PHARMACEUTICAL INSPECTION CONVENTION

PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

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ANNUAL REPORT 2018

Prepared by the Secretariat

TABLE OF CONTENT

What is PIC/S?

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 2018, 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 2018.

ANNUAL REPORT 2018

THE YEAR IN A NUTSHELL

Boon Meow Hoe (Singapore / HSA) becomes PIC/S' first Chairman from Asia

1.   On 1st January 2018, Mr Boon Meow Hoe from Singapore's Health Sciences Authority (HSA) became the twenty-third Chairman of PIC/S as well as the first Chairman from Asia in PIC/S' history. His mandate will be for two years (2018-19).

Singapore / HSA has traditionally been a leading Agency in Asia in the field of GMP. It was the first Regulatory Authority from Asia to adopt the PIC/S GMP Guide. It was also the first Asian Regulatory Authority to join PIC/S in 2000.

Photo: Mr Boon Meow Hoe, PIC/S Chairman

2.   Mr Boon chaired the PIC/S Committee meetings: first in Geneva (Switzerland) on 17-18 April 2018, and then in Chicago (USA), on 24-25 September 2018, in conjunction with the annual PIC/S Seminar hosted by the US Food and Drug Administration (FDA).

PIC/S' expansion continues

3.   2018 was yet another successful year for PIC/S, which started with the accession of three new Participating Authorities (PAs) on 1st January:

Iran Food and Drug Administration (IFDA), which applied in September 2010, became PIC/S' 50th PA;

The Turkish Medicines and Medical Devices Agency (TMMDA), which applied in May 2013, became PIC/S' 51st PA;

Mexico's Federal Commission for the Protection Against Sanitary Risks (COFEPRIS), which applied in December 2014, became PIC/S' 52nd PA.

4.   The Bulgarian Drug Agency (BDA) applied for PIC/S membership on 27 August 2018 while the Jordan Food and Drug Administration (JFDA) submitted a complete pre-accession application on 9 August 2018.

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

Members
Applicants
Pre-Applicants
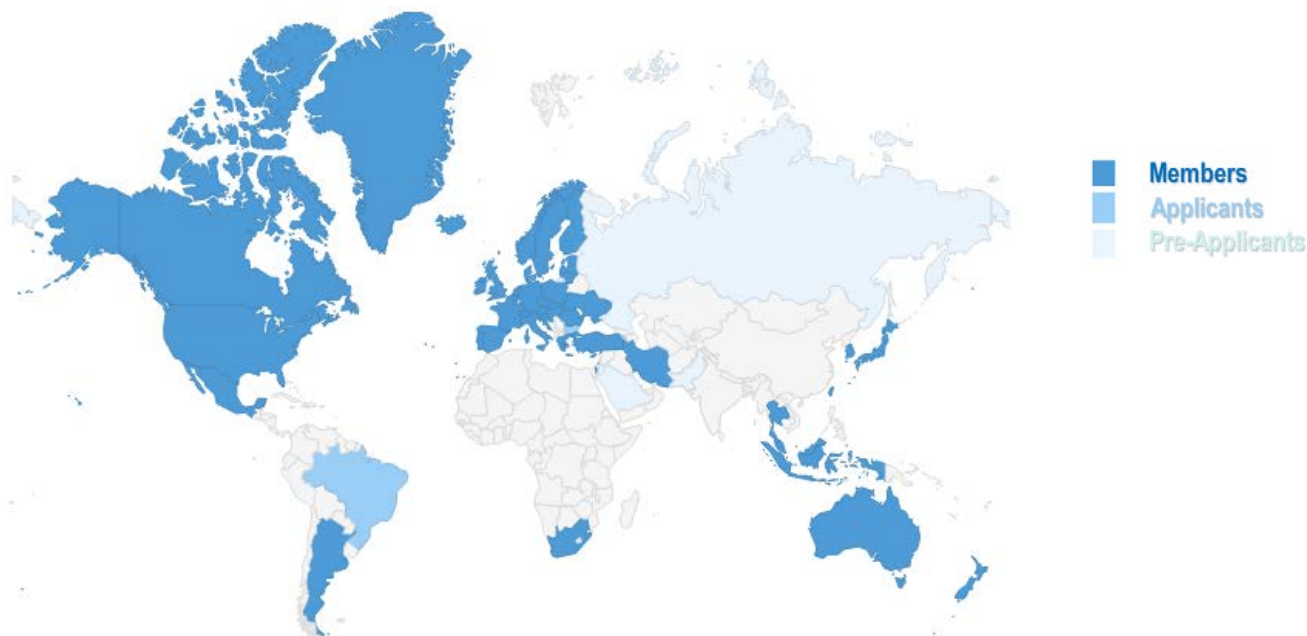
GMP Inspection Reliance

6.   The increasing number of inspections is not only a concern to industry; it is also a considerable challenge to Regulatory Authorities, which are under pressure to always do more with fewer resources. To address this challenge, the Committee adopted a Guidance on Inspection Reliance (PI 048-1), which entered into force on 1 June 2018. 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 guidance is based on a draft developed by the International Coalition of Medicines Regulatory Authorities (ICMRA).

Classification of Deficiencies, Cross-Contamination, Data Integrity

7.   PIC/S continued to lead expert discussions on critical, contemporary GMP topics and to develop related guidance documents for inspectors, which are also very useful for industry.

8.   In 2018, the Committee adopted a Guidance on the Classification of Deficiencies (PI 040-1) as well as an Aide-Memoire on Cross-Contamination in Shared Facilities (PI 043-1). It also submitted its draft "PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments" (PI 041-1 (Draft 3)) for public consultation.

Record participation in 2018 Annual Seminar in Chicago

9.   The US FDA hosted the PIC/S annual seminar in Chicago on 26-28 September 2018.   Over 200 participants from 46 countries around the world discussed the "Management of Risk through the Product Life-Cycle". This is the largest attendance of a PIC/S Seminar ever.

Opening ceremony of the 2018 PIC/S Seminar

New Executive Bureau (2018-19)

10.   A newly composed PIC/S Executive Bureau (EB) took office on 1 January 2018 for a 2-year term. It consists of:

➢ 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 Paul Hargreaves (United Kingdom / MHRA), immediate past PIC/S Chairman;

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

➢ Mr Paul Gustafson (Canada / RORB), 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) ; and

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

11.   The EB met twice: first in Geneva (Switzerland) on 16-17 April 2018, and then in Chicago (USA), on 24 September 2018. EB meetings are traditionally devoted to the preparation of the Committee's meeting; it also discusses financial, administrative and staff related issues as well as strategic orientations. Brainstorming sessions are occasionally organised in order to address particular issues.

