PHARMACEUTICAL INSPECTION CONVENTION

PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

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17 July 2020

ANNUAL REPORT 2019

Prepared by the Secretariat

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

www.picscheme.org

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What is PIC/S?

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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 2019, PIC/S comprised 52 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 PAs' 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 2019.

A N N U A L   R E P O R T   2 0 1 9

THE YEAR IN A NUTSHELL

Successful chairmanship for Singapore / HSA

1.   2019 was the second year of the chairmanship of Mr Boon Meow Hoe from Singapore's Health Sciences Authority (HSA). Under the efficient leadership of Mr Boon, who is the first Chairman from Asia in PIC/S' history, PIC/S was able to achieve a great number of successes during the year under review (see below).

Mr Boon chaired two PIC/S Committee meetings: first in Geneva (Switzerland) on 9-10 April 2019, and then in Toyama (Japan), on 11-12 November 2019, in conjunction with the annual PIC/S Seminar hosted by Japan's Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA).

Photo: Mr Boon Meow Hoe, PIC/S Chairman

PIC/S' expansion continues

2.   PIC/S' membership continued to expand in 2019. At its meeting in Toyama, the Committee invited Italy's Directorate General for Animal Health and Veterinary Medicinal Products (DGSAF) to join PIC/S as the 53rd Participating Authority as from 1 January 2020.

Italy / DGSAF applied for PIC/S membership on 26 August 2016 and an on-site assessment visit took place on 14-18 January 2019. DGSAF is the 4th agency, exclusively competent for veterinary medicinal products, to join PIC/S.

3.   A successful on-site assessment visit also took place on 9-21 October 2019 at Brazil's Agência Nacional de Vigilância Sanitâria (ANVISA). The visit report will be tabled to the Committee at its next meeting.

4.   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.

Members
Applicants
Pre-Applicants
Former Pre-Applicants
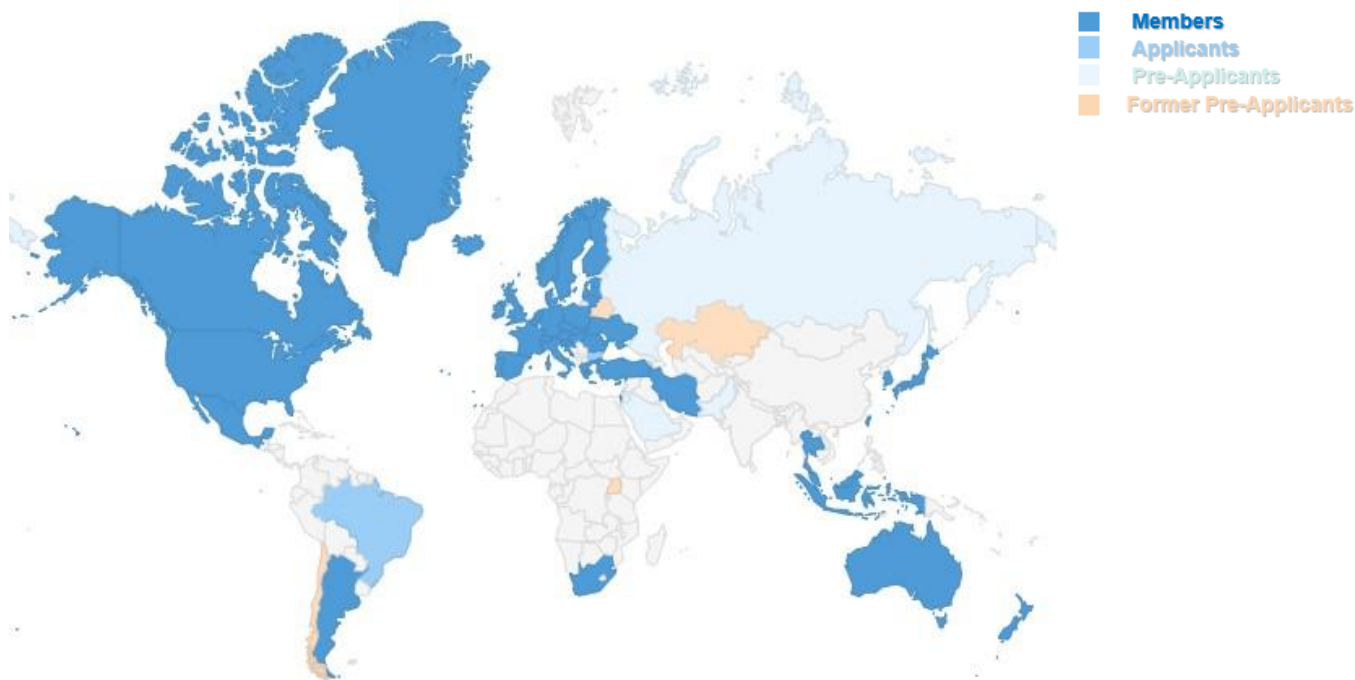
PIC/S Inspectorates' Academy (PIA) unfolds

5.   The development of the PIC/S Inspectorates' Academy (PIA) was further advanced in 2019. 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.

6.   At its meeting in Toyama, the Committee endorsed in principle a number of key documents for the development of PIA. These documents outline an architecture for a harmonised PIA Training Programme (including training curricula and training cycle) and qualification process. A pilot demo of an e-learning module, based on a Curriculum on QRM for GMP Inspectorates, was also presented.

7.   With these key documents as well as the pilot on QRM e-learning module, PIA will now be able to unfold, subject to the availability of financial resources. To explore new financial resources to support PIA and other PIC/S projects, a Working Group on Third-Party Funding was established under the PIC/S Executive Bureau.

Revision of Annexes 1 & 2 of the PIC/S GMP Guide

8.   PIC/S continued to contribute to expert discussions on contemporary GMP issues such as the manufacture of sterile products (Annex 1 of PIC/S GMP Guide) and the manufacture of biological medicinal substances and products for human use (Annex 2 of PIC/S GMP Guide).

9.   In 2019, the joint PIC/S-EMA Working Group on Annex 1 (manufacture of sterile medicinal products) continued its review of the 6,300 comments received during the public consultation. This resulted into a new draft of the revised Annex 1, which will be submitted to a focused stakeholder consultation in early 2020.

10.   In parallel, the 2019 Annual Training Seminar of PIC/S focused on the revision of Annex 1, in particular the Quality Assurance of Sterile Medicinal Products. The Seminar was organised by Japan's Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) in Toyama (Japan) on 13-15 November 2019. It was attended by over 160 inspectors from approximately 50 jurisdictions around the world. The Seminar provided participants with a better understanding of Annex 1, based on issues discussed during its current revision and through case studies of sterility assurance.

2019 PIC/S Seminar
Official Photo

11.   In 2019, the PIC/S Working Group on the revision of Annex 2 of the PIC/S GMP Guide prepared (i) a new Annex 2A for the Manufacture of Advanced Therapy Medicinal Products (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.

12.   These two documents were advanced to Step 1 (consultation of PAs) and then to Step 2 (public consultation) in the form of a targeted stakeholder consultation with the assistance of professional organisations, which ended on 20 December 2019. They were also discussed during the 25th meeting of the Expert Circle on Human Blood, Tissues, Cells and ATMPs, hosted by Indonesia / NADFC, in Jakarta on 8-10 October 2019.

Effectiveness of a Pharmaceutical Quality System (PQS) in relation to risk-based change management

13.   In 2019, the PIC/S Expert Circle on Quality Risk Management (QRM) developed a new draft recommendation, which provides guidance on how to evaluate and demonstrate the effectiveness of a PQS in relation to risk-based change management (PI 054-1 (Draft 1)).

14.   This document is very important, as the PIC/S GMP Guide requires companies to demonstrate the effectiveness of their PQS and to apply quality risk management (QRM) principles to change control activities. It is also important for the future implementation of ICH Q12.

15.   The draft recommendation will be applied on a 6-month trial basis by PIC/S Participating Authorities; it is not open for comments by industry.   The draft recommendation and the related concept note are available on the PIC/S website.

Changes in the Executive Bureau

16.   The Executive Bureau (EB) met twice in 2019: first in Geneva (Switzerland) on 9 April and then in Toyama (Japan), on 11 November. EB meetings are traditionally devoted to the preparation of the Committee's meeting; the EB also discusses strategic orientations as well as financial and administrative issues. In the course of the year, the EB also held bilateral meetings with China / NMPA (on 8 April and 14 November) and with the Chair of the ICH Management Committee (on 13 November 2019).

PIC/S Executive Bureau in 2019 (from left to right): Jacques Morénas (France / ANSM); Mark Birse (UK / MHRA); Susan Laska (US FDA); Paul Gustafson (Canada / RORB); Boon Meow Hoe, PIC/S Chairman (Singapore / HSA); Andreas Krassnigg (Austria / AGES); Anne Hayes, PIC/S Deputy Chairperson (Ireland / HPRA); Ger Jan van Ringen (Netherlands / IGJ).

