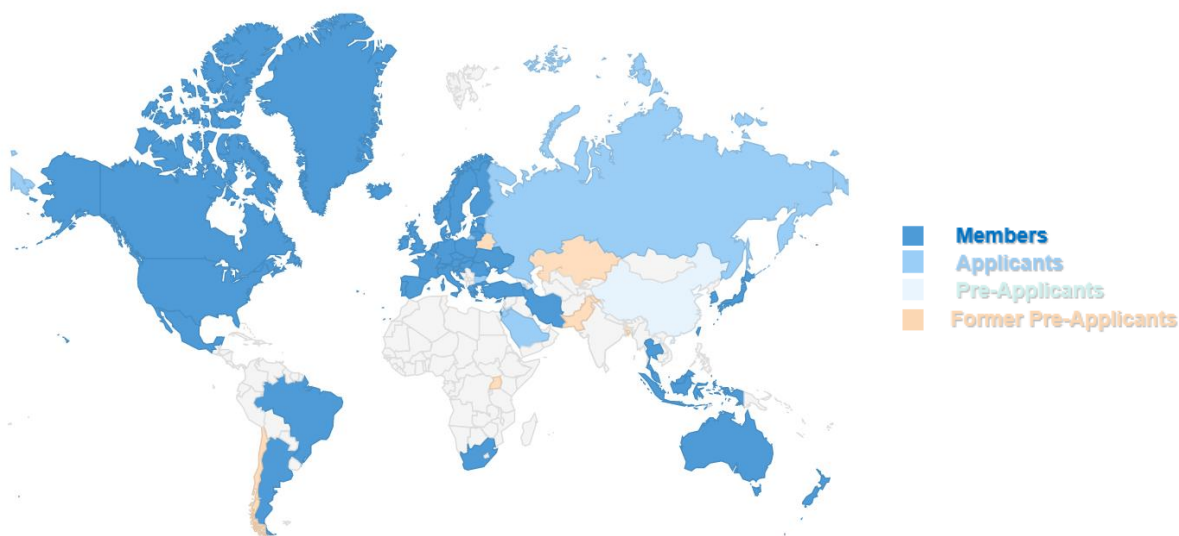
China's National Medical Products Administration (NMPA) submitted an application for pre-accession to PIC/S. The application was received on 24 September 2021. The PIC/S Committee nominated Jacques Morenas (France / ANSM) as Rapporteur.



The Jordan Food and Drug Administration (JFDA) lodged a membership application on 20 January 2021. The full membership application was received shortly after the closure of the pre-accession process on 31 December 2020. The appointed Rapporteur is Henning Willads Petersen (Denmark / DKMA).

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





## 1.4 Virtual training events

As an alternative to in-person training events, PIC/S transitioned to virtual training events in 2020. In 2021, as face-to-face events were still too challenging to organise due to travel and other sanitary restrictions, PIC/S organised, or co-organised, four virtual training events. These were (in chronological order):

- A PIC/S webinar for inspectors on ICH Q12 (Pharmaceutical Product Lifecycle Management) was organised by the PIC/S Working Group on Training Material for ICH Q12, with the support of the PIC/S Secretariat, on 11 May 2021. It was attended by around 350 participants from 50 agencies and 44 different jurisdictions (for more information, see section 19).
- A webinar on Distant assessment / Remote Virtual Inspection was jointly organised by the PIC/S Expert Circle on Human Blood, Tissues, Cells & ATMP and the EU Commission Expert Sub-Group on Inspections in the Blood, Tissues and Cells Sectors (IES). It took place on 18 June 2021 and was attended by around 325 participants (for more information, see section 15.1).
- The 2021 PIC/S annual seminar was hosted by the Ministry Food and Drug Safety (MFDS), Republic of Korea, on the topic “GMP Assessment Approaches in Post COVID-19 Era”. This virtual seminar took place on 9-11 November 2021 and was attended by 315 inspectors from 54 authorities (for more information, see section 21.4).
- The 2<sup>nd</sup> meeting of the PIC/S Expert Circle on Controlling Cross-Contamination in Shared Facilities (CCCISF) was virtually hosted by WHO on 14-15 December 2021. It was attended by 375 participants from all over the world (for more information, see section 21.2).

## 1.5 Revision of GMP Guide & GPG for Blood Establishments

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 GMP Guide), the manufacture of biological medicinal substances and products for

human use (Annex 2 of PIC/S GMP Guide), and Good Practice Guidelines (GPG) for Blood Establishments and Hospital Blood Banks (PE 005).

2021 was a very productive year for PIC/S and several guidance documents were successfully adopted while others progressed significantly. This was notably the case of:

- Annex 2A for the Manufacture of ATMP for Human Use and Annex 2B for the Manufacture of Biological Medicinal Substances and Products for Human Use were successfully adopted on 1 April 2021 and entered into force on 1 May 2021 (for the revised GMP Guide, see PE 009-15).
- The PIC/S Guidance on Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments (PI 041-1) as well as a restricted Aide Memoire on inspection of data management and integrity (PI 049), available to PIC/S inspectors only, were adopted on 1 June 2021 and entered into force on 1 July 2021.
- The PIC/S Good Practice Guidelines for Blood Establishments and Hospital Blood Banks (PE 005) and the PIC/S Aide Memoire to Inspections of Blood Establishments and Plasma Warehouses (PI 008) were adopted on 9 April 2021 and entered into force on 1 June 2021.
- The joint PIC/S-EMA Working Group on Annex 1 reviewed the comments received during the second public consultation in 2020 and issued a revised Annex 1 by the end of 2021, which was ready to be tabled for parallel adoption by PIC/S, the European Medicines Agency (EMA) and the World Health Organization (WHO) by early 2022.

## 1.6 The PIC/S Inspectorates' Academy (PIA) continues to develop

The PIC/S Inspectorates' Academy (PIA) continued to unfold in 2021. 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.