PIC/S Executive Bureau 2018-2019 (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); Paul Hargreaves (UK / MHRA).

PIC/S Sub-Committee Structure

12. Since 2014, 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).

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

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PIC/S' Organisational Chart
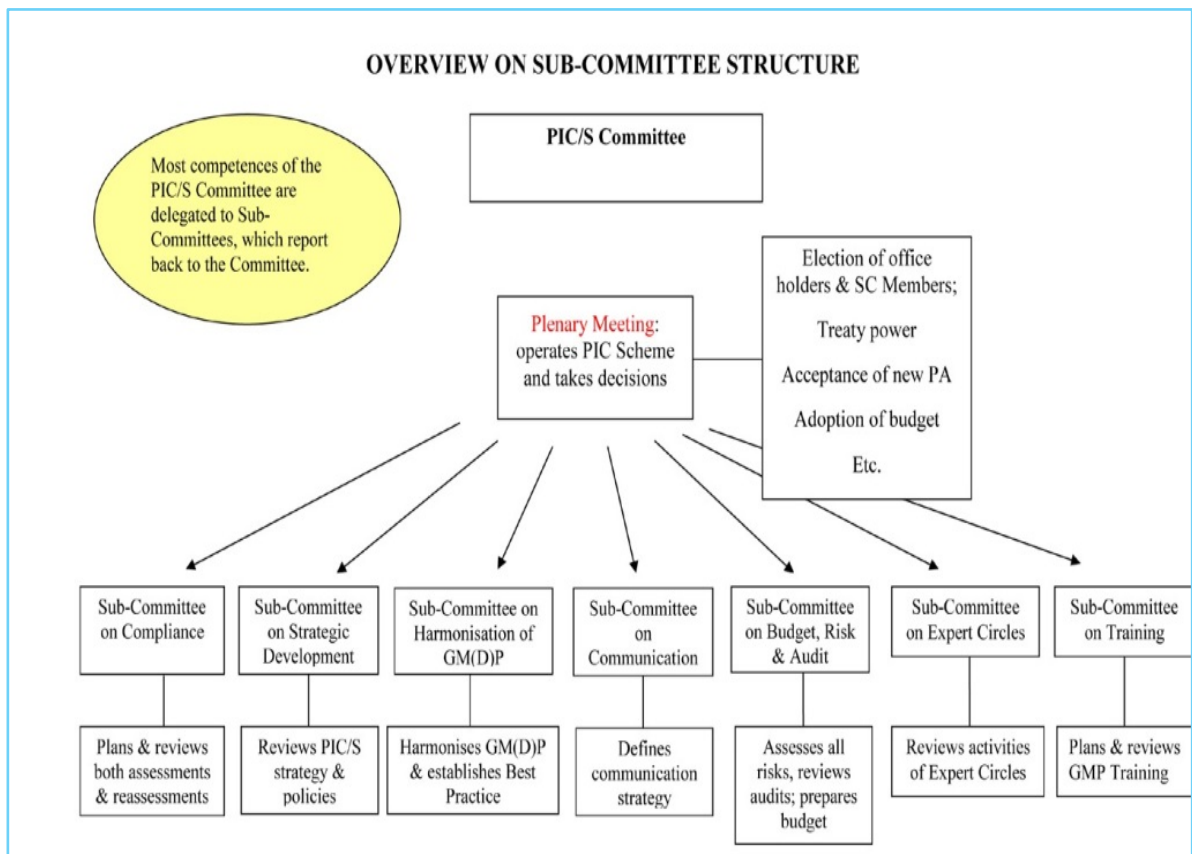
COMPLIANCE

14.   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 paragraph 4 of 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.

15.   This task has been entrusted to the Sub-Committee on Compliance (SCC) under 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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16.   The SCC held four teleconferences in 2018: on 31 January, 5 April, 19 July and 6 September 2018. 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

17.   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

18.   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 / RORB), is developing 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.

19.   The Working Group has completed its review of the 48 critical indicators (phase 1) and is now covering very important and important indicators (phase 2).

Working Group on the Drafting of Pre-Accession Guidelines

20.   The Working Group on the Drafting of Pre-Accession Guidelines, led by Jacques Morénas (France / ANSM), was established in 2018.   It aims at developing guidelines specific to the pre-accession process and providing interested Agencies with a better understanding of PIC/S expectations and requirements.

21.   The pre-accession process will be streamlined to avoid the duplication of work between "accession" and "pre-accession". The main objective will be to explain the 78 indicators to the Pre-Applicant so that he/she is able to carry out himself/herself the gap analysis whereas so far, the gap analysis was done by PIC/S.

Working Group on the Revision of the Accession Guidelines

22.   The Working Group on the revision of the Accession Guidelines and related documents (in particular those related to the PIC/S Joint Reassessment Programme [JRP]) was established in 2018. It will become operational once the Working Group on the Drafting of Pre-Accession Guidelines has completed its work.

23.   At the Committee meeting in Chicago, the SCC Chairperson presented selection criteria, which have been identified by the SCC, in order to determine the size of Assessment and Re-assessment Teams. These criteria will be incorporated in the relevant procedure.

Membership Applications

24.   In the course of 2018, PIC/S continued the assessment of the following four membership applications (in alphabetical order):

Armenia / SCDMTE

25.   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, when the last missing documents were submitted.

26.   At its meeting in Geneva in April 2018, the Committee nominated Michel Keller (Switzerland / Swissmedic) as Rapporteur, Mark Cilia (Malta / MAM) as Co-Rapporteur, and Rachel Shimonovitz (Israel / ISCP) as Team Member. The Rapporteur and Co-Rapporteur have started with the paper evaluation.

Bulgaria / BDA

27.   The Bulgarian Drug Agency (BDA) submitted a complete membership application on 27 August 2018. As BDA recently went through an audit under the EMA Joint Audit Programme (JAP) and the report shared with PIC/S, the application process will be abridged.

36.   At its meeting in Chicago in September 2018, the Committee appointed Jacques Morénas (France / ANSM) as Rapporteur and Ana Rita Martins (Portugal / INFARMED I.P.) as Co-Rapporteur.

Brazil / ANVISA

28.   Brazil's Agência Nacional de Vigilância Sanitária (ANVISA) lodged a partial membership application in 2010, which was completed in October 2014.