17.   The composition of the EB in 2019 was the following:

➤ Mr Boon Meow Hoe (Singapore / HSA), PIC/S Chairman;

➢ Ms Anne Hayes (Ireland / HPRA), PIC/S Deputy Chairperson and Chair of the Sub-Committee on Compliance (SCC);

➢ Mr Jacques Morénas (France / ANSM), Chair of the Sub-Committee on Training (SCT);

➢ Mr Paul Gustafson (Canada / ROEB), Chair of the Sub-Committee on GM(D)P Harmonisation (SCH);

➢ 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 Mark Birse (United Kingdom / MHRA), Chair of the Sub-Committee on Communication (SC COM) (until 30 November 2019); and

➢ Ms Susan Laska (US FDA), Chair of the Sub-Committee on Strategic Development (SCSD).

18.   At its meeting in Toyama, the PIC/S Committee elected Ms Anne Hayes (Ireland / HPRA) as Chairperson for the period 2020-2021. Ms Hayes has represented HPRA in the PIC/S Committee since 2005. She has chaired the Sub-Committee on Compliance and been an EB Member since 2013.

Outgoing PIC/S Chairman (2018-2019), Mr Boon Meow Hoe (Singapore / HSA), welcoming incoming PIC/S Chairperson (2020-2021), Ms Anne Hayes (Ireland / HPRA).

19.   The PIC/S Committee renewed the composition of the EB, which will assist the Chairperson in her task for the period 2020- 2021. The EB will consist 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 Anctil (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).

PIC/S Sub-Committee Structure

20.   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.

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

OVERVIEW ON SUB-COMMITTEE STRUCTURE
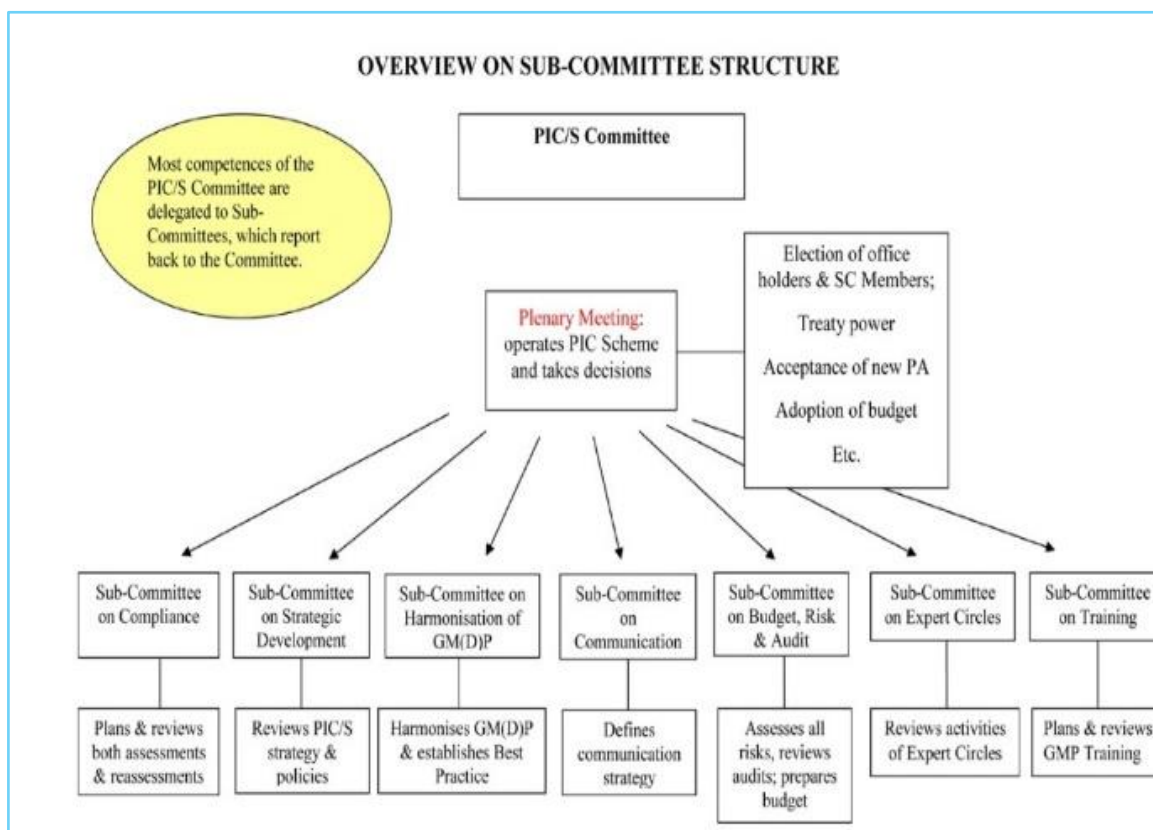
COMPLIANCE

22.   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.

23.   This task has been entrusted to the Sub-Committee on Compliance (SCC) under the chairmanship of Anne Hayes (Ireland / HPRA). 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

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24.   The SCC held four teleconferences in 2019: on 21 March, 31 July, 26 September and 17 December 2019. It discussed membership applications, pre-

accession applications, assessment and reassessment procedures as well as contacts with non-Members, as detailed below.

Evaluation and Re-evaluation Procedures

25.   Three Working Groups are operating under the SCC and reviewing evaluation and re-evaluation procedures:

  ➤ Working Group on the Interpretation of the Audit Checklist
  ➤ Working Group on the Drafting of Pre-Accession Guidelines
  ➤ Working Group on the Revision of the Accession Guidelines

Working Group on the Interpretation of the Audit Checklist

26.   The Working Group on the interpretation of the Audit Checklist is run in co-operation with the EMA Compliance Group on the Joint Audit Programme (JAP). The Working Group, led by Louise Kane (Canada / ROEB), has developed an interpretation guideline on the 78 indicators contained in the PIC/S-JAP Audit Checklist, which is based on the Evaluation Guide for GMP Regulatory Compliance Programme of Health Canada. A first draft of the interpretation guideline has been circulated to Members for comments on 15 October 2019 with a deadline until 30 November 2019.

Working Group on the Drafting of Pre-Accession Guidelines

27.   At its meeting in Toyama, the Committee adopted new PIC/S Pre-Accession Guidelines (PS/W 12/2019), developed by the Working Group on the Drafting of Pre-Accession Guidelines, led by Jacques Morénas (France / ANSM). The draft Guidelines were reviewed by the SCC and submitted to Members for comments on 1 July 2019 with a deadline until 31 July 2019.

28.   The main objective of pre-accession is to explain PIC/S requirements, notably the 78 indicators of the PIC/S audit checklist, to the Pre-Applicant so that it is then able to identify the gaps between PIC/S requirements and the requirements under its own national GMP Regulatory Compliance Programme. It is then up to the Pre-Applicant to make a gap analysis, based on its understanding of PIC/S requirements. Up to this point, the gap analysis was done by PIC/S leading to a duplication of work between "accession" and "pre-accession".

Working Group on the Revision of the Accession Guidelines

29.   The Working Group on the revision of the Accession Guidelines and related documents, in particular those of the PIC/S Joint Reassessment Programme (JRP), is led by Jacques Morénas (France / ANSM). It has prepared the following documents:

  ➤ revised PIC/S Guidelines for Accession;
  ➤ revised PIC/S Questionnaire for Assessment;
  ➤ new Assessment Report Template (harmonised with the EMA JAP Assessment Report Template).

Membership Applications

30.   In the course of 2019, PIC/S continued the assessment of the following four membership applications (in alphabetical order):

Armenia / SCDMTE

31.   Armenia's Scientific Center of Drug and Medical Technologies Expertise (SCDMTE) applied for PIC/S membership on 8 September 2017, further to addressing the Corrective and Preventive Actions (CAPA) resulting from the PIC/S pre-accession gap analysis conducted in 2013. The application was formally completed on 13 April 2018. However, due to a change in Government in Armenia in 2018 and the adoption of new regulations, SCDMTE requested sufficient time to update the questionnaire and translate the regulations. A new Head of Agency was also appointed to SCDMTE in 2019.

32.   As a result of these changes, the appointed Rapporteur, Michel Keller (formerly Switzerland / Swissmedic), and the Co-Rapporteur, Mark Cilia (Malta / MAM), are awaiting the revised application, which should be submitted in Q1 2020, before completing the paper evaluation.

Bulgaria / BDA

33.   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.

34.   The appointed Rapporteur, Jacques Morénas (France / ANSM), and 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. The planned on-site assessment visit is expected to take place in 2020.

Brazil / ANVISA

35.   Brazil's Agência Nacional de Vigilância Sanitária (ANVISA) lodged a partial membership application in 2010, which was completed in October 2014. In April 2018, the Committee granted a one-year stop-clock in order for ANVISA to update the membership application following the reorganisation of its inspection system.