Following the successful establishment of a PIA Learning Management System (LMS), the development of a pilot e-learning module on Quality Risk Management (QRM) was initiated alongside with a curriculum on QRM for GMP Inspectorates. The general outline ("skeleton") for relevant curricula on the inspection of APIs, ATMPs, biologicals, blood, non-sterile, sterile, etc. was also prepared.

In parallel with the development of this pilot module, new training materials were published on a continual basis on PIA and project and budget plans were prepared to facilitate the financing of PIA.

## 1.7 PIC/S strategic plan (2023-2027)

The Executive Bureau has established a Working Group, which is mandated to develop the next PIC/S strategic plan for 2023-2027 to be presented at the PIC/S 50<sup>th</sup> anniversary in 2022. In 2021, in line with its project plan, the Working Group reached out to PIC/S Sub-Committees, PIC/S inspectors, Partner Organisations and selected Non-Members to gather their views on PIC/S' future orientation and activities.

## 1.8 Changes in the Executive Bureau

The Executive Bureau (EB) was elected in Toyama (Japan) for a 2-year term starting on 1 January 2020 and ending on 31 December 2021. It consisted of:

- Ms Anne Hayes (Ireland / HPRA), PIC/S Chairperson;
- Mr Paul Gustafson (Canada / ROEB), PIC/S Deputy Chairman and Chair of the Sub-Committee on GM(D)P Harmonisation (SCH);
- Mr Boon Meow Hoe (Singapore / HSA), immediate past PIC/S Chairman;
- 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);
- Ms Susan Laska (US FDA), Chair of the Sub-Committee on Strategic Development (SCSD).
- Ms Stephanie Ancil (Canada / ROEB), Chair of the Sub-Committee on Compliance (SCC); and
- Mr David Churchward (United Kingdom / MHRA), Chair of the Sub-Committee on Communication (SC COM).

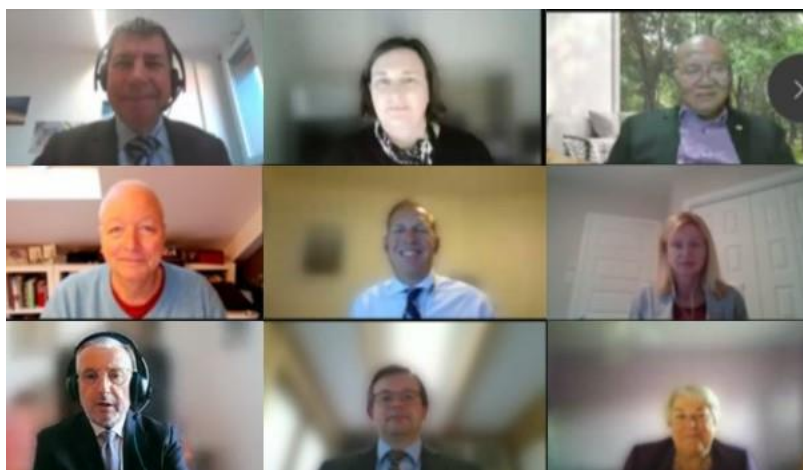


Photo of the EB for the period 2020-21:

Andreas Krassnigg - Anne Hayes (Chair) - Boon Meow Hoe  
Ger Jan Van Ringen - Paul Gustafson - Stephanie Ancil  
Jacques Morénas - David Churchward - Susan Laska

Due to the pandemic, the renewal of the EB for the period 2022-23 was carried out by written procedure, successfully completed on 13 December 2021. The PIC/S Committee unanimously elected Mr Paul Gustafson (Canada / ROEB) as Chairperson for the period 2022-2023. Mr Gustafson will be able to rely on the support of other EB Members elected for the same period. As from 1 January 2022, the full EB will consist 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).



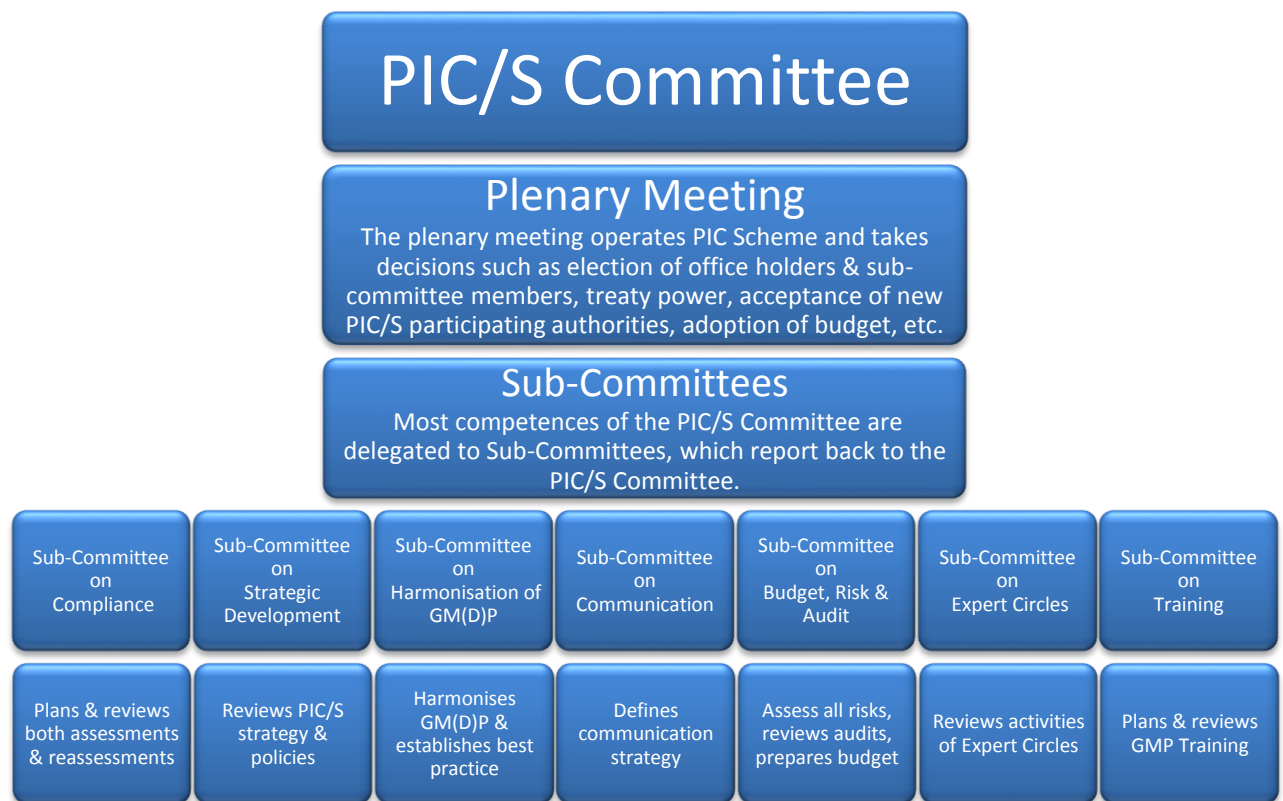
Ms Anne Hayes (Ireland / HPRA), outgoing PIC/S Chairperson, and Mr Paul Gustafson (Canada / ROEB), incoming PIC/S Chairperson