29.   At its meeting in Geneva in April 2018, the Committee granted ANVISA, at the latter's request, a 1-year stop-clock in order to update the membership application. In exchange, ANVISA was invited to confirm in writing its readiness to host the PIC/S assessment team in late 2019.

30.   The Rapporteur for the assessment of ANVISA's membership application is Mark Birse (UK / MHRA), who is assisted by Ana Rita Martins (Portugal / INFARMED I.P.), Co-Rapporteur.

Italy (Vet) / DGSAF

31.   Italy's Directorate General for Animal Health and Veterinary Medicinal Products (DGSAF) applied for PIC/S membership on 26 August 2016 following an audit under the EMA Joint Audit Programme (JAP), which was shared with PIC/S.

32.   At its meeting in Chicago in September 2018, the Rapporteur, Jason Todd (UK / VMD), announced that the on-site assessment visit to Italy (Vet) / DGSAF would take place on 14-18 January 2019. The PIC/S audit team will consist of the Rapporteur and Grégory Verdier (France / ANSES-ANMV). The main purpose of the visit will be to verify the implementation of the CAPAs undertaken by DGSAF following the JAP audit and an observed GMP inspection on sterile products.

Pre-Accession Applications

33.   PIC/S' Accession Guidelines, which are currently in force, provide for the possibility for a Competent Authority to ask PIC/S to carry out a pre-assessment. This includes a gap analysis on the basis of which a recommendation may be given to the Competent Authority either to apply for membership or to take the necessary measures in order to comply with PIC/S requirements.

34.   In the course of 2018, the following 5 pre-accession applications were under review:

Jordan / JFDA

35.   The Jordan Food and Drug Administration (JFDA) submitted a complete pre-accession application on 9 August 2018. The Rapporteur, Izabela Majić (Croatia / HALMED), was appointed by the PIC/S Committee by written procedure.

Kazakhstan / CCMPA

36.   The pre-accession process of Kazakhstan's Committee for the Control of Medical and Pharmaceutical Activities (CCMPA) was closed on 17 November 2017. On 13 February 2018, Kazakhstan / CCMPA (NCED) submitted a CAPA, which was reviewed by the Rapporteur, Rosmarie Neeser (Switzerland / Swissmedic), and noted by the Committee at its meeting in Chicago.

Pakistan / DRAP

37.   The Drug Regulatory Authority of Pakistan (DRAP) submitted a pre-accession application on 18 September 2017, which the Rapporteur, Petra Müllerová (Czech Republic / ISCVBM), started to review in the course of 2018.

Russian Federation / Minpromtorg and FSI SID&GP

38.   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.

39.   The Rapporteur, Jacques Morénas (France / ANSM), and the Co-Rapporteur, Michel Keller (Switzerland / Swissmedic), explained the 78 indicators of the audit checklist to a Delegation by Minpromtorg Russia and FSI "SID & GP" at a meeting in Paris on 29 March 2018. The Delegation promised to update the audit checklist.

40.   In a letter dated 24 September 2018, the Department of Pharmaceutical and Medical Industry Development, Minpromtorg, undertook to establish an inter-ministerial working group between Minpromtorg and the Federal Service for Surveillance in Healthcare (Roszdravnadzor), which is in charge of licensing, in order to work on the audit checklist. An inter-agency agreement on co-operation was also initiated.

Saudi Arabia / SFDA

41.   The Saudi Food and Drug Authority (SFDA) submitted a pre-accession application on 31 July 2017. The Rapporteur is Jacques Morénas (France / ANSM) and the Co-Rapporteur is Muhammad Lukmani Ibrahim (Malaysia / NPRA).

42.	At a meeting in Paris on 1 February 2018, the 78 indicators were explained to SFDA, which then updated the audit checklist, thus demonstrating a good understanding of PIC/S requirements. At the Committee meeting in Chicago, Saudi Arabia / SFDA announced that it would submit a membership application, as soon as the pre-accession process had been formally completed.

Reassessment of Participating Authorities

43.	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 also combined with the MRA Maintenance program of Health Canada, which are following a similar approach and contribute to saving in resources for regulators and reducing the burden for the audited party.

<u>Re-assessment in 2017</u>

44.	Two reassessments took place in September 2017 and the related reports were discussed by the Committee at its meeting in Geneva in April 2018.

Reassessment of Australia / TGA

45.	The on-site visit took place on 18-22 September 2017 in the regional office of TGA in Melbourne, where most inspectors are located. Where necessary, interviews with the headquarters and the control laboratories, located in Canberra, were arranged via video or teleconferencing. The PIC/S Team was led by Anne Hayes (Ireland/HPRA) with Team Members from South Africa / SAHPRA and US FDA. The reassessment report was reviewed by the SCC and the conclusions endorsed by the Committee, according to which TGA is considered equivalent under the PIC Scheme.

Reassessment of Singapore / HSA

46.	The on-site visit took place on 18-22 September 2017 at the HSA offices in Singapore. The Team, which was led by Jacques Morénas (France / ANSM), included Members from Australia / TGA, Malaysia / NPRA, and New Zealand / Medsafe. 3 observed inspections were carried out. The reassessment report was reviewed by the SCC and the conclusions endorsed by the Committee. HSA will be considered equivalent under the PIC Scheme in 2020, once Singapore has adopted a new regulation on APIs.

<u>Re-assessments in 2018</u>

47.	The following re-assessments took place in the last quarter of 2018 (the related reports will be discussed in 2019):

➢ The reassessment of Argentina / INAME, led by Jacques Morénas (France / ANSM), took place on 5-9 November 2018;

➢ The reassessment of Switzerland / Swissmedic, led by Susan Laska (US FDA), took place on 15-19 October 2018. It was combined with a MRA re-assessment

by Health Canada and co-ordinated with the EMA JAP audit of Liechtenstein / AG;

➢ The reassessment of Ukraine / SMDC, led by Ana Rita Martins (Portugal / INFARMED I.P.), took place on 22-26 October 2018.

Re-assessments in 2019 / 2020

48.   The Committee also decided to reassess Canada / RORB and South Africa / SAHPRA in 2019 and Indonesia / NADFC and New Zealand / Medsafe in 2020.

Non-Members

49.   Close contacts were kept with a number of non-Members, in particular India's Central Drugs Standard Control Organisation (CDSCO) and China's National Medical Products Administration (NMPA) with which bilateral meetings with the Executive Bureau were organised in the margins of the 2018 Seminar in Chicago.