36.   The Brazilian Health Surveillance System is based on a decentralised system, which includes 27 States, 5,568 Municipalities, the Federal District of Brasilia and ANVISA. Following the implementation of two strategies in the field of GMP inspections, the number of GMP actors has been reduced to 7 States, 2 Municipalities and ANVISA.

37.   On 17 April 2019, Brazil / ANVISA submitted its updated membership application. The PIC/S Committee nominated an Audit Team consisting of the Rapporteur, Mark Birse (UK / MHRA), the Co-Rapporteur, Ana Rita Martins (Portugal /

INFARMED I.P.), and 2 Team Members from Hong Kong SAR / PPBHK and Malta / MAM.

38.   The on-site assessment visit took place on 9-21 October 2019. The Assessment Team reviewed the Quality System at ANVISA's Headquarters, in Sao Paulo municipality as well as in the State of Minas Gerais. It also observed inspections in Sao Paulo and Minas Gerais. The visit was successful and the report will be presented at the next Committee meeting.

Italy (Vet) / DGSAF

39.   Italy's Directorate General for Animal Health and Veterinary Medicinal Products (DGSAF) applied for PIC/S membership on 26 August 2016 following a JAP audit, which was shared with PIC/S. As a result, the application process consists of a partial assessment taking into account the EMA JAP audit.

40.   The on-site assessment visit took place on 14-18 January 2019. The audit team consisted of the Rapporteur, Jason Todd (UK / VMD), and a Team Member from France / ANSES-ANMV. They followed up on the CAPA following the EMA JAP audit, observed an inspection of a biological manufacturer and visited two testing laboratories. The report was reviewed by the SCC.

41.   Based on the visit' report and the team's recommendation, the Committee invited Italy / DGSAF to join PIC/S as the 53rd Participating Authority as from 1 January 2020.

Pre-Accession Applications

42.   In the course of 2019, the following 5 pre-accession applications were under review:

Bangladesh / DGDA

43.   Bangladesh's Directorate General of Drug Administration (DGDA) applied for pre-accession on 26 February 2019. At its meeting in Geneva, the Committee appointed Henning Willads Petersen (Denmark / DKMA) as Rapporteur.

Jordan / JFDA

44.   The Jordan Food and Drug Administration (JFDA) submitted a complete pre-accession application on 9 August 2018. A new Rapporteur, Belinna Binti Abu Bakar (Malaysia / NPRA), was appointed at the PIC/S Committee meeting in April 2019. A preliminary gap analysis was shared with Jordan / JFDA in November 2019. It still needs to be reviewed by the SCC.

Pakistan / DRAP

45.   The Drug Regulatory Authority of Pakistan (DRAP) submitted a pre-accession application on 18 September 2017. DRAP was established in 2012 and is operational since 2015. It employs 25 inspectors. The PIC/S GMP Guide, which has been adopted, will be implemented during a transitional period (1 July 2020 – 31 December 2021).

46.   The Rapporteur, Petra Müllerová (Czech Republic / ISCVBM), reviewed the pre-accession application in 2018 and 2019. A report will be provided at the next PIC/S Committee meeting.

<u>Russian Federation / Minpromtorg and FSI SID&GP</u>

47.   The Ministry of Industry and Trade of the Russian Federation (Minpromtorg Russia) and the Federal State Institution "State Institute of Drugs and Good Practices" (FSI "SID & GP") jointly submitted a pre-accession application on 28 August 2017. The Federal Service for Surveillance in Healthcare (Roszdravnadzor), which is in charge of licensing and quality defects, joined the pre-accession process in the course of 2019.

48.   The pre-accession process was conducted in line with the new Guidelines on Pre-Accession (see paragraphs 27-28 above), which means that the Rapporteur, Jacques Morénas (France / ANSM), explained the PIC/S requirements to Minpromtorg, FSI SID&GP and Roszdravnadzor, which together completed the self-assessment (the 78 indicators of the PIC/S audit checklist). No assessment of the documentation as such was done by the Rapporteur.

49.   At the PIC/S Committee meeting in Toyama, the Rapporteur presented a short high-level report indicating that the Russian competent authorities had a good understanding of PIC/S requirements. The report was endorsed by the PIC/S Committee and the pre-accession process closed.

<u>Saudi Arabia / SFDA</u>

50.   The Saudi Food and Drug Authority (SFDA) submitted a pre-accession application on 31 July 2017. The pre-accession process was conducted in line with the new Guidelines on Pre-Accession (see paragraphs 27-28 above).

51.   At the PIC/S Committee meeting in Geneva, the Rapporteur, Jacques Morénas (France / ANSM), presented a short high-level report indicating that Saudi Arabia / SFDA had a good understanding of PIC/S requirements. The report was endorsed by the PIC/S Committee and the pre-accession process was closed. Saudi Arabia / SFDA indicated that it intended to apply for membership.

Reassessment of Participating Authorities

52.   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.

53.   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.

54.   In 2019, the Committee reviewed the preparation and reporting of the following reassessments (in alphabetical order):

Reassessment of Argentina / INAME

55.   The reassessment of Argentina / INAME took place on 5-9 November 2018. The Audit Team Leader, Jacques Morénas (France / ANSM), was assisted by auditors from Israel / ISCP, Netherlands / IGJ, and Spain / AEMPS. The Team reviewed the quality system and observed three inspections: one sterile, one non-sterile and one API. The reassessment report was discussed by the SCC and the conclusion endorsed by the Committee at its meeting in Geneva. Argentina / INAME continues to be considered equivalent under the PIC Scheme.

Reassessment of Canada / ROEB

56.   The on-site reassessment visit took place on 7-11 October 2019. The Audit Team consisted of three Members: the Team Leader, Richard Andrews (UK / MHRA), and two auditors from Australia / TGA and Switzerland / Swissmedic. The reassessment report as well as the team's conclusions will be reviewed by the SCC and the Committee in 2020.

Reassessment of Indonesia / NADFC

57.   The reassessment of Indonesia / NADFC is due in 2020. In 2019, a call was made for the constitution of an Audit Team for the reassessment of Indonesia / NADFC.

Reassessment of New Zealand / Medsafe

58.   New Zealand / Medsafe is due for a reassessment in 2020. In 2019, the Committee appointed the Audit Team, which consists of the Team Leader, Jacques Morénas (France / ANSM), who will carry out his on-site assessment visit back to back with the 2020 Seminar in Thailand, and an auditor from Ireland / HPRA, who will observe an inspection of an aseptic manufacturer in December 2019.

Reassessment of South Africa / SAHPRA

59.   The re-assessment of South Africa / SAHPRA was postponed twice at the request of SAHPRA: first, to Q4 2019 and then to June 2020. SAHPRA took over from the Medicines Control Council (MCC) on 1 February 2018 and its reorganisation has taken longer than scheduled. The Team Leader is Jacques Morénas (France / ANSM).

60.   At its meeting in Toyama, the PIC/S Committee decided to send an official letter asking South Africa / SAHPRA to confirm the dates of the reassessment.

Reassessment of Switzerland / Swissmedic (2018-19)

61.   The reassessment of Switzerland / Swissmedic took place on 15-19 October 2018. It was combined with an MRA re-assessment by Health Canada and co-ordinated with the EMA JAP audit of Liechtenstein / AG.

62.   The Audit Team, led by Susan Laska (US FDA), consisted of auditors from Health Canada, Germany / ZLG and UK / MHRA. The reassessment consisted of a

review of the documentation, an on-site assessment at Swissmedic, a visit to the laboratories and one observed inspection. The reassessment report was discussed by the SCC and the conclusion endorsed by the Committee at its meeting in Toyama. Switzerland / Swissmedic continues to be considered equivalent under the PIC Scheme.

Reassessment of Ukraine / SMDC (2018-19)

63.   The reassessment of Ukraine / SMDC took place on 22-26 October 2018. The Team Leader, Ana Rita Martins (Portugal / INFARMED IP), was assisted by two audit team members from Chinese Taipei / TFDA and Denmark / DKMA. Two inspections (one sterile, one non-sterile) were observed and the quality system reviewed at SMDC. The reassessment report was discussed by the SCC and the conclusions endorsed by the Committee at its meeting in Geneva. Ukraine / SMDC is considered equivalent under the PIC Scheme, subject to the completion of Corrective and Preventive Actions (CAPA), which was successfully implemented under the monitoring of the SCC in the course of 2019.

Corrective Action / Update by recently acceded PAs or PAs under Reassessment

64.   The SCC continued to monitor corrective actions by recently acceded PIC/S PAs or PIC/S PAs under reassessment. In 2019, the CAPA were closed for Australia / TGA and Ukraine / SMDC while the CAPA for Iran / IFDA was removed from the list.