## 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 Stephanie Ancil (Canada / ROEB); the Deputy Chair is Jenny Hantzinikolas (Australia / TGA). The SCC held four virtual meetings in 2021: on 26 March, 29 June, 2 November and 10 December 2021. 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. The

SCC and the PIC/S Committee also discussed the need to increase the number of trained auditors, as the number of (re)assessments and pre-accession processes continuously increases. Several options are under consideration.

## 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 only Working Group operating under the auspices of the SCC is the Working Group on the Revision of the Accession Guidelines.

The Working Group on the revision of the accession guidelines and related documents is led by Jacques Morénas (France / ANSM). It is revising 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). Nine procedures were submitted to PIC/S Members for comments by written procedure, which ended on 1 April 2021. Once documents have been finalised, they will be circulated for adoption. Six other documents are still in the process of being revised by the Working Group.

## 5. Membership Applications

In 2021, PIC/S continued the assessment of the following five membership applications (in alphabetical order):

### 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. A preliminary report, summarising their findings, will soon be shared with SCDMTE.

### 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 EMA 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 EMA 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 and agreed with Health Canada on the need to observe two inspections: one by Canada on sterile manufacturing and one by PIC/S on non-sterile manufacturing. BDA has submitted

updated documents, which the Rapporteur and Co-Rapporteur have reviewed. The on-site assessment visit has been postponed due to the pandemic and will take place depending on BDA's availability as well as the lifting of travel restrictions.

### **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 from Brazil / ANVISA).

### **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").

Considering the complexity of the Russian GMP framework, the SCC has recommended setting up a larger team consisting of a Rapporteur and several Co-Rapporteurs which is expected to be nominated by early 2022.

### **5.6 Saudi Arabia / SFDA**

The Saudi Food & Drug Authority (SFDA) applied for PIC/S membership on 17 February 2020. The Rapporteur, Jacques Moréas (France / ANSM), the Co-Rapporteur, Ferenc Lukács (Hungary / NIPN), and a Team Member, Gülşen Yılmaz (Turkey / TMMDA), were appointed on 26 March 2021. The paper review has progressed well during 2021 and a preliminary report will soon be shared with the SCC.

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

In 2021, the following four 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.

## **6.2 Bangladesh / DGDA**

Bangladesh's Directorate General of Drug Administration (DGDA) applied for pre-accession on 26 February 2019. The Rapporteur, Henning Willads Petersen (Denmark / DKMA), engaged with DGDA, however, the 2-year timeframe for the pre-accession of Bangladesh / DGDA expired on 25 February 2021. Upon recommendation of the SCC, the Committee agreed on 26 March 2021 to close the pre-accession process and to invite DGDA to re-apply.

## **6.3 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 Morenas (France / ANSM), a Co-Rapporteur, Raphael Yeung (Hong Kong SAR, China / PPBHK) and a trainee Co-Rapporteur, Kathleen Sinninger (US FDA).

## **6.4 Pakistan / DRAP**

The Drug Regulatory Authority of Pakistan (DRAP) submitted a pre-accession application on 18 September 2017. The Rapporteur, Petra Müllerová (Czech Republic / ISCVBM), assessed the pre-accession application. Her gap analysis report was endorsed by the Committee in March 2021 and the pre-accession application closed on 31 March 2021. Pakistan / DRAP was invited to apply for membership, subject – amongst other matters – to the implementation of the PIC/S GMP Guide.

# **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 2021, 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. The SCC proposed a 2-step approach, which was endorsed by the Committee. The approach consists of appointing a Rapporteur and Co-Rapporteur to perform the document review to be followed by an on-site visit, once travelling restrictions have been lifted.

A Co-Rapporteur and a Team Member were identified in the course of 2021; however, the position of Rapporteur is still vacant.

### **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 JRP procedures, currently under revision. Medsafe was invited to submit all requested documents for its reassessment by 31 December 2021.

### **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 SAHPRA and the Rapporteur, Jacques Morénas (France / ANSM), SAHPRA submitted all reassessment documents on 30 September 2021. The next step will consist in the Rapporteur reviewing the documents.

### **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**

Contacts were established with a number of non-Members such as Cameroon's Laboratoire National de Contrôle de Qualité des Médicaments et d'Expertise, China's Institute of Veterinary Drug Control, Cuba's Centro para el Control Estatal de

Medicamentos, Equipos y Dispositivos Médicos (CECMED), and Montenegro's Institute for Medicines and Medical Devices.

## 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 EMA, the GMDP IWG, the 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 Paul Gustafson (Canada / ROEB), who is assisted by Ian Jackson (UK / MHRA), Deputy Chair. In the course of 2021, the SCH held four virtual meetings: on 25 February, 20 May, 23 September and 9 December 2021. 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:

- 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.