50.   The new Director General of the Philippines Food and Drug Administration (PFDA) attended the Committee meeting in Chicago and confirmed the intent of Philippines / PFDA to submit a new PIC/S membership application. Contacts with other Non-Members during 2018 included Bangladesh / DGDA, Belarus / MoH, Ethiopia / FDA, Korea (Vet) / QIA, Libya / MoH, Moldova / MMDA, New Zealand (Vet) / MPI, Sénégal / MSAS, Sri Lanka / NMRA, Tunisia / MoH, Sudan / NMPB and Vietnam / DAV.

GMDP

51.   The harmonisation of Good Manufacturing Practice (GMP) and – more recently – of Good Distribution Practice (GDP) is at the very heart of PIC/S. 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;
♦ to facilitate the removal of barriers to trade in medicinal products.

52.   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.

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

54.   The SCH held four teleconferences on 8 February, 3 May, 6 September and 13 December 2018, 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

55.   Seven Working Groups are operating under the SCH.

Working Group on Annex 1 / Sterile Manufacturing

56.   The PIC/S Working Group on Annex 1 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. In 2018, the joint PIC/S-EMA Drafting Group was led by Andrew Hopkins (UK / MHRA) and included representatives of the Competent Authorities of PIC/S and EEA as well as WHO.

57.   Following a second written consultation of PIC/S PA and EU/EEA Competent Authorities on the draft revision of Annex 1, which ended in January 2017, the Working Group reviewed comments and prepared a revised draft.

58.   The revision of Annex 1 was advanced to Step 2 on 20 December 2017, when it was published for public consultation jointly with the EU and WHO. The consultation ended on 20 March 2018. Over 6,300 comments were received and reviewed by the Working Group during the year.

<u>Working Group on the revision of Annex 2</u>

59.   Following the adoption by the European Commission of the EU Guidelines on GMP for Advanced Therapies Medicinal Products (ATMPs) and the revised 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).

60.   The Working Group was established at the Committee meeting in Geneva: 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 has volunteered to act as Deputy Chair.

61.   The Working Group has started drafting a new Annex 2A on Advanced Therapy Medicinal Products (ATMPs), which will part of the PIC/S GMP Guide, and an Annex 2B, which will based on the revised EU Annex 2 for the remaining biological products. This way, EU and PIC/S GMP requirements will remain harmonised.

62.   A first rough draft of Annex 2A has been prepared by the Working Group and discussed by the SCH in December. PIC/S PAs will be consulted in early 2019.

<u>Working Group on Data Integrity</u>

63.   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. 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.

64.   Two other documents, developed by the Working Group on Data Integrity, have been submitted to comments to PAs (step 1):

> ➢ 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)).

65. Guidance documents on DI, which have been developed by other Agencies (e.g. MHRA, EMA) or professional organisations (e.g. ISPE, ECA) have been reviewed by the Working Group and will be made available to inspectors in the Members' Area of the PIC/S website.

Working Group on Harmonisation of the Classification of Deficiencies

66. 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 more consistent responses among international regulatory authorities when responding to GMP deficiencies and GMP non-compliance.

67. The first draft of the Guidance on the Classification of Deficiencies was submitted to PIC/S Members and Partner Organisations on 7 January 2016. It was also shared with inspectors during the 2016 and 2017 PIC/S Seminars. The Working Group then reviewed the comments and developed a revised draft in 2017, which was submitted to a second internal consultation on 23 November 2017 for a period of three months (PI 040-1 (Draft 3)). Based on these comments, which were reviewed by the Working Group in the course of 2018, the guidance was finalised.

68. At its meeting in Chicago, the Committee adopted the PIC/S Guidance on Classification of Deficiencies (PI 040-1) with an entry into force on 1 January 2019.

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

69. The goal of the Working Group on Controlling Cross-Contamination in Shared Facilities is to draft an Aide Memoire which will focus on harmonising and standardising terminology used in relation with the control of cross-contamination in shared facilities and address questions which inspectors should ask themselves during inspections – in particular in relation with risk management. This will allow inspectors to better assess the risks of cross contamination in shared facilities.

70. A first draft (PI 043-1 (Draft 1)) was developed by the Working Group, chaired by Graeme McKilligan (UK / MHRA), and submitted to Members' comments on 21 April 2017. Comments were then reviewed by the Working Group and a revised draft (PI 043-1 (Draft 2)) submitted to PAs by written procedure on 20 February 2018. At its meeting in Geneva, the Committee adopted the Aide-Memoire on Cross-Contamination in Shared Facilities (PI 043-1), which entered into force on 1 July 2018.

71. The Committee also agreed to turn the Working Group into an Expert Circle, which will aim at developing training material for inspectors.

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

72. The Working Group of Experts 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 EU Good Practices Guidelines for blood establishments.

73.   The Working Group, chaired by Christian Schärer (Switzerland / Swissmedic), started revising the PIC/S GMP Guide for Blood Establishment (PE 005-3) and presented a first draft to the Expert Circle on Human Blood, Tissue, Cells & ATMPs in Warsaw (Poland) on 23-25 October 2018. The SCH also reviewed the draft at its teleconference in December 2018, which will be submitted to PAs in 2019.

74.   The PIC/S Guide to Inspections of Source Plasma Establishment and Plasma Warehouses (PI 008-3) will be revised according to the same lines.

Working Group on the revision of PI 006

75.   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.

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

76.   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.

77.   In 2018, the SCH continued to harmonise and transpose GM(D)P guidance documents:

➢ It finalised the revision of Chapters 3 (Premise and Equipment), 5 (Production), and 8 (Complaints and Product Recalls) of the PIC/S GMP Guide, which entered into force on 1 July 2018.

➢ It transposed a revision of EU Annex 13 (Investigational Medicinal Products) for PIC/S purposes, which will be submitted for comments in 2019.

➢ It discussed a proposal to adapt EU Annex 16 (Certification by an Authorised Person & Batch Release) for PIC/S purposes. As neither the PIC Scheme nor the PIC/S GMP Guide deal with import or import controls, the implementation for import-related activities will be voluntary for non-EU/EEA PAs of PIC/S.

78.   PIC/S experts are also involved in EMA Drafting Groups on the revision of the following Chapters and Annexes of the EU-PIC/S GMP Guide:

➢ Chapter 1 (Pharmaceutical Quality System): PIC/S has been invited to appoint an Expert to the EMA Drafting Group.

➢ Chapter 4 (Documentation) and Annex 11 (Computerised Systems): PIC/S is represented by experts from Australia / TGA and Canada / RORB.