Non-Members

65.   Close contacts were kept with a number of non-Members, in particular with China's National Medical Products Administration (NMPA). Two meeting were organised between the Executive Bureau and China / NMPA to discuss accession-related issues: the first meeting took place in Geneva (Switzerland) on 8 April 2019 and the second meeting was held in Toyama (Japan) on 14 November 2019.

GMDP

66.   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 ensure the maintaining of high standards of quality assurance 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.

67.   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.

68.   The mandate of the Sub-Committee on the Harmonisation of GM(D)P (SCH), chaired by Paul Gustafson (Canada / ROEB), 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

69.   The SCH held three teleconferences on 21 February, 16 May, and 19 September 2019, during which it discussed the revision of the PIC/S GMP Guide and the drafting of guidance documents. It also monitored and reviewed the work carried out by a number of Working Groups, detailed below.

Working Groups under the SCH

70.   Eight Working Groups are operating under the SCH.

Working Group on Annex 1

71.   The PIC/S Working Group on Annex 1 (manufacture of sterile medicinal products) was established at the Rome meeting on 15-16 May 2014. At the Paris meeting on 20-21 October 2014 the WG was 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. Since 2019, it is led by Abdelaali Sarakha (France / ANSM).

72.   Following two written consultations of PIC/S PA 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 and 2019. This resulted into a new draft of the revised Annex 1.

73.   At its meeting in Toyama, the PIC/S Committee endorsed a proposal by the WG to launch a focused stakeholder consultation on the draft revision of Annex 1. The joint PIC/S-EU-WHO focused stakeholder consultation will be launched in early 2020 with the support of industry associations, which will compile comments to specific questions.

Working Group on the revision of Annex 2

74.   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, the Committee decided to establish a Working Group on the revision of Annex 2 of the PIC/S GMP Guide (Manufacture of biological medicinal substances and products for human use).

75.   The Working Group was established in 2018; it is chaired by Francesco Cicirello (Australia / TGA) and consists of 18 experts from PAs as well as 2 Partner Organisations: EMA and WHO. WHO is acting as Deputy Chair.

76.   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.

77.   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 consists in a targeted stakeholder consultation with the assistance of professional organisations (ECA, IFPMA, ISCT, ISPE, PDA and SQA), which have agreed to collect comments from stakeholders on behalf of PIC/S.

Working Group on Data Integrity

78.   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 aims at developing a PIC/S data integrity guidance document for inspectors to provide them 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.

79. 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 has taken the form of a "focused consultation" seeking comments from industry on specific questions. ECA, IFPMA, ISPE and PDA have agreed to compile the comments from their members. In parallel, PIC/S PAs have been re-invited to apply the revised draft guidance on a trial basis.

80. In 2019, the WG reviewed comments received during the focused stakeholder consultation.

81. Two other documents have been developed by the Working Group on Data Integrity and submitted to Members for comments in 2019:

➤ PIC/S Aide-Memoire on Inspection of Data Management and Integrity (PI 049-1 (Draft 1)); and

➤ PIC/S Data Integrity System Specific Guidance on Chromeleon 7 Chromatography Data Systems and Server/Client Systems (PI 050-1 (Draft 1)).

82. During its meeting in Geneva, the Committee agreed that these two guidance documents for inspectors should be advanced to Step 3.

Working Group on Harmonisation of the Classification of Deficiencies

83. The Working Group on Harmonisation of the Classification of Deficiencies, led by Jenny Hantzinikolas (Australia / TGA), has been mandated to draft a guidance document, which includes a tool for Inspectorates to improve harmonised risk classification of GMP deficiencies. Recommendations to facilitate harmonised compliance and enforcement approaches to address GMP non-compliance are included. These efforts are hoped to facilitate a more consistent approach among international regulatory authorities when responding to GMP deficiencies and GMP non-compliance.

84. At its meeting in Chicago in September 2018, the Committee adopted the PIC/S Guidance on Classification of Deficiencies (PI 040-1) with an entry into force on 1 January 2019. The Working Group did not have any activities in 2019.

85. In order to align the PIC/S SOP on Inspection Report Format (PI 013-3) with PI 040-1, 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.

86. The PIC/S Guidance on Classification of Deficiencies has also been shared with the Expert Circle on GDP, which will review it and discuss the possibility to adapt it for GDP purpose.

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

87. The Working Group on Controlling Cross-Contamination in Shared Facilities has drafted 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. This Aide Memoire will allow inspectors to better assess the risks of cross contamination in shared facilities.

88.   At its meeting in Geneva in April 2018, the Committee adopted the Aide-Memoire on Cross-Contamination in Shared Facilities (PI 043-1), which entered into force on 1 July 2018.

89.   The Working Group was then turned into an Expert Circle with the aim of developing training material for inspectors.

90.   At its meeting in Toyama, the Committee adopted a mandate (PS/W 34/2019 (Draft 1)) for a new Working Group on Cross-Contamination Control in Shared Facilities CCCISF, which will operate along the Expert Circle on CCCISF. The WG will update the Aide Memoire on Cross-Contamination in Shared Facilities (PI 043-1).

91.   In addition, the Expert Circle on Controlling Cross-Contamination in Shared Facilities (CCCISF), chaired by Graeme McKilligan (UK / MHRA), has reviewed the comments received during Step 1 (internal consultation of PIC/S PA), which ended on 31 July 2019, of the following two documents:

➢ PI 052-1 (Draft 1): Aide-memoire on the Inspection of Health Based Exposure Limit (HBEL) Assessments and Use in Quality Risk Management;

➢ PI 053-1 (Draft 1): Questions and Answers on Implementation of Risk-based Prevention of Cross-contamination in Production and 'Guideline on Setting HBEL for Use in Risk Identification in the Manufacture of Different Medicinal Products in Shared Facilities'.

92.   It is expected that these documents will be advanced for adoption in early 2020.

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

93.   The Working Group of Experts, 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 (PE 008-3) with a view to harmonise them with the EDQM-EC Good Practices Guidelines for blood establishments.

94.   The Working Group presented a first draft revision of the PIC/S GMP Guide for Blood Establishment (PE 005-4) 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. Comments received during Step 1 have been reviewed by the Working Group.

95.   The Working Group has also initiated a revision of the PIC/S Guide to Inspections of Source Plasma Establishment and Plasma Warehouses (PI 008-4 (Draft 1)) in order to align it with PE 005-4. The Guide has been converted into an Aide-Memoire, which was advanced for Step 1 (PIC/S-internal consultation) with a deadline until 6 December 2019.

96.   At its meeting in Geneva, the Committee decided to advance the revision of PIC/S Good Practice Guidelines for Blood Establishments and Hospital Blood Banks (PE 005-4 (Draft 2)) to Step 2 (consultation of national industry associations). The

mandate of the Working Group was also amended in the course of 2019 in order to allow for a revision of the related Site Master Files (SMF).

Working Group on the revision of PI 006

97.   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.

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

98.   A call has been made to Members to appoint experts for the new Working Group for a PIC/S Aide Memoire on Tissues and Cellular Therapy Products Inspections. The Working Group is not operational yet.

Revision of the PIC/S and EU GMP Guides and Annexes

99.   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.

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

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

101.   Due to relocation of EMA and the related Contingency Plan, the revision of Chapter 1 has been put on hold for most of 2019. PIC/S will be represented by an Expert in this Drafting Group.

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

102.   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. Due to the relocation of EMA, the work of this Drafting Group has been put on hold for most of 2019.

Annex 1 (Sterile Manufacturing) of PIC/S-EU GMP Guide

103.   See paragraphs 71-73.

Annex 2 (Manufacture of biological medicinal substances and products for human use) of PIC/S GMP Guide

104.   See paragraphs 74-77.

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

105. 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.

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

106. 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 activities be voluntary for non-EU/EEA PAs of PIC/S.

107. Step 1 (internal consultation of PIC/S PAs) of Annex 16 ended on 10 February 2019. At its meeting in Geneva, 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 decided to consult PAs on this issue.

108. At its meeting in Toyama, the SCH Chairman reported on the consultation, which showed that a majority of respondents were in favour of retaining provisions on import, which could be applied on a voluntary basis. As a result, the revision of Annex 16 will be advanced to Step 2.

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

109. PIC/S is represented by Switzerland / Swissmedic in the IWG Drafting Group on Annex 21 of the EU GMP Guide. Following a review of the first draft, the SCH recommended to the PIC/S Committee to not transpose the new EU Annex 21 for PIC/S purposes. A formal decision will be taken by the Committee at its next meeting on the basis of the new Annex, which will be published by the European Commission for public consultation.

Guidance Documents and Procedures

110. A number of guidance documents have been developed by PIC/S Working Groups, notably on cross-contamination, data integrity, the classification of deficiencies, etc. (see paragraphs 70-98 above). Guidance documents not developed by a Working Group are listed below.

111. 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.