### 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 Authorities of PIC/S and EEA as well as WHO. From 2014 to 2019, the Working Group was chaired 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 with a majority relating to Chapter 8 (Production and Specific Technologies), Chapter 4 (Premises), and Chapter 9 (Viable and non-viable environmental & process monitoring). The Working Group reviewed the comments 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.

On 12 October 2021, PIC/S PAs were consulted on a proposal to advance the revised Annex 1 to Step 3 of the PIC/S adoption process unless substantial comments were received by 5 November 2021. An implementation period of 1 year has been proposed by the WG with alternative implementation periods to be considered for some sections of Annex 1. A finalised version of Annex 1 is expected to be tabled for adoption by 2022.

## **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 consists of 18 experts from PAs as well as 2 Partner Organisations (EMA and WHO). It was first chaired by Francesco Cicirello (Australia / TGA) until May 2020 and then by Christina Meissner (Austria / AGES).

The Working Group has 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.

Both documents were advanced to Step 1 (consultation of PAs) on 25 March 2019 and then to Step 2 (public consultation) on 20 September 2019. The 3-month public consultation consisted in a targeted stakeholder consultation with the assistance of a number of professional and industry organisations, which agreed to collect comments from stakeholders on behalf of PIC/S. A total of 240 comments were received and then reviewed by the Working Group. The revised draft Annexes were submitted to PAs on 18 August 2020 with an opportunity to comment by 27 November 2020. The finalised Annexes 2A and 2B were submitted for adoption on 5 March 2021 by written procedure, successfully completed on 1 April 2021. Both Annexes then entered into force on 1 May 2021 (for the revised GMP Guide, see PE 009-15).

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

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

The draft “PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments” (PI 041-1 (Draft 2)) was published on 10 August 2016 and implemented on a trial-basis for a period of 6 months. In parallel, PAs were invited to report back on the implementation of the guidance document.

The draft guidance was then revised based on Members’ comments and submitted for public consultation for a period of three months on 30 November 2018 (PI 041-1 (Draft 3)). The consultation took the form of a “focused consultation” seeking comments from selected stakeholders on specific questions. In parallel, PIC/S PAs were re-invited to apply the revised draft guidance on a trial basis. In 2019-20, the WG reviewed all comments received, whether from PAs or stakeholders.

The Working Group also developed an aide-memoire along with other tools to support data integrity inspections. These documents are accessible only to PIC/S inspectors.

On 1 June 2021 the Committee adopted the PIC/S Guidance on Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments (PI 041-1), which was published on the PIC/S website. It adopted in parallel a restricted Aide Memoire on inspection of data management and integrity (PI 049), which has been made available to inspectors on the password-protected Members Area. Both documents entered into force on 1 July 2021.

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

The Working Group on Harmonisation of the Classification of Deficiencies, led by Jenny Hantzinikolas (Australia / TGA), has been given the mandate to draft a PIC/S Guidance on Classification of Deficiencies (PI 040-1). The latter was successfully adopted and entered into force on 1 January 2019.

In order to align the PIC/S SOP on Inspection Report Format (PI 013-3) with 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.

#### **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) 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), will operate 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 has worked first on a revision of PE 005, which was renamed “PIC/S Good Practice Guidelines for Blood Establishments and Hospital Blood Banks”. A first draft was submitted to the Expert Circle on Human Blood, Tissue, Cells & ATMPs in Warsaw (Poland) on 23-25 October 2018. The draft was then reviewed by the SCH and advanced to Step 1 (PIC/S-internal consultation) on 11 March 2019 with a deadline for comments by 30 April 2019. A revised draft was advanced to Step 2 (consultation of national industry associations) with a deadline for comments until 17 April 2020.

The Working Group has then revised the PIC/S Guide to Inspections of Source Plasma Establishment and Plasma Warehouses (PI 008), which was converted into an Aide-Memoire (“PIC/S Aide Memoire to Inspections of Blood Establishments and Plasma Warehouses”) and advanced to Step 1 (PIC/S-internal consultation) with a deadline for comments until 6 December 2019.

In 2020, the Working Group completed the revision of both “PE 005: “PIC/S Good Practice Guidelines for Blood Establishments and Hospital Blood Banks” and “PI 008: PIC/S Aide Memoire to Inspections of Blood Establishments and Plasma Warehouses”. The finalised documents were then advanced to Step 3 and adopted on 9 April 2021. They entered into force on 1 June 2021.

The Working Group will now work 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 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 from some Members.

In 2021, the Committee was consulted on whether Members intended to consult their national stakeholders on the revised recommendations. The outcome showed that only one PA intended to do so. During the Committee meeting in October 2021, a majority of Members indicated their preference for a focused stakeholder consultation with selected industry and professional organisations.

### **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**

Due to the effects of the UK withdrawal from the European Union and EMA's Business Continuity Plan, the revision of Chapter 1 has been put on hold since 2019. 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. While the work of this Drafting Group had also been put on hold in 2019 due to EMA's Business Continuity Plan, the revision of Annex 11 was restarted in 2021.

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

Together with EMA, the PIC/S Working Group on Veterinary Medicinal Product (VMP), chaired by Grégory Verdier (France / ANSES-ANMV), is planning to revise Annexes 4 & 5 (manufacture of veterinary medicinal products other immunological veterinary medicinal products, and manufacture of immunological veterinary medicinal products).



On 23 September 2021, Members were invited to endorse the concept papers on the revision of Annex 4 and Annex 5 with a deadline for comments by 22 October 2021.

#### **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.

On 8 July 2021 Members were consulted on whether to advance Annex 13 on the Manufacture of Investigational Medicinal Products to Step 3 (adoption). There were no objections by the end of the deadline (1 September 2021). Comments were received from a number of Members and reviewed by the SCH.

As a next step, PIC/S Annex 13 will be submitted for adoption in order to enter into force at the same time as EC Regulation No. 536/2014 on Clinical Trials, replacing EU Annex 13, which is expected to be in early 2022.