➢ Annex 1 (Sterile Manufacturing): See paragraphs 56-58.

> Annex 17 (Real Time Release Testing, previously Parametric Release): the IWG Drafting Group on Annex 17 comprises experts from Australia / TGA and Canada / RORB. Steps 1 and 2 were successfully completed under the PIC/S-EMA Joint Consultation Procedure. The revised draft was then adopted by the EMA IWG and PIC/S (Step 3) and entered into force on 1 July 2018.

> Annex 21 (GMP Obligations for Importation to the EU): PIC/S is represented in the IWG Drafting Group on Annex 21, which has prepared a first draft. PIC/S may decide to develop a PIC/S-specific Annex.

Guidance Documents and Procedures

GMP guidance documents

79.   A number of guidance documents have been developed by PIC/S Working Groups, notably on cross-contamination, data integrity, the classification of deficiencies, etc. (for more information, see paragraphs 56-74 above).

80.   Older GMP guidance documents are periodically revised to comply with updated GMP requirements and technological progress.

81.   The need to update 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.

GDP guidance documents

82.   At its meeting in Madrid (Spain) on 16-18 October 2018, the PIC/S Expert Circle on GDP, led by Peter Blundell (UK / MHRA), reviewed the comments from Members on the draft Aide-Memoire on Inspection of Manufacturers and Wholesale Distributors for Compliance with GDP and the draft Q&A for the PIC/S GDP Guide.

EMA guidance documents

83.   At its meeting in Geneva in April 2018, the Committee adopted the following EMA guidance documents, which were transposed by the SCH for PIC/S purpose:

- Guidelines on the formalised risk assessment for ascertaining the appropriate Good Manufacturing Practice for excipients of medicinal products for human use (PI 045-1);
- Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (PI 046-1);
- Guidelines on the principles of Good Distribution Practices for active substances for medicinal products for human use (PI 047-1).

84.   The Guidelines entered into force on 1 July 2018.

Guidance on Total Parenteral Nutrition (TPN)

85.   Following a request from the EMA IWG that PIC/S takes over a guidance on Total Parenteral Nutrition (TPN) and a consultation of PAs, the Committee approved a recommendation by the SCH that the EMA Guidance on TPN be adopted by PIC/S as an appendix to the PIC/S "Guide to good practices for the preparation of medicinal

products in healthcare establishments" (PE 010-4). Whether a limited revision of the said Guide is sufficient in order to include the Guidance will be investigated by the SCH (NB: TPN is subject to manufacturing authorisation in some PIC/S countries.)

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

PIC/S Library

87.   The SCH continued its work on establishing a PIC/S library, which will include documents related to GM(D)P inspection drafted by Members and Partners and which will be integrated into the PIC/S Inspectorates' Academy (PIA). A first compilation, based on information provided by 12 PAs, was made available as a draft on the password-protected PIA website.

TRAINING

88.   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 an essential activity of PIC/S. Recently, PIC/S has also opened its training programme to inspectors active in other areas such as Good Distribution (GDP), Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP).

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

The mandate of the SCT is to:

1.   Identify training needs

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

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

4.   Monitor the Joint Visits Programme and the Coached Inspection Programme and carry out a review of reports in order to identify divergences on GMP interpretation and inspection practices

5.   Ensure the rotation of training between the various regions, taking into consideration the expansion of PIC/S

6.   Consider proposals for co-operation with professional organisations (e.g. ISPE, PDA) in the field of training

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> 7.   Report back to the PIC/S Committee, as provided for in the Terms of References, and make proposals / recommendations

90.   The Sub-Committee on Training (SCT) is chaired by Jacques Morénas (France / ANSM), and held two teleconferences in 2018: on 22 February and 11 June 2018. One of its main duties is to review the preparation and outcome of PIC/S training activities.

91.   During these teleconferences, the SCT discussed future training priorities and agreed to pay particular attention to the development of inspections skills and inspection methodology during PIC/S training events, as this is PIC/S' main added value in terms of training. The SCT also proposed increasing synergies by working more closely together with the Sub-Committee on Expert Circles (SCEC); there are many interactions between the two Sub-Committees, in particular since Expert Circles also provide training to inspectors.

92.   The following PIC/S training activities were held in 2018 (in chronological order):

Date	Place	Activity	Organised by
11-13 September 2018	Taipei (Chinese Taipei)	Expert Circle meeting and Advanced Training on Quality Risk Management (QRM)	Chinese Taipei / TFDA
26-28 September 2018	Chicago (USA)	PIC/S 2018 Seminar on " Management of Risk through the Product Life-Cycle "	US FDA
16-18 October 2018	Madrid (Spain)	PIC/S Expert Circle on Good Distribution Practice (GDP)	Spain / AEMPS
23-25 October 2018	Warsaw (Poland)	PIC/S Expert Circle on Human Blood, Tissues, Cells and ATMPs	Poland / CPI
26-30 November 2018	Tochigi (Japan)	PMDA-ATC GMP Inspection Seminar	Japan / PMDA (with the support of PIC/S)

Annual Training Seminar

93.   PIC/S arranges every year a 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.

2018 Seminar

94. In 2018, the Seminar was organised by the US Food and Drug Administration (US FDA) Chicago (USA) on 26-28 September 2018. The topic of the seminar was the "Management of Risk through the Product Life-Cycle" and focused on how to assess and manage risks from inspectional and product-cycle point of views.

PIC/S 2018 Seminar Logo

95. The Seminar was the first organised in the USA since FDA joined PIC/S in 2011. It was attended by over 200 inspectors from 46 countries – the largest ever attendance in a PIC/S seminar. All continents were represented. The Seminar was opened by US FDA Associate Commissioner for Regulatory Affairs, Ms Melinda Plaisier (photo on the left).

96. She emphasised the role and responsibilities of inspectors for public health through their work. The Seminar topic addressed the fact that regulators are continually assessing risk: from the risk that helps determine which sites to inspect to the risk of what critical aspects to inspect. These responsibilities, along with the growing complexity and emerging technologies of drug products, present regulatory challenges. Organisations such as PIC/S are instrumental in ensuring that inspectors from across the world are assessing GMPs in a harmonised way. PIC/S is uniquely positioned to lead this harmonisation effort.

PIC/S 2018 Seminar audience, Chicago (USA)

PIC/S chairmanship with US FDA Delegation.