Aide-Memoire on the Inspection of Pharmaceutical Quality Control Laboratories

112. The revision of the PIC/S Aide-Memoire on the Inspection of Pharmaceutical Quality Control Laboratories (PI 023-2) was discussed by experts during the 2017 Seminar on Quality Control Laboratories Related in Taipei (Chinese Taipei). Related comments were reviewed by Chinese Taipei / TFDA in 2018. In 2019, Chinese Taipei / TFDA, continued to work on the revision of the Aide-Memoire.

Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments

113.   The PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments (PE 010-4), which has been revised to include an EMA / EU Parenteral Nutrition guidance as an appendix, will be advanced by electronic means by early 2020.

Aide-Memoire on the Inspection of APIs

114.   The Expert Circle on APIs continues to work on the revision of the Aide-Memoire on the Inspection of APIs (PI 030-1).

PIC/S Library

115.   A first compilation of the PIC/S library, based on information provided by 12 PAs, has been prepared-. 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.

116.   In conjunction with the PIC/S library, ECA, ISPE and PDA continued to share GMP-related guidance documents with PIC/S, which were published on the password-protected website.   These guidance documents contain very useful technical information.

TRAINING

117.   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).

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

The mandate of the SCT is to:

1.   Identify training needs

2.   Co-ordinate and monitor PIC/S training activities

3.   Review the planning and organisation of annual training seminars, in particular:
-       propose and validate the seminar topic,
-       review the seminar programme,
-       assess the seminar report,
-       make recommendations for future seminars,
-       propose amendment to the Aide Memoire on the Organisation of Seminars (PI 003).

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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

119.   The Sub-Committee on Training (SCT) is chaired by Jacques Morénas (France / ANSM), and held three teleconferences in 2019: on 17 January, 4 September and 16 October 2019.

120.   During these teleconferences, the SCT discussed the development of the PIC/S Inspectorates' Academy (PIA), the revision of the Joint Visits Programme, the outcome of the survey on future training priorities, and the organisation (and subsequent) assessment of the following PIC/S training events organised in 2019 (in chronological order):

Date	Place	Activity	Organised by
19-21 June 2019	Taipei (Chinese Taipei)	1st Expert Circle on Controlling Cross Contamination in Shared Facilities (CCCISF)	Chinese Taipei / TFDA
7-9 October 2019	Madrid (Spain)	9th Expert Circle on Active Pharmaceutical Ingredients (APIs)	Spain / AEMPS
8-10 October 2019	Jakarta (Indonesia)	25th Expert Circle on Human Blood, Tissues, Cells and ATMPs	Indonesia / NADFC
13-15 November 2019	Toyama (Japan)	PIC/S 2019 Seminar on " Quality Assurance of Sterile Medicinal Products – Annex 1"	Japan / MHLW & PMDA

Annual Training Seminar

121.   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.

2019 Seminar

122. In 2019, the Seminar was organised by Japan's Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) in Toyama (Japan) on 13-15 November 2019. The topic of the Seminar was "Quality Assurance of Sterile Medicinal Products – Annex 1".

PIC/S 2019 Seminar Logo

123. The Seminar was the first organised in Japan since MHLW, PMDA and the Japanese Prefectures joined PIC/S in 2014. It was attended by over 160 inspectors from approximately 50 countries / entities. All continents were represented. The Seminar was opened by the Governor of the Toyama Prefecture, Mr Takakazu Ishii (photo on the left), along with PMDA Senior Executive Director and the PIC/S Chairman.

124. Paying tribute to PIC/S, PMDA Senior Executive Director, Dr Yoshikazu Hayashi (photo on the right), said: *"It is impossible for a single regulatory authority to understand complicated systems correctly, and lead to adequate and timely regulatory guidance. It is an effective 'international harmonisation and cooperation' among regulatory authorities that protects health and lives of the patients."*

125. The Seminar, through a mix of presentations and workshops, provided participants with a better understanding of Annex 1, based on issues discussed during its current revision and through case studies of sterility assurance. The revision of Annex 1 is led by a PIC/S-EMA Working Group with WHO participation.

PIC/S 2019 Seminar audience, Toyama (Japan)

126. In addition to the revision of Annex 1, the programme covered topics related to Process Simulation Test (PST), Clean Room Management and Clean Room

Qualification and Environmental Monitoring, Management of Water for Injection (WFI), Quality Control and Stable Supply of Single-Use Systems, Restricted Access Barriers Technology (RABS) and Isolators as well as Rapid Microbiological Methods.

127.   The Seminar also allowed participants to acquire skills on how to make risk-based decisions during GMP inspections of sterile products and to discuss examples of observations for sterile products. Discussions were stimulated through the innovative use of videos taken of practical manufacturing operations, screened during the workshops.

128.   As a result of the successful Seminar, PIC/S is considering establishing a new Expert Circle dedicated to Sterile Manufacturing as well as a new Working Group on Emerging New Technologies.

129.   For more details regarding the Seminar, please refer to the PIC/S press release dated December 2019.

Past and Future Seminars

130.   In 2019, the SCT and the Committee reviewed:

-    The evaluation report on the 2018 Seminar on the "Management of Risk through the Product Life-Cycle", organised by US FDA in Chicago (USA) on 26-28 September 2018.

-    The preparations of the 2020 Seminar on "How to be a Good GMP Inspector in 2020". The seminar will be hosted by Thailand / Thai FDA in Bangkok (Thailand) from 16-20 November 2020.

131.   The Committee accepted invitations from:

➢   Ireland / HPRA to host the 2021 Seminar and the 50th PIC/S anniversary in Dublin (Ireland) in June 2021. The proposed topic of the Seminar will be "Inspecting the Pharmaceutical Quality System (PQS)".

➢   Finland / FIMEA to host the 2022 Seminar in Turku (Finland) in Q2 2022. The proposed seminar topic will be the inspection of new technologies.

➢   Korea (Republic of) / MFDS to host the 2023 Seminar in Q4 2023.

Joint Visits Programme / Coached Inspection Programme

132.   At the end of 2019, there were more than 15 Joint Visit Groups involving around 45 inspectors in the PIC/S Joint Visits Programme (JVP) and Coached Inspections Programme (CIP). The JVP and the CIP are essential PIC/S tools helping to ensure global GMP harmonisation (see box below).

133.   The JVP is open to PIC/S inspectors only and is particularly appreciated by inspectors specialised in specific fields of GMP, GDP, GCP and GVP.

> ### *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.*

134.   The participation in the JVP has been progressively extended from GMP inspectors to GDP, GCP[1] and GVP[2] inspectors. Joint Visits Groups for GCP/GVP are co-ordinated by the PIC/S Working Group on GCP/GVP (see paragraphs 176-178).

135.   In 2017, the Committee decided to open the JVP to GCP/GVP inspectors from PIC/S Applicant Authorities and from PIC/S countries/entities, where the competence for GCP/GVP is not with the PA.

136.   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 revised JVP Guidelines were presented to the PIC/S Committee meeting in Geneva and then circulated to Members for comments.

137.   Since 2019, several new JVP groups have been established notably in the field of ATMP.

138.   At its meeting in Toyama, the Committee noted a report prepared by the PIC/S Working Group on GCP & GVP, led by UK / MHRA, on PIC/S Joint Visits Programme groups for GCP and GVP. The report includes a summary of recommendations and feedback on the basis of 27 JVP reports over the period 2013-17.

PIC/S New Inspector Training Course

139.   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 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.

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1   Good Clinical Practice
2   Good Vigilance Practice / Pharmacovigilance

140.   The last NITC was held in Dublin (Ireland) on 23-27 October 2017. The next course, which was scheduled to take place in 2019, has been postponed to Q3 2020. It will be organised by Ireland / HPRA in Dublin.

PIC/S Inspectorates' Academy (PIA)

141.   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.

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 52 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.

142.   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.

143.   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.

144.   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.

145.   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.

146.   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.

147.   New training materials are developed and published on a continual basis on PIA. As of 31 December 2019, 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.

148.   In 2018, the Committee discussed the priorities for the next stages and agreed on the following:

➢ To modify the order of development of PIA by moving the "certification system" from Stage 2 to Stage 3 and the "training curriculum" from Stage 3 to Stage 2;

➢ To mandate the SCT to update the outcome of the 2014 Training Questionnaire regarding the identification of training needs through a supplementary questionnaire;

➢ To develop a "training curriculum" and training modules starting with basic training.

149.   These priorities were implemented in 2019. On 4 February 2019 a questionnaire was circulated to Members on PIC/S training priorities, taking into account training priorities of HMA and EMA. 21 replies out of 52 have been received by the end of 2019. The deadline to provide input was thus further extended.

150.   A separate call to Members was issued on 7 March 2019 in order to identify Agencies, which have already developed e-learning systems and which are ready to share their experience with PIC/S.

151.   At its meeting in Toyama, the Committee endorsed in principle a number of key documents for the development of PIA. These documents outline an architecture for a harmonised PIA Training Programme (including its related training Curricula and Cycle) 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.