#### **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 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.

Step 1 (internal consultation of PIC/S PAs) of Annex 16 ended on 10 February 2019. Following this consultation, the Committee discussed whether imports should be completely excluded from Annex 16, as the scope of the GMP Guide is normally limited to manufactured medicinal products. It consulted PAs on this issue in the course of 2019. The consultation showed that a vast majority of respondents were in favour of retaining provisions on imports, which would be applied on a voluntary basis.

Annex 16 was advanced to step 2 (public consultation) on 15 June 2021 for a 3-month period (i.e. until 15 September 2021). Comments were then reviewed by the SCH. As a next step, Annex 16 will be submitted for adoption in order to enter into force at the same time as Annex 13.

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

PIC/S is represented by Switzerland / Swissmedic in this Drafting Group on Annex 21 of the EU GMP Guide. The European Commission launched a public consultation on EU Annex 21 in 2020. Following a review of the draft, the SCH recommended to the PIC/S Committee to not transpose the new EU Annex 21 for PIC/S purposes. A formal decision by the Committee will be taken on the basis of the finalised EU Annex 21.

## 12. Guidance Documents and Procedures

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

## 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. 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 / next page.

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 three times in 2021: on 3 February, 27 May and 16 September 2021.

During these virtual meetings (mainly videoconferences), the SCT discussed the development of the PIC/S Inspectorates' Academy (PIA) as well as the planning of training events, which are all virtual due to the COVID-19 pandemic.

The following virtual training events were successfully organised by PIC/S in 2021 (in chronological order):

Date	Virtual Place	Activity	Organised by
11 May 2021	Geneva (Switzerland)	Webinar on ICH Q12 Training Material for Inspectors	PIC/S WG on ICH Q12 & PIC/S Secretariat
9-11 November 2021	Seoul (Republic of Korea)	PIC/S 2021 Seminar on Distant Assessment of GMP Compliance	Korea (Republic of) / MFDS
14-15 December 2021	Geneva (Switzerland)	Webinar by the PIC/S Expert Circle on Controlling Cross-Contamination in Shared Facilities (CCCISF)	WHO

## 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 2021 Seminar

The 2021 seminar was hosted by the Ministry Food and Drug Safety (MFDS), Republic of Korea, on the topic “GMP Assessment Approaches in Post COVID-19 Era”. This virtual seminar took place on 9-11 November 2021 and was attended by 315 inspectors from 54 authorities. All continents were represented.



This was the first time that Korea (Republic of) / MFDS hosted a PIC/S Seminar since it acceded to PIC/S in 2014. The seminar was officially opened by MFDS Minister, Mr KIM Ganglip. It focused on the on the current status of distant assessment approaches and relevant experiences as well as on the sharing of information on GMP inspection results based on mutual reliance.

The seminar consisted in presentations, case studies, panel discussions and virtual workshops, which were repeated twice to accommodate different time zones: on 9 November, for Asia and Europe (morning); and on 10 November, for America and Europe (afternoon).

The parallel workshops focused on the following topics:

- Current status on distant assessment among regulatory authorities and latest distant assessment technologies;
- Advantages and challenges of sharing information on GMP inspection results between regulatory authorities based on reliance.

The last day consisted in a common live plenum broadcasted to all participants simultaneously, during which the workshop results were presented and discussed.

### 15.2 Past and Future Seminars

In 2021, the SCT and the Committee reviewed:

- The evaluation report on the 2020 Seminar on “Distant Assessment of GMP Compliance”, which was virtually hosted by Finland / FIMEA on 8-10 December 2020.
- The preparations of the 2022 Seminar on “Inspecting the Pharmaceutical Quality System (PQS)” to be hosted by Ireland / HPRA in Dublin on 5-7 October 2022.

## 16. Joint Visits Programme / Coached Inspection Programme

Due to the pandemic, the PIC/S Joint Visits Programme (JVP) and Coached Inspections Programme (CIP) continued to be suspended due to COVID-19 related travel restrictions.

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 be able 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.

In 2018, the SCT started working on a revision of the JVP Guidelines in order to clarify and improve the operation of the programme. The revision process is ongoing.

### **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

Since 2011, 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.

## 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.



### 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 600 training materials and 250 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.

Cont'd

PIA was officially established at the PIC/S Committee meeting in Paris (France) on 20-21 October 2014. At its meeting in Nusa Dua (Indonesia) on 5-6 October 2015, the PIC/S Committee adopted the official PIA logo and its motto, which is “**Inspection Excellence through Harmonised Training**”. In July 2016, stage 1 of the Academy was launched successfully with its website and since then the incorporation of 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. This will include basic, specialised and ongoing levels, which will consist in a fine balance between e-learning modules and webinars designed to needs and face-to-face training. Delivery and monitoring are to be optimised and the training curriculum steps to result in recognised certification.

In 2019, the Committee endorsed the outline of a harmonised PIA Training Programme, including its related training Curricula and Cycle (see chart below) and Qualification Process. The PIA Training Programme aims to define harmonised minimum training requirements (and related curricula) in specific fields (e.g. API, sterile, biologicals, etc.). Training will be based on high quality training materials focusing on GMP requirements and inspection skills, to be delivered through various formats. The formats are to be provided either through training tools offered by PIA or by the PIC/S PAs or both.

In 2020, the Committee endorsed, subject to the availability of financial and human resources, the development of a Learning Management System (LMS) including e-learning modules. Thanks to a generous grant by Chinese Taipei / TFDA, a LMS was successfully developed. The LMS is the backbone for the management of PIA’s training tools and content.



Outline of PIA Training Cycle

In 2021, the PIC/S Secretariat, together with the assistance of the Expert Circle on QRM, started to develop a pilot e-learning module on Quality Risk Management (QRM) while a curriculum on QRM for GMP Inspectorates was published on the password-protected

part of the PIA website. The general outline (“skeleton”) for relevant curricula on the inspection of APIs, ATMPs, biologicals, blood, non-sterile, sterile, etc. was also prepared.