From left to right: US FDA Assistant Commissioner for Medical Products and Tobacco Operations, Ms Ellen F. Morrison; PIC/S Deputy Chairperson Ms Anne Hayes, (Ireland / HPRA); PIC/S Chairman, Mr Boon Meow Hoe (Singapore / HSA); US FDA Associate Commissioner for Regulatory Affairs, Ms Melinda K. Plaisier; PIC/S Chair of Sub-Committee on Strategic Development and US FDA Senior Advisor Medical Products, Ms Susan Laska (US FDA)

97.   The 2.5 day Seminar consisted of a mix of presentations and parallel workshops. The first day addressed "Process and Production Plant Risks" and started with a panel discussion on the risk through the product life-cycle and presentations on quality oversight of APIs and process control, which were followed by two parallel workshops on:

> ➢ Risk Related to Raw Materials and Contract Services (Workshop leader: UK / MHRA);
> ➢ Emerging Technologies (Workshop leader: Health Canada)

98.   The second day focused on "risk to the product" with presentations on quality oversight of finished products and risk-based inspections, which were followed by two parallel workshops on:

> ➢ Risk in the Distribution Chain (Workshop leaders: Singapore / HSA and New Zealand / Medsafe);
> ➢ Risk Based Inspections (Workshop leader: Ireland / HPRA and US FDA).

99.   The outcome of the workshops was discussed on the third and last day, followed by a series of presentations on "risk to patients and personnel", including drug shortage risk and inspector safety.

2018 Seminar - Official photo with participants

Past and Future Seminars

100.   In 2018, the SCT and the Committee reviewed:

-   The evaluation report on the 2017 Seminar on "Quality Control Laboratories – How to Inspect", hosted by Chinese Taipei / TFDA. The seminar, which was attended by 158 participants, will result in the revision of the PIC/S Aide Memoire on inspection of pharmaceutical quality control laboratories (PI 023-2). The seminar was highly rated, as shown by the outcome of the seminar evaluation, which ranked from very good to excellent.

- The preparations of the 2019 Seminar, which will be hosted by Japan / MHLW and PMDA in Toyama (Japan) on 11-15 November 2019. The topic of the seminar will be "Quality Assurance of Sterile Medicinal Products – Annex 1".

101. The Committee accepted an invitation by the Thai FDA Secretary General to host the 2020 Seminar in Bangkok (Thailand) in the 2nd or 3rd week of November 2020. The topic is under consideration.

102. The Committee also agreed to establish a Working Group on whistle-blowers as a follow-up to the 2016 Seminar, which will be co-led by UK / MHRA and US FDA.

Joint Visits Programme / Coached Inspection Programme

103. At the end of 2018, there were approximately 19 active Joint Visit Groups involving around 57 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).

104. The JVP is open to PIC/S inspectors only and is particularly appreciated by inspectors specialised in specific fields of GMP (e.g. sterile manufacturing).

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.

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105. The participation in the JVP has been progressively extended from GMP inspectors to GDP, GCP[1] and GVP[2] inspectors. At the end of 2018, there were 12 active Joint Visits Groups for GCP/GVP co-ordinated by the PIC/S Working Group on GCP/GVP (see paragraphs 137-139).

106. 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.

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[1] Good Clinical Practice
[2] Good Vigilance Practice / Pharmacovigilance

107.   In 2018, the SCT started working on a revision of the JVP Guidelines in order to clarify and improve the operation of the JVP. Following a call made in June 2018, several new JVP groups in the field of ATMP were established.

PIC/S New Inspector Training Course

108.   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.

109.   The last NITC was held in Dublin (Ireland) on 23-27 October 2017; 34 inspectors attended. The course was run by HPRA with the assistance of trainers from UK / MHRA and US FDA. The feedback from participants was very positive. The report on the course, prepared by HPRA, was reviewed by the SCT and the Committee in 2018. The next course is scheduled to take place in 2019.

PIC/S Inspectorates' Academy (PIA)

110.   The PIC/S Inspectorates' Academy (PIA) is the most prominent project under development in PIC/S. It is a global capacity building and training initiative developed by PIC/S Participating Authorities aiming at delivering inspection excellence through harmonized training in the field of Good Manufacturing Practices (GMP) 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 more than 650 training materials and 250 training videos
-    webinars, on-line learning tools, forum which are in development
-    a library of relevant GMP references.

111.   This web-based educational centre is placed under the PIC/S umbrella with the purpose of providing GMP training, which has been harmonised and standardised, at an international level. PIA 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 is being implemented in stages. It is run and monitored by the Sub-Committee on Training. (NB: the PIA Project Management Steering Committee ("PMSC") was merged with the SCT in 2018 in order to improve efficiency and avoid duplications).

112. 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. 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.

113. 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.

114. In March 2018, a review of approximately 500 PIC/S training materials available on PIA was achieved which will allow these materials to be rated according to their relevance and level (e.g. for new inspectors) with respect to a future training curriculum. New materials are being developed and published on a continual basis. Responding to the need for more focus on inspection skills and methodology, short videos on soft skills developed by Paul Hargreaves (UK / MHRA), were added to PIA in 2018.

115. The SCT and the Committee also discussed the priorities for the next stage of development of PIA and agreed on the next concrete steps for Stage 2, subject to available funding and resources. These will be:

➢ 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.

116. The Committee also discussed the possible contribution that professional organisations could make to PIA and the possibility of reviewing and assessing materials from particular organisations for inclusion, including, for example, from ISPE and the European Compliance Academy (ECA).

117. A presentation brochure on PIA and its features was finalised and will be published in 2019.

PMDA Training Course supported by PIC/S

118.   Japan / PMDA and the Asia Training Center (ATC) organised a third GMP Training Course, which was held in Tochigi (Japan) from 26-30 November 2018, with the support of PIC/S.   The seminar focused on risk-based mock-inspections for biological APIs and attracted participants from Bangladesh, Brazil, Chinese Taipei, Hong Kong, India, Indonesia, Malaysia, Mexico, Myanmar, Philippines, Russia, Sri Lanka, Thailand, Vietnam and WHO.

Co-operation with other Organisations

119.   The EMA invited PIC/S inspectors to an EU GMP inspector training on Health Based Exposure Limits (HBEL) and cross-contamination control. The course took place at EMA on 5-6 July 2018. An invitation was also extended to PIC/S by the EMA to participate in a training on GMP for ATMPs on 27-28 September 2018. EMA has agreed that trainings materials from both these courses can be made available to PIC/S, similarly to the EMA-EDQM Webinar Water for Injections by Non-Distillation Technologies in September 2017, which has since been published on the PIA.