Draft Outline of PIA Training Cycle

152.   In addition, a first example of a curriculum in the form of a draft Curriculum on QRM for GMP Inspectorates was endorsed in principle by the Committee in Toyama. This curriculum has been developed by the PIC/S Expert Circle on QRM, led by Kevin O'Donnell (Ireland / HPRA). Other curricula could be developed by other Expert Circles or Working Groups in the future.

153.   A pilot demo of an e-learning module on QRM, developed on the basis of the Curriculum on QRM, was also presented to the Committee. This pilot may serve as model for the development of future e-learning modules taking into account the key features of the future Learning Management System (LMS) for PIA.

154.   Subject to the availability of financial and human resources, the Committee endorsed in principle the development of a LMS including e-learning modules on the basis of the demo given as part of Step 2 of the development of PIA.

155.   Finally, an information brochure on PIA was issued in the course of the year following its review by the EB, SCT and SC COM.

PMDA Training Course supported by PIC/S

156.   The annual GMP Training Course, organised by Japan / PMDA and the Asia Training Center (ATC), was held jointly with the PIC/S Annual Seminar in Toyama (Japan) – see paragraphs 122-129.

Co-operation with other Organisations

157. EMA accepted in principle to share with PIC/S the training materials resulting from training events organised by EMA in 2018 on Health Based Exposure Limits (HBEL) and cross-contamination as well as on ATMP.

158. The SCT Chairman met with WHO representatives in Geneva on 9 April 2019 in order to discuss opportunities for co-operation in the field of training.

EXPERT CIRCLES

159. 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.

160. 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

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161. The SCEC is chaired by Andreas Krassnigg (Austria / AGES). In 2019, it held two teleconferences: the first on 20 March and the second on 10 September 2019. A number of Expert Circles and Working Groups operate under the SCEC – their activities are described below.

Expert Circle on API

162. The 9th Expert Circle meeting was organised by Spain / AEMPS in Madrid on 7-9 October 2019. 80 attendants from 50 countries / entities participated in the event, which included presentations (e.g. on cross-contamination, continuous manufacturing,

etc.), workshops on case studies, and discussions on PIA as well as the revision of the Aide Memoire on the inspection of APIs.

163.   The Committee commended Ms Matilde Moreno (Spain / AEMPS) for organising a successful event as well as chairing, on an acting capacity, the Co-ordinating Committee. At the PIC/S Committee meeting in Toyama, France / ANSM offered to take over the chairmanship.

164.   The Expert Circle meets on average every two years. The date and venue of the next meeting have not been determined yet.

Expert Circle on API in Madrid

Expert Circle on Controlling Cross Contamination in Shared Facilities

165.   The Expert Circle on Controlling Cross Contamination in Shared Facilities (CCCISF) was established in 2017. It is chaired by Graeme McKilligan (UK / MHRA).

166.   Chinese Taipei / TFDA hosted the 1st Expert Circle meeting in Taipei on 19-21 June 2019. The meeting was designed to share and develop understanding of challenges facing inspectors on inspection of risk of (chemical) cross contamination in shared facilities and the inspection approaches required to successfully inspect for compliance with PIC/S GMP. 82 delegates from 20 different countries / entities took part in the event, during which 8 plenary presentations, 2 workshops and 4 case studies were delivered. Video recordings of this training event were also made by Chinese Taipei / TFDA, and published on PIA.

167.   The next Expert Circle meeting will be hosted by WHO in the beginning of 2021.

Expert Circle on Controlling Cross Contamination in Shared Facilities in Taipei

Expert Circle on GDP

168.	The Expert Circle on Good Distribution Practice (GDP) was established in 2013 and organised four meetings between 2013 and 2017 in line with the Expert Circle's first mandate, which ended in 2017.

169.	In 2018, a new Co-ordinating Committee was set up under the chairmanship of Peter Blundell (UK / MHRA) and a new mandate adopted by the Committee. The 5th Expert Circle meeting was hosted by Spain / AEMPS in Madrid on 16-18 October 2018 and the related report reviewed by the Committee at its meeting in Geneva in April 2019.

170.	The 6th Expert Circle meeting will be hosted by Ukraine / SMDC in Kyiv (Ukraine).

Expert Circle on Human Blood, Tissues, Cells & ATMPS

171.	The Expert Circle on Human Blood, Tissues and Cells is the oldest Expert Circle in PIC/S. In 2015, the Expert Circle expanded to include Advanced Therapies Medicinal Products (ATMPs). It is chaired by Marisa Delbò (Italy / AIFA).

172.	The 25th meeting of the Expert Circle on Human Blood, Tissues, Cells and ATMPs was hosted by Indonesia / NADFC in Jakarta on 8-10 October 2019. The meeting was attended by 94 participants from 24 PAs, 3 Non-Member Agencies and 3 organisations (EDQM, EMA, and WHO). The focus of this meeting was "Blood, Tissues, Cells and ATMPs: How to Inspect and Current Trends" and consisted in presentations and workshops on topics related to the Expert Circle's mandate on the inspection of on Human Blood, Tissues, Cells and ATMPs.

Expert Circle on Blood, Tissue, Cells & ATMPs in Jakarta

Expert Circle on QRM

173.   The Expert Circle on Quality Risk Management (QRM) was established in 2007. Between 2014 and 2017 it organised three Advanced QRM Training Courses in Tokyo (Japan), Los Angeles (USA), London (UK). A new mandate was adopted by the Committee in September 2017. The Expert Circle is chaired by Kevin O'Donnell (Ireland / HPRA) since 2019.

174.   In 2019, the Committee reviewed the report on the meeting of the Expert Circle on QRM and the related training event, which was organised by Chinese Taipei / TFDA in Taipei on 11-13 September 2018. The Committee also endorsed a Concept Paper and a draft 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 (Draft 1)), which was prepared by the Expert Circle on QRM. The recommendation has been published on the PIC/S website and will be applied by PAs on a trial basis

175.   The Co-ordinating Committee of the Expert Circle also developed a draft Curriculum on QRM for GMP Inspectorates, which was endorsed in principle by the Committee (see paragraph 152).

Working Group on GCP / GVP

176.   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. The Working Group is chaired by Mandeep Rai (UK / MHRA).

177.   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, which entered into force on 1 January 2018.

178.   In 2019, the Committee reviewed a summary report prepared by the Working Group on the basis of 27 JVP reports during the period 2013-17: this summary report highlights recommendations by the various JVP groups as well as similarities and differences in the way GCP/GVP inspections are carried out.

Working Group on Medicinal Products for Veterinary Use (VMP)

179.   In 2016, the Committee established an Ad Hoc Working Group on Veterinary Medicinal Products (VMP) in order to assess the need to have a VMP-specific platform in PIC/S. Following a survey, which revealed the need for such a platform, the Committee adopted a mandate for a new Working Group on VMP, which was established in April 2019.

180.   The Working Group on VMP held a first meeting in October 2019. It comprises experts from Canada / ROEB, Czech Republic / ISCVBM, France / ANSES-ANMV, Germany / ZLG, Switzerland / Swissmedic, UK / VMD, and US FDA. It is chaired by Grégory Verdier (France / ANSES-ANMV) with Jason Todd (UK / VMD) acting as Deputy Chairman.

Working Group on Computerised Systems

181.   The Working Group on Computerised Systems comprises 9 experts and is chaired by Denmark / DKMA. Its task is to revise the PIC/S Good Practices for Computerised Systems (PI 011), which requires revision. The Working Group was 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.

STRATEGIC DEVELOPMENT & CO-OPERATION

182.   The Sub-Committee on Strategic Development was set up in 2009 in order to discuss, amongst other matters, the outcome of a survey on how to improve the operation of the Scheme. It elaborated a concrete proposal on how to set up and implement a Sub-Committee structure.

183.   The mandate of the SCSD has since then been widened to define PIC/S' strategy and future policy and to make proposals on how to improve the structure and the operation of PIC/S as well as co-operation with PIC/S 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

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> 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

184.　　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.

185.　　The SCSD is chaired by Susan Laska (US FDA). It held two teleconferences on 19 February and 18 September 2019.

186.　　Three Working Groups operate under the SCSD:

Working Groups operating under the SCSD

Unique Facility Identifiers (UFI)

187.　　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. The Working Group is led by US FDA and consists of representatives of Canada / ROEB, EDQM, EMA, Spain / AEMPS and UK / MHRA. Its mandate was adopted in 2017. The purpose of the Working Group is to have a harmonised and consistent system in order to localise a manufacturing site.

188.　　The Working Group held one teleconference in 2018 and has not met since, although preliminary work regarding the recommended precision of geolocalisation has been made by US FDA. The Working Group is expected to resume its activities in 2020.