In parallel with the development of training modules, new training materials are published on a continual basis on PIA. As of 31 December 2021, over 850 PIC/S training materials and videos were available on PIA and most of them had been rated according to their relevance and level (e.g. for new inspectors) with respect to a future training curriculum.

To facilitate the financing of PIA, which is critical for its success, a project plan on PIA has been prepared and circulated to all PIC/S Heads of Agencies. The project plan, which aims to ensure the adequate and timely planning of the project, has been developed alongside of a 5-year Budget Plan for the period 2020-2024. Calls for voluntary contributions from PAs were made at the end of 2020 and 2021.

## 19. ICH Q12 Training Material

In 2020, the Committee established a PIC/S Working Group on Training Material for ICH Q12 (Pharmaceutical Product Lifecycle Management) under the chairmanship of the SCT Chairman, Jacques Morénas (France / ANSM). WG Members were appointed in May 2020. The WG started to develop training material jointly with the PIC/S Expert Circle on QRM, in particular:

- a PIC/S recommendation on how to evaluate / demonstrate the effectiveness of a PQS (PI 054-1);
- a PIC/S procedure for exchanging information on serious non-compliance related to PQS to inform about PQS failures; and
- a format for notification of effectiveness of a PQS.

This training material was presented to PIC/S inspectors at a PIC/S webinar on ICH Q12 Training Material for Inspectors, which was conducted on 11 May 2021 and financed by a grant by ICH. It was attended by around 350 participants from 50 agencies and 44 different jurisdictions. The webinar allowed to identify that most of the 50 participating agencies had no regulatory framework and no implementation guidance in place on ICH Q12.

## 20. 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 November 2021.

A Memorandum of Understanding (MoU) was signed with ISPE on 8 June 2021 to allow for a trial review by PIC/S of ISPE’S e-learning offer in relation with the development of PIA.



## 21. 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 30 March 2021. A number of Expert Circles and Working Groups operate under the SCEC – their activities (in the alphabetical order of the Expert Circle) are described below. Most Expert Circles' activities have been impacted by the pandemic since March 2020.

### 21.1 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. Due to the pandemic, the date and venue of the next meeting have not been determined. The Co-ordinating Committee of the Expert Circle, chaired by Linda Gallais (France / ANSM), did not meet in 2021.

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

The Expert Circle on Controlling Cross Contamination in Shared Facilities (CCCISF) 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 supposed to be hosted by WHO at its European Regional Office in Copenhagen (Denmark) in 2021. However, due to the pandemic, it was virtually hosted by WHO on 14-15 December 2021.

The webinar was attended by 375 participants and consisted in a mix of presentations and case studies. Inspectors discussed an update to the PIC/S aide-memoire; GMP requirements for contamination and cross-contamination; and cleaning validation.

## **21.3 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. The last meeting, planned in Kyiv (Ukraine) in May 2020, was cancelled due to the pandemic. The Expert Circle is considering organising a virtual meeting, provided that a host can be found.

The Co-ordinating Committee of the Expert Circle on GDP met in April and July 2021 in order to develop a new mandate, which will be submitted to the SCEC for review.

## **21.4 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 (Italy / AIFA).

At its last meeting in Jakarta on 8-10 October 2019, the Expert Circle agreed that its next meeting would be held in 2021. However, due to the pandemic, this did not materialise. The Co-ordinating Committee of the Expert Circle investigated alternative meeting opportunities in co-operation with other organisations.

A webinar on Distant Assessment (DA) / Remote Virtual Inspection (RVI) was jointly organised by the Expert Circle and the EU Commission Expert Sub-Group on Inspections in the Blood, Tissues and Cells Sectors (IES). The webinar, which was run twice to accommodate different time zones, took place on 18 June 2021 and was attended by around 325 participants. The objective of this webinar was to present activities and guidance documents in the field of DA/RVI, share experience of Competent Authorities and highlight differences between DA and RVI. 3 sessions were organised:

- a general session with presentations on DA/RVI;
- a specific session on the experience on DA/RVI gathered by some agencies (AGES, Health Canada, PEI, TGA, and US FDA) as well as a blood establishment (German Red Cross); and
- a final session to collect comments and questions from the audience as well as draw some conclusions.

Following contacts between PDA and the Co-ordinating Committee of the Expert Circle, PDA generously granted free virtual access to PIC/S inspectors attending the “2021 PDA Advanced Therapy Medicinal Products Conference” in Baltimore (USA) on 26-27 October 2021. The Chair of the PIC/S Working Group on Annex 2 also gave a presentation and participated, along with representatives from Health Canada, in panel discussions on Day 2 of this conference.

### **21.5 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.

The Expert Circle, chaired by Kevin O'Donnell (Ireland / HPRA), organised a very successful webinar on 24 September 2020, which was hosted by Turkey / TMMDA (see previous Annual Report). It also drafted a “PIC/S Recommendation on How to Evaluate / Demonstrate the Effectiveness of a Pharmaceutical Quality System in relation to Risk-based Change Management” (PI 054-1), which was successfully adopted on 30 June 2021 and entered into force on 15 July 2021.

The Co-ordinating Committee of the Expert Circle also developed a new mandate, which has been endorsed by the SCEC, SCT and SC COM on 4 October 2021. As a next step, it will be submitted to the PIC/S Committee for adoption.

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).

### **21.6 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.

On 11 October 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.

## 21.7 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). Following this positive assessment, a Working Group on VMP 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, the Working Group started to work on a concept paper 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.

These concept papers were finalised in 2021 following a review by the SCH, the PIC/S Committee and the EMA IWG on GMDP. They were then advanced for public consultation on 9 November 2021 for a 2-month period. As a next step, the joint EMA-PICS drafting group will review the comments received during the public consultation.

## 21.8 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.

# 22. 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

More recently, 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 held two virtual meetings in 2021: the first on 11 March and the second on 7 September. 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.