120.   A meeting took place in the margins of the PIC/S Seminar in Chicago between the SCT Chairman and the Chair of the ICH Sub-Committee on Training to discuss current respective training activities and explore possible collaborations.

EXPERT CIRCLES

121.   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.

122.   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

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

123.   The SCEC is chaired by Andreas Krassnigg (Austria / AGES). In 2018, it held one teleconferences on 31 January 2018. A number of activities were carried out by e-mails.

Expert Circle on API

124.   The chairmanship of the Expert Circle on Active Pharmaceutical Ingredients (API) rotates between the three Members of its Co-ordinating Committee: Greg Orders (Australia / TGA), Florence Benoit-Guyod (EDQM) and Michel Keller (Swissmedic).

125.   In 2018, the Co-ordinating Committee prepared a new mandate as well as a work plan. It also discussed the organisation of the 9th Meeting of Expert Circle Meeting on API, which will be hosted by Spain / AEMPS in the second half of 2019. No meeting was organised in 2018.

126.   At its meeting in Geneva, the Committee adopted the new mandate of the Expert Circle. It also noted the report on the last Expert Circle meeting hosted by Australia / TGA in Melbourne on 5-7 April 2017.

Expert Circle on Human Blood, Tissues, Cells & ATMP

127.   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).

128.   The 24th meeting of the Expert Circle on Human Blood, Tissues, Cells and ATMPs was hosted by Poland / CPI in Warsaw on 23-25 October 2018. The meeting was attended by around 80 participants from 43 authorities. Discussions focused on contemporary issues in the field of blood components, plasma derivatives and tissues with a particular focus on ATMPs. A presentation was given on the differences between PIC/S Annex 2 and the EU guidelines on GMP for ATMPs. The revision of the PIC/S GMP Guide for Blood Establishments was actively discussed. Participants were also given the possibility to visit an ATMP manufacturing site and a tissue bank in Poland.

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

129.   The 25th Expert Circle meeting will be hosted by Indonesia / NADFC in 2019.

Expert Circle on QRM

130.   The Expert Circle on Quality Risk Management (QRM) was established in 2007. Between 2014 and 2016 it organised three Advanced QRM Training Courses in Tokyo (Japan), Los Angeles (USA) and London (UK). In 2017-2018, the Expert Circle was chaired by Karmin Saadat (Austria / AGES).

131.   In 2018, Chinese Taipei / TFDA hosted an Expert Circle meeting and Advanced Training on QRM in Taipei on 11-13 September 2018. Around 70 participants from 16 countries took part. Similar training, as given back in 2016, was provided at this occasion.

132.   At its meeting in Geneva, the Committee noted the outcome of a survey, prepared by the Chairman of the Expert Circle, on future QRM training as well as the use of the PIC/S recommendation on risk-based inspection planning.

Expert Circle on GDP

133.   The Expert Circle on Good Distribution Practice (GDP) was established in 2013 and organised four meetings between 2013 and 2017. A new Co-ordinating Committee was set up in 2017 with experts from UK / MHRA, Spain / AEMPS, South Africa / MCC and Sweden / MPA. The Chairman of the Co-ordinating Committee is Peter Blundell (UK / MHRA).

134.   In 2018, the Co-ordinating Committee developed a new mandate, which was adopted by the Committee at its meeting in Chicago. It also reviewed the organisation of the 5th Expert Circle meeting on GDP, which was hosted by Spain / AEMPS in Madrid on 16-18 October 2018. 66 participants from 38 countries attended. Participants were

given an introduction to Quality Management Systems in GDP and were asked to contribute to a new guide on the practical implementation of QRM in the GDP environment. Updates were also provided on regulatory changes such as the EC Falsified Medicines Directive (safety features). Interactive sessions were organised e.g. on re-visiting Q&As for the PIC/S website and the Aide-Memoire for GDP inspections

Expert Circle on Controlling Cross Contamination in Shared Facilities

135.   The Expert Circle on Controlling Cross Contamination in Shared Facilities (CCCISF) was established in 2017. Originally, the first meeting was scheduled to take place in the UK. However, since the EMA decided to host a similar training in 2018 and the MHRA moved offices, it was agreed to move the location to another region.

136.   Chinese Taipei / TFDA proposed to host the 1st Expert Circle meeting, which will take place in Taipei on 19-21 June 2019. The 2nd and 3rd Expert Circle meetings are planned to be hosted by UK / MHRA (2020) and WHO (2021).

Working Group on GCP / GVP

137.   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).

138.   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.

139.   In 2018, approximately 10 new JVP groups were established.

Working Group on Medicinal Products for Veterinary Use (VMP)

140.   Following a survey on veterinary competencies of PIC/S PA, the Committee established an Ad Hoc Working Group on Veterinary Medicinal Products (VMP). The Group, which comprises experts from France / ANSES-ANMV and UK / VMD, prepared a questionnaire seeking input from PIC/S PAs on the need to have a VMP-specific platform in PIC/S. The questionnaire was circulated to PAs on 4 December 2017 with a deadline for replies until 31 January 2018. In 2018, the Ad Hoc Working Group assessed the replies. A majority of the respondents indicated that they were in favour of (i) revising and developing Annexes 4 and 5 of the PIC/S-EU GMP Guide (dealing with VMP and immunological VMPs); (ii) developing VMP-specific training as well as VMP-specific guidance documents.

141.   At its meeting in Chicago, the Committee adopted a mandate of the Working Group on VMP, which was followed by a call of the Secretariat to nominate Working Group Members.

Working Group on Computerised Systems

142.   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 is partially outdated. The Working Group was temporarily 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

143.   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. Following a suggestion by the Irish Medicines Board (now HPRA) to establish more Sub-Committees under the PIC/S Committee, the SCSD elaborated a concrete proposal on how to set up and implement a Sub-Committee structure.

144.   The mandate of the SCSD is to define PIC/S' strategy and future policy and make proposals on how to improve the structure and the operation of PIC/S as well as co-operation with PIC/S Partners. 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

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> 4. Discuss new projects for PIC/S and make proposals on the possible "expansion" of PIC/S' mandate to other areas
>
> 5. Address implementation of new projects and resource management – in particular funding (e.g. external) – in consultation with PIC/S PA and Heads of Agencies
>
> 6. Review co-operation with Partners and make proposals / recommendations for the possible improvement of the co-operation
>
> 7. Promote the participation of authorities interested in the PIC Scheme
>
> 8. Report back to the PIC/S Committee, as provided for in the Terms of References and make proposals / recommendations

145. 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 PA as well as to facilitate mutual reliance on a voluntary basis.