Travel Safety

189.　　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, which is led by UK / MHRA, comprises representatives from Australia / TGA, Brazil / ANVISA[3], Canada / ROEB, EDQM, Indonesia / NADFC, Ireland / HPRA, Netherlands / IGJ, Sweden / MPA, Thailand / Thai FDA, UK / MHRA, and US FDA.

190.　　The aim of the Working Group is to consider means to mitigate health, security or site-related risks affecting inspectors. The Working Group did not meet in 2019. It will resume its activities in 2020.

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[3]　　　Applicant Authority

<u>Informants</u>

191.   The Working Group on Informants, co-led by UK / MHRA and US FDA, was set up in 2019 following the adoption of its mandate at the Committee meeting in Geneva. It has not met yet.

192.   The Working Group will focus its work on three priorities: the definition and distinction between "informants" and "whistle blowers"; the limitations regarding inspectors' involvement; and how to handle intelligence from informants.

Amendment of the Scheme

193.   The Committee has agreed in principle of amending the PIC Scheme. The main purposes of the revision are the following:

➢ To clarify the definition of PIC/S Member and that of Non-Member wishing to apply for membership;
➢ To describe PIC/S' legal status and PIC/S principles; and
➢ To streamline the language.

194.   The revision process has been split into various steps:

➢ Step 1:   Consultation of SCSD and Executive Bureau (Q1-Q2 2018)
➢ Step 2:   First reading by PIC/S Committee (Q3 2018)
➢ Step 3:   Consultation of PIC/S Committee Members (Q4 2018)
➢ Step 4:   Review of comments and new draft (Q1 2019)
➢ Step 5:   Consultation of SCSD and Executive Bureau (Q1 2019)
➢ Step 6:   Second reading by PIC/S Committee (Q2 2019) followed by legal scrubbing (Q2 2019)
➢ Step 7:   Written consultation of PIC/S Participating Authorities (Q3 2019)
➢ Step 8:   Adoption at the PIC/S Committee (Q4 2019).

195.   In 2019, the SCSD reviewed the comments and proposals made by Members of the Committee during the written consultation, which ended on 31 December 2018. The revised draft was subjected to legal scrutiny and then submitted to a formal consultation of all PIC/S Participating Authorities, which ended on 6 September 2019. The amended Scheme was then successfully adopted by the Committee at its meeting in Toyama with an entry into force on 1 January 2020.

Inspection Reliance

196.   In the context of increased foreign inspections, PIC/S has taken a number of measures over the past few years to reduce duplicate foreign inspections such as through the maintenance of a list of planned foreign inspections – which in 2019 included around 660 planned inspections globally – as well as through various procedures such as the PIC/S procedure for team inspections (PI 031-1) and the "Procedure to inform Foreign Regulatory Agencies of Foreign Inspections to be conducted in their Jurisdiction" (PI 039-1).

197.   A survey on "same scope inspections" was carried out amongst all PIC/S PAs to understand how Members deal with "same scope inspections", which are GMP inspections having exactly the same scope and which are thus redundant. The survey

was updated in 2019 by PAs, which acceded to PIC/S on 1 January 2018 (i.e. Iran / IFDA, Mexico / COFEPRIS, Thailand / Thai FDA, and Turkey / TMMDA) and which provided their input on how they deal with "same scope inspections". The survey provides an excellent overview on similarities and differences between PAs in accepting (or refusing) information on GMP inspections from other PAs.

198. In 2017, the Committee accepted an offer from International Coalition of Medicines Regulatory Authorities (ICMRA) to take over the ICMRA GMP project and to adapt the 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.

199. In 2019, PAs were invited to collect statistics on desk-top assessments. The purpose of these statistics is to document the efforts made by PIC/S PAs to rely on existing inspection reports rather than duplicate foreign GMP inspections. The first annual statistics will be available in 2020.

200. In addition, in order to have a better understanding of how desk-top assessments work, Australia / TGA and Canada / ROEB presented at the Committee meeting in Geneva their processes of performing remote inspections. Australia / TGA highlighted that 2,700 overseas manufacturers rely on desk-top clearance and the experience has been very positive. The same conclusion was reached by Health Canada, which indicated that in almost all cases, the desk-top assessment comes to the same conclusion as the initial inspection. A re-inspection is only decided in borderline cases as well as when the dosage form is different.

201. The Committee also discussed whether to adopt, for PIC/S purposes, the EU Compliance Management Procedure. This procedure focuses on borderline compliant cases, where a GMP certificate has been issued but the manufacturer is under increased surveillance. It agreed to launch a pilot on "borderline cases" between interested PAs to determine (i) public health and regulatory benefits, and (ii) the actual level of administrative burden to share information. The pilot will be launched in 2020.

Co-operation with Associated Partners and other Organisations

Associated Partners (EDQM, EMA, UNICEF and WHO)

202. PIC/S continued to co-operate with its Associated Partners, namely EDQM, EMA, UNICEF and WHO.

203. Close co-operation was maintained with the European Medicines Agency (EMA), in particular in the field of harmonisation of GMP guides and guidance documents. The European Directorate for the Quality of Medicines & Healthcare (EDQM), UNICEF and the World Health Organization (WHO) continued to actively contribute to the PIC/S list of planned foreign GMP inspections. EMA, PIC/S and WHO also co-operated on the revision of Annex 1 of the EU-PIC/S GMP Guide.

Other organisations

ASEAN

204.   In 2019, Singapore / HSA, acting as ASEAN Liaison Authority, provided an update on activities in ASEAN, which are of interest to PIC/S. It reported that the ASEAN Pharmaceutical Product Working Group (PPWG) accepted in principle a PIC/S proposal for an exchange of letters in order to establish a basis for the future co-operation between PIC/S and the ASEAN PPWG in GMP matters. The exchange of letter was signed by the PIC/S Chairman in January 2019 and by the Chairman of the ASEAN PPWG in May 2019.

205.   The Committee was also updated on the activities of the ASEAN Joint Sectoral Committee on GMP Inspection (JSC GMP MRA) and on the status of the ASEAN draft GMP Guide for Traditional Medicines (TM), which has been developed by the ASEAN TMHS Product Working Group. In this context, the Committee supported a recommendation by the SCSD to initiate a similar exchange of letters with the ASEAN Traditional Medicines Health Supplements Product Working Group (TMHS PWG).

Heads of EEA Medicines' Agencies

206.   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 continue to 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.

ICH

207.   Since 1 June 2017, PIC/S has become an observer with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). In 2018, the PIC/S representative to ICH, David Churchward (UK / MHRA), attended the ICH Assembly meetings in Amsterdam (Netherlands) on 5-6 June 2019 and in Singapore on 19-20 November 2019.

208.   In 2019, PIC/S nominated Jacques Morénas (France /ANSM) and Jenny Hantzinikolas (Australia / TGA) to represent PIC/S in Q13 (Continuous Manufacturing). Jacques Morénas (France / ANSM) provided an update on Q13 at the Committee meeting in Toyama.

209.   The Committee also nominated Gail Francis (UK / MHRA) in E6 (GCP).

210.   At its meeting in Toyama, the Committee was informed of a proposal made by the ICH Management Committee (MC) for more routine engagement between ICH and PIC/S. A bilateral meeting between the Chair of the ICH MC, Dr Theresa Mullin (US FDA), and the EB took place in Toyama on 13 November 2019 in order to further discuss the proposal.

IPRP

211.   The PIC/S representative in ICH, David Churchward (UK / MHRA), gave a presentation on PIC/S at the meeting of the International Pharmaceutical Regulators Programme (IPRP) in Singapore on 20-21 November 2019.

ISPE

212.   PIC/S was invited to the several ISPE conferences, in particular the ISPE Europe Annual Conference in Dublin (Ireland) on 1-4 April 2019; the Inaugural ISPE Asia Pacific Pharmaceutical Manufacturing Conference in Singapore on 30 September -1 October 2019; and the ISPE 2019 Annual Meeting in Las Vegas (USA) on 27-30 October 2019.

213.   The Global Pharmaceutical Manufacturing Leadership Forum (GPMLF), which is driven by the International Society of Pharmaceutical Engineering (ISPE), offered its assistance in helping in the implementation of inspection reliance, notably by collecting statistics on the duplication of inspections.

PDA

214.   The PIC/S Deputy Chairperson was invited to present at the PDA Europe Meeting in Amsterdam (Netherlands) on 25-26 June 2019.

World Organisation for Animal Health (OIE)

215.   PIC/S and the World Organisation for Animal Health (OIE) formalised their co-operation on the basis of an informal exchange of letters, which was completed on 16 December 2019.

BUDGET, RISK & AUDIT

216.   The Sub-Committee on Budget (SCB) was established back in 2004. With the introduction of the new Sub-Committee structure in 2014 its mandate has been widened in order to encompass issues related to risk and audit. For the full mandate, see box below.