## 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 Working Group consists of representatives of Canada / ROEB, EDQM, EMA, Spain / AEMPS, UK / MHRA and US FDA. The purpose of the Working Group is to have a harmonised and consistent system in order to localise a manufacturing site.

The Working Group, co-chaired by Susan Laska (US FDA) and Jennifer Maguire (US FDA), held four meetings in 2021 and presented its operational conclusions to the PIC/S Committee at its virtual meeting in October 2021. The proposal of the WG on UFI is 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 aid in the identification of global pharmaceutical manufacturing facilities, for both national and third country inspections.

The proposal of the UFI WG was submitted to PAs by written procedure on 16 December 2021 with a deadline for comments until 28 January 2022. A number of other steps will need to be taken before the proposal can be implemented, amongst others, a survey to ensure that the geocodes can be included in the databases of all inspectorates.

## **23.2 Travel Safety**

The Working Group on inspectors' travel safety 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 was submitted for comments to PIC/S Members on 24 March 2021. After a review of the comments, the finalised guidance was adopted by the Committee on 30 June 2021. It entered into force on 15 July 2021.

## **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, the Working Group has been put on hold. It is expected to resume its activities in 2022.

## **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 have been invited to collect statistics on the number of desk-top assessments, which allow agencies to possibly waive a foreign inspection on the basis of an already existing GMP certificate or GMP inspection report.

The PIC/S Committee reviewed annual statistics, which shows that over 7,000 inspections were waved annually by PIC/S PAs in 2019 and 2020. The statistics also show that a number of 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 Chairman of the Working Group made a proposal to the PIC/S Committee at its virtual meeting in October 2021 to amend the template for yearly statistics on inspection reliance in order to add more questions on potential barriers and thus get more detailed replies on why a number of PAs do not make use of inspection reliance.

### **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. This was followed up by a call for volunteers. The Working Group was formally established on 1 October 2021. It is chaired by Jenny Hantzinikolas (Australia / TGA) and comprises 25 WG Members from 16 PAs and 2 Partner Organisations (EDQM and EMA).

A first meeting was held on 29 October 2021, during which the WG discussed its mandate. The mandate will be submitted to the PIC/S Committee in early 2022. There is a consensus in PIC/S that the WG should develop a common approach (including shared definitions) and training material on remote assessment without duplicating efforts made by other organisations or agencies.

## **24. 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. An informal poll, conducted during the Committee meeting, showed that there was strong support for the proposed policy. PAs will be duly consulted on the policy on 14 December 2021 with a deadline until 28 January 2022 to provide their feedback.

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

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

In 2020, 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).

This co-operation is particularly evident in fields covered by the respective co-operation agreements 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.

In addition to the above-mentioned organisations, PIC/S accepted in 2021 to grant the status of Associated Partner Organisation to the European Commission. The latter was invited to attend the Committee meeting in April 2021, during which Lenita Lindström-Gommers and Olivier Gross, Directorate-General for Health and Food Safety, Unit B4 (Medicinal Products – Quality, Safety, Innovation), proposed to establish an institutionalised relationship between PIC/S and the EC. Such a relationship should allow the EC (i) to support third countries' competent authorities in their efforts to join PIC/S; (ii) to refer to PIC/S in official Commission documents; and (iii) to interact efficiently with PIC/S in other areas such as GMDP standards (in particular the GMP Guide), Quality System requirements for inspectorates, the Joint Audit Programme (JAP), MRA audits, the training of inspectors, inspection reliance, etc.

### 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

On 20 May 2021, the PIC/S Chairperson gave a virtual presentation on “Application and Implementation of PIC/S” at a DIA China Annual Meeting in Suzhou (China).



## **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 2021, PIC/S and EMA continued to shared audit reports as well as information on upcoming (re)assessments.

## **ICMRA**

PIC/S regularly exchanges with the International Coalition of Medicines Regulatory Authorities (ICMRA) on regulatory collaboration. In 2021, exchanges focused on the interaction between with the ICMRA WG on distant assessment, which is led by UK / MHRA, and the PIC/S Working Group on Distant Assessment with the aim to avoid a duplication of efforts.

## **IFPMA**

The PIC/S Chairperson gave a presentation on “Overview of GMP Harmonisation - PIC/S’ Role” at an IFPMA event held virtually 28 May 2021.

## **ISPE**

The PIC/S Chairperson presented on the topic of “Remote/Distant Assessments” at the ISPE Global Pharmaceutical Regulatory Summit, held virtually on 28 April 2021. The PIC/S Deputy Chairperson attended the ISPE Pharmaceutical Manufacturing Leadership Forum 2021, held virtually on 17 May 2021.

## **PDA**

PDA granted free virtual access to PIC/S inspectors attending the “2021 PDA Advanced Therapy Medicinal Products Conference” in Baltimore (USA) on 26-27 October 2021. See also Section 21.4.

## **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 on next page.

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:
    - (i) the regularity of the receipt, custody and disposal of all funds and other financial resources of PIC/S;
    - (ii) the conformity of commitments and expenditures with the budget voted by the PIC/S Committee;
    - (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 was, until October, Marta Alicia Cicero (Argentina / INAME), who sadly passed away. The SCB held three virtual meetings: on 23 March, 16 September, and 17 November 2021. During these meetings, it reviewed the 2020 PIC/S accounts, prepared the 2022 budget and the 2022-24 budget plan, and discussed the financing of PIC/S as well as that of PIA, as detailed below.

## 27. 2020 Accounts

The SCB reviewed the report on the 2020 accounts by the external auditor, Moore Stephens Refidar S.A. as well as the Statement of Accounts for the Financial Year 2020. In line with the SCB's recommendation, the Committee approved by written procedure the Statement of Accounts for the Financial Year 2020. It also agreed to transfer the

2020 balance and the bank interests for a total of CHF 25,378.77 to the PIC/S Reserve Fund and to discharge the Secretary of his responsibility for the 2020 accounts.

The SCB also reviewed the financial report on the 2020 annual seminar virtually hosted by Finland / FIMEA, which resulted in a surplus of € 38,820. FIMEA generously donated this surplus to PIC/S.

## 28. 2021 Accounts

The SCB reviewed the status of income and expenditures of the 2021 accounts during the year while the Committee appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2021 accounts, which is scheduled to take place in early 2022.

## 29. 2022 Budget

As recommended by the SCB, the Committee approved by written procedure, which was successfully completed on 10 December 2021, the 2022 PIC/S Budget for an amount of CHF 1,331,265 (compared with CHF 1,064,270 the year before). The increase of the budget is mainly due to the organisation of PIC/S' 50<sup>th</sup> anniversary in Dublin in 2022.

## 30. Budget Plans & Future Financing

In the course of 2021, the SCB discussed three budget plans: a staff increase budget plan (2021-23); a 3-year budget plan (2022-24); and a 5-year budget plan specific for PIA (2020-24). In line with PIC/S Financial Regulations, budget plans are established by the SCB to assess future commitments and income.

- The staff increase budget plan for the period 2021-23 was successfully adopted by the PIC/S Committee on 11 June 2021. It foresees a gradual raise of the annual fee over the period 2022-23, which will allow for an increase of human resources at the Secretariat in order to match the significant expansion of PIC/S activities over the past two decades.
- The PIC/S 3-year budget plan (2022-24) was reviewed by the SCB based on estimated income and expenditure for the next three years.
- The PIA 5-year budget plan for the period 2020-24 was developed with the aim of securing the financing of PIA in line with its development, as described in the PIA Business Plan. The PIA budget plan foresees an escalation of income and expenses in the first four years (2020-2023), corresponding to the building up of PIA, followed by a stabilisation of the budget (from 2024) focusing on maintenance.

The SCB also discussed and endorsed a SCT position paper on the development of PIA financing, which was presented to the Committee at its October virtual meeting. The paper reviews four sources of potential funding for PIA, i.e.: (i) voluntary contributions from PA; (ii) third-party funding; (iii) new income; and (iv) other income (e.g. non-Member fees). A proposed format for voluntary contributions by PIC/S PAs, contained in the position paper, was supported by Members during the meeting.

## 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, chaired by David Churchward (MHRA / UK), held one virtual meeting 3 September 2020, during which it discussed 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). The PIC/S representative to ICH is the SC COM Chairman, who attends ICH Assembly meetings. In 2021, he participated in the virtual ICH Assembly meetings on 2-3 June and 16-17 November 2021. A number of PIC/S experts also take part 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).

In 2019, the ICH Management Committee (MC) made a proposal to PIC/S for more routine engagement between the two organisations. Following a bilateral meeting between the ICH MC Chair, Dr Theresa Mullin (US FDA), and the Executive Bureau in Toyama, a pilot on was successfully launched in April 2020. It covers co-operation on ICH Q Guidelines between the two organisations in two specific ICH EWG: Q9 and Q12. For Q12 related training for inspectors, see Section 19.

To facilitate the involvement of PIC/S in ICH EWGs, the SC COM has drafted an SOP, which was circulated for comments to the PIC/S Committee in November 2020. Its finalisation was put on hold in 2021 due to other priorities.

### 33. Foreign Inspections

Due to the pandemic and related travel restrictions, almost no foreign inspections took place in 2021. As a result, the list of foreign inspections planned by PIC/S PAs and Partner Organisations was neither circulated nor updated. Instead, a survey has been conducted to identify PAs, which have resumed with foreign inspections, either on-site or at distance. This survey has proven to be useful in the context of increased inspection reliance between PIC/S PAs.

The SC COM reviewed past data on foreign inspections and concluded that only a few sites are inspected by several PIC/S PAs. In 2019, out of a PIC/S list containing approximately 700 foreign inspections, only 7 sites were inspected more than once. However, since not all PAs contribute to the PIC/S List of Foreign Inspections, the figure may be higher. All PAs are thus encouraged to participate to future lists.

The SC COM also consulted Members by poll during the April Committee meeting on whether the actual date (if different from the planned date) of the foreign inspection should be mentioned in the PIC/S List of Foreign Inspections. Most Members supported the inclusion of the actual date but they also noted a risk of duplication with other existing databases.

### 34. Other SC COM issues

The SC COM, together with the Secretariat, has continued to work on the following issues:

- PIC/S stakeholder mapping;
- List of GMDP Inspectors employed by PIC/S PA and Partners.
- List of PIC/S Single Contact Points (SCP);
- New standard presentation on PIC/S and promotional video on PIC/S;
- Questionnaire to determine the utilisation and implementation of PIC/S guidance documents;
- PIC/S presence on social media.

With regard to the Working Group in charge of transposing, for PIC/S purposes, the revised EMA procedures on (i) Managing Reports of Suspected Quality Defects in Medicinal Products; and (ii) Handling Rapid Alerts Arising from Quality Defects, it has remained on hold for most of 2021 while waiting for the relevant EMA procedures to be adopted and published. This was eventually the case on 26 October 2021 and the Working Group was reactivated by the end of 2021.

PAs as well as Partner Organisations continued to make use of virtual meetings or e-mails to communicate on important changes in their respective agencies.

## 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**  
(as of 31 December 2021)

(in the alphabetical order of the jurisdiction in which they are located)

	<b>PARTICIPATING AUTHORITY</b>	<b>ACRONYM</b>
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>	<i>Agence nationale de sécurité du médicament et des produits de santé (French National Agency for Medicines and Health Products Safety)</i>	ANSM
	<i>Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (French Agency for Food, Environmental &amp; Occupational Health Safety)</i>	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.



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	National Agency for Drug and Food Control	NADFC
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
	Directorate General for Animal Health and Veterinary Medicinal Products (Direzione generale della sanità animale e dei farmaci veterinari)	DGSAF
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 DGSAF 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

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<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.