The mandate of the SCB is to:

1.   In line with good governance:

1.1   Assess regulatory risk, financial risk, reputational risk and risk management and make proposals / recommendation to minimise such risk

1.2   Appraise the performance, efficiency, effectiveness and adequacy of internal and external controls

1.3   Evaluate internal and external audits and the implementation of their recommendations

1.4   Ensure that PIC/S adheres to good governance practices

2.   In line with PIC/S' Financial Rules (PS/W 1/2004):

2.1   Establish a budget proposal to the PIC/S Committee

2.2   Propose updates and amendments of the Financial Rules to ensure effective financial administration, the exercise of economy and consistency in financial reporting

2.3   Maintain an internal financial control and examine financial transactions in order to ensure:
(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

217.   The Sub-Committee on Budget, Risk and Audit (SCB) is chaired by Ger Jan van Ringen (Netherlands / IGJ). It held two teleconferences on 11 March and 23 September 2019, during which it reviewed the PIC/S accounts and prepared the budget, as detailed below.

2018 Accounts

218.   The SCB examined the audit report on the 2018 accounts by the external auditor, Moore Stephens Refidar S.A. The accounts were closed with a small surplus. The SCB also reviewed the financial part of the report on the 2018 annual seminar, which was found to be in line with those of previous seminar reports.

219.   On the basis of the external auditor's report, the Committee approved the Statement of Accounts for the Financial Year 2018 and agreed to transfer the 2018 balance to the PIC/S Reserve Fund. It discharged the Secretary of his responsibility for the 2018 accounts.

220.   The Committee thanked the 2018 Seminar Organiser, US FDA, for the generous donation of the seminar surplus to be used for the development of a training curriculum under PIA.

2019 Accounts

221.   The SCB reviewed the status of income and expenditures of the 2019 accounts during the year while the Committee appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2019 accounts.

222.   The 2019 accounts operate under revised PIC/S Financial Rules, which entered into force on 31 October 2018.

2020 Budget and 3-Year Budget Plan

223. As recommended by the SCB, the Committee approved the 2020 Budget for an amount of CHF 773,730 as well as a revised 3-year budget plan for the period 2020-2022.

External Funding

224. At its meeting in Toyama, the Committee adopted a revised draft mandate for the Working Group on Third-Party Funding, which will be composed of EB Members, donating PAs, the Secretariat and interested staff members. The Working Group will become operational in 2020.

225. The Executive Bureau also discussed on how to promote voluntary donations from PIC/S PAs. A call will be made in 2020 to financially support specific projects under PIA.

COMMUNICATION

226. PIC/S regularly communicates on its activities through press releases, annual reports and its web site. Good communication between PAs through PA representatives is one of PIC/S' recognised benefits, which derives from membership. Communication has also become an important tool to promote PIC/S. As a result, the PIC/S Committee has decided to establish a specific Sub-Committee on Communication.

227. 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. For the complete mandate, see box on next page.

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. Monitor and propose changes to the PIC/S web site

4. Work on improving communications with PA, in particular with Heads of Agencies, as well as PIC/S Partners

5. Identify the most suitable speakers for (regional or international) conferences where PIC/S has been invited to speak

6. Report back to the PIC/S Committee, as provided for in the Terms of References and make proposals / recommendations

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228. The Sub-Committee on Communication (SC COM) held two teleconferences on 25 February and 11 September 2019 under the chairmanship of Mark Birse (MHRA / UK). The Committee also discussed a number of communication-related topics, as listed below.

2020 Annual Work Plan

229.   The Committee adopted a PIC/S Annual Work Plan for 2020 based on the contributions made by PIC/S' seven Sub-Committees.

PIC/S Working Group on Quality Defects Procedures

230.   The Committee established a PIC/S 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. The WG, to be led by Ireland / HPRA, is composed of experts from Canada / ROEB, Poland / CPI, Ukraine / SMDC and WHO.

Implementation of PIC/S Guidance Documents

231.   Based on a recommendation by the SC COM, the Committee agreed in principle the launch of a survey among PAs in order to determine the use and implementation of PIC/S guidance documents. The survey will be based on a checklist, which needs to be finalised before being circulated to PAs.

List of PIC/S Foreign Inspections

232.   Following the advice by the SC COM, the Committee decided against a possible extension of the list of foreign inspections to include domestic inspections, as it would require PIC/S to establish a suitable database. Instead, PAs will be invited by the Secretariat to identify which PAs publish a list of domestic inspections; this information will then be made available to all Members.

233.   The list of planned foreign inspections for 2019 was issued on 6 May 2019, updated on 10 October 2019, and finalised on 14 January 2020.

Communications from Participating Authorities

234.   A number of PAs took advantage of PIC/S Committee meetings in Geneva and Toyama to report on important changes or projects concerning their Agencies / Inspectorates.

235.   Australia / TGA announced that it has introduced a voluntary programme on GCP inspections in the form of a pilot over a period of 12 months.

236.   UK / MHRA reassured Members that Brexit would not affect MHRA's activities in PIC/S.

237.   US FDA reported on the implementation of its project on a "New Inspection Protocol Project" (NIPP), which introduces a new way for assessing, recording, and reporting data from surveillance and pre-approval inspections for sterile drug products.

238.   EMA and US FDA jointly announced that all 28 EU Competent Authorities had been successfully assessed by US FDA as part of the US-EU implementation phase. The extension of the MRA to veterinary medicinal products was under way with the FDA's Center for Veterinary Medicine (CVM) being assessed by the EU.

PIC/S Website

239.   The PIC/S website was regularly updated throughout the year and some changes were made to the password-protected Members' Area such as developing an on-line renewal of the confidentiality agreement and absence of conflict of interests and introducing an on-line application for participation in Sub-Committee(s) or Working Group(s).

Other SC COM issues

58.   The Committee noted that:

➢ The new standard presentation on PIC/S and the stakeholder mapping tool, both developed by the SC COM, will be finalised in 2020.

➢ The list of GM(D)P Inspectors, employed by PIC/S PAs and Partners, was updated on 8 April 2019.

➢ A dedicated team will be established to develop a PIC/S promotional video with the assistance of US FDA.

PIC/S Committee meeting in Toyama

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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 2019)

(in the alphabetical order of the country / entity in which they are located)

	PARTICIPATING AUTHORITY	ACRONYM
Argentina	Instituto Nacional de Medicamentos (National Institute of Drugs)	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 (Federal Agency for Medicines and Health Products)	AFMPS
Canada	Health Canada - Regulatory Operations and Enforcement Branch (ROEB) (Santé Canada - Direction générale des opérations réglementaires et de l'application de la loi (DGORAL))	ROEB
Chinese Taipei	Taiwan Food and Drug Administration	TFDA
Croatia	Agency for Medicinal Products and Medical Devices of Croatia (Agencija za lijekove i medicinske proizvode)	HALMED
Cyprus	Pharmaceutical Services	CyPHS
Czech Republic[4]	Státní Ústav pro Kontrolu Léčiv (State Institute for Drug Control)	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv (Czech Institute for State Control of Veterinary Biologicals and Medicines)	ISCVBM
Denmark	Danish Medicines Agency	DKMA
Estonia	State Agency of Medicines	SAM
Finland	Finnish Medicines Agency	FIMEA
France [5]	Agence nationale de sécurité du médicament et des produits de santé (French National Agency for Medicines and Health Products Safety)	ANSM
	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (French Agency for Food, Environmental & Occupational Health Safety)	ANSES

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[4]   SÚKL and ÚSKVBL count as two distinct Participating Authorities.
[5]   ANSM and ANSES count as two distinct Participating Authorities.

Germany [6]	Bundesministerium für Gesundheit *(Federal Ministry of Health)*	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten *(Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices)*	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων *(National Organization for Medicines)*	EOF
Hong Kong SAR	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	Agenzia Italiana del Farmaco	AIFA
Japan [7]	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 *(State Agency of Medicines)*	ZVA
Liechtenstein	Amt für Gesundheit *(Office of Healthcare)*	AG
Lithuania	State Medicines Control Agency	SMCA
Malaysia	National Pharmaceutical Regulatory Agency	NPRA
Malta	Medicines Authority Malta	MAM
Mexico	Federal Commission for the Protection Against Sanitary Risks *(Comisión Federal para la Protección contra Riesgos Sanitarios)*	COFEPRIS
Netherlands	Inspectie voor de Gezondheidszorg en Jeugd *(Health and Youth Care Inspectorate)[8]*	IGJ

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6   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.

7   MHLW, PMDA and the Japanese Prefectures count as one Participating Authority. The Japanese Prefectures are represented by MHLW.

8   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.

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 (*National Authority of Medicines and Health Products IP*)	INFARMED IP
Romania	National Agency for Medicines and Medical Devices	NAMMD
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 *(Spanish Agency for Medicines and Medical Devices)[9]*	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[10]	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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[9]   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.

[10]   MHRA and VMD count as two distinct Participating Authorities.