146. The SCSD is chaired by Susan Laska (US FDA). It held two teleconferences on 14 March and 29 August 2018.

147. Three Working Groups operate under the SCSD:

Working Groups operating under the SCSD

Unique Facility Identifiers (UFI)

148. 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 / RORB, 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.

149. The Working Group held one teleconference in 2018. The main issues discussed by this WG relate to the geolocalisation codes, in particular their format and precision as well as what part of the manufacturing site should be recorded and where.

Travel Safety

150. The Working Group on inspectors' travel safety was established following the 2016 Seminar in Manchester. The Working Group comprises representatives from Australia / TGA Canada / RORB, EDQM, Indonesia / NADFC, Ireland / HPRA, Netherlands / IGZ, Sweden / MPA, Thailand / Thai FDA, UK / MHRA, US FDA, and Brazil / ANVISA[3]. Since 2018, it is led by UK / MHRA. The aim of the Working Group is to consider means to mitigate health or security issues affecting inspectors. These means will be summarised in an Aide Memoire.

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3   Applicant Authority

151.   At its meeting in Chicago, the Committee adopted the mandate of the Working Group on Inspector Travel Safety, which covers security risks, heath risks and site-related risks.

<u>Confidential Informants</u>

152.   The PIC/S Committee decided to establish in principle a Working Group on Confidential Informants, co-led by UK / MHRA and US FDA, which will discuss possible strategies on how to deal with confidential informants. Once operational, the Working Group will be under the SCSD.

<u>Road Map Summary</u>

153.   At its meeting in Geneva, the Ad-Hoc Working Group on Summarising the Road Map, led by Ilisa Bernstein (US FDA), presented the public version of the PIC/S Road-Map for 2018-2020, which was adopted by the Committee and then published on the PIC/S website.

Amendment of the Scheme

154.   In 2018, the Committee discussed two proposals on amending the PIC Scheme.

155.   The first proposal concerned the possibility to allow Inspection Units of Partner Organisations to join PIC/S as Members. EDQM, UNICEF and WHO were consulted on a possible interest but declined to become Members. Therefore this proposal was withdrawn.

156.   The second proposal concerned the redefinition of what a "Participating Authority" is as well as a clarification on the legal status of PIC/S. A proposal by the Secretariat and PIC/S' legal advisor, Professor Andreas Ziegler (University of Lausanne), was reviewed by the SCSD and EB and then submitted to the Committee for a first reading in Chicago. It was then circulated to Members for comments by written procedure on 9 November 2018. The revision process is likely to take one year.

Inspection Reliance

157.   In the context of increased foreign inspections, PIC/S has taken a number of measures to reduce duplicate foreign inspections such as through the maintenance of a list of planned foreign inspections – which in 2018 included around 1,200 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).

158.   In 2014, the SCSD carried out a survey on "same scope inspections". Same scope inspections, which are to be distinguished from multiple inspections for which industry is responsible, are GMP inspections, which have exactly the same scope and which are consequently redundant and unnecessary.

159.   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.

160.   The PIC/S draft Guidance on Inspection Reliance was submitted to comments to PIC/S PAs on 30 November 2017 with a deadline until 31 January 2018. It was adopted by the Committee at its meeting in Geneva in April 2018 with an entry into force on 1 June 2018 (PI 048-1). It was published on the PIC/S website.

161.   At its meeting in Chicago in September 2018, the Committee adopted a template to collect statistics on desk-top assessments as from 1st January 2019. 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.

Co-operation with Associated Partners and other Organisations

Associated Partners (EDQM, EMA, UNICEF and WHO)

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

163.   Close co-operation was maintained with the European Medicines Agency (EMA), in particular in the field of harmonisation of GMP guides and guidance documents. PIC/S was duly informed on the EMA's business continuity plan (BCP) to ensure operational continuity while the Agency prepares for its relocation to Amsterdam (Netherlands) in 2019.

164.   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

165.   Thailand / Thai FDA, the current ASEAN Liaison Authority, provided an update on activities in ASEAN, which are of interest to PIC/S. In 2018, 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 process will be formally completed in 2019.

166.   The Committee nominated Singapore / HSA as new PIC/S – ASEAN Liaison Authority for the period 2019-2020.

Heads of EEA Medicines' Agencies

167.   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 & IPRP

168.   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 on 6-7 June 2018 in Kobe (Japan) as well as in Charlotte, North Carolina, USA, on 15-16 November 2018.

169.   The Committee discussed PIC/S' contribution to GMP-related papers and working groups developed by ICH, which impacts on GMP inspectors. This is notably the case of Q12 (Pharmaceutical Product Lifecycle Management), where PIC/S provided comments in December 2018 as part of ICH's public consultation.

170.   The Committee also discussed PIC/S' possible involvement in ICH Working Groups such as on Analytical Procedure Development and Revision of Q2(R1) Analytical Validation (Q2(R2)/Q14) or Continuous Manufacturing (Q13).

171.   In the margins of the ICH Assembly in Charlotte, the PIC/S representative to ICH met with the Co-Chairs of the International Pharmaceutical Regulators Programme (IPRP), to discuss possible co-operation

ISPE

172.   PIC/S was invited to the several ISPE conferences , in particular the ISPE Europe Annual Conference in Rome (Italy) on 19-21 March 2018; the Indonesia Affiliate's Annual Conference in Jakarta on 8-9 May 2018; the ISPE Thailand Annual meeting in Bangkok on 16-17 July 2018; and the Singapore Conference and Exhibition on 29-31 August 2018.

Organisation for Economic Co-operation and Development (OECD)

173.   At the invitation of the OECD, PIC/S has taken part in July 2018 in a second survey on International Regulatory Co-operation.

PDA

174.   The PIC/S Chairman was invited to present at the 2018 PDA Annual Singapore Conference on 30-31 October 2018. PDA also invited PIC/S inspectors to attend some of its other conferences which took place in 2018 in the Asia Pacific region.

World Organisation for Animal Health (OIE)

175.   The World Organisation for Animal Health (OIE) was invited to attend the PIC/S Committee in Geneva as a guest. It was represented by Jean-Pierre Orand (France / ANSES-ANMV), who gave a presentation on OIE activities. The harmonisation of GMP for VMP is an area where PIC/S and OIE could possible co-operate in the future.

BUDGET, RISK & AUDIT

176.   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

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177.   The Sub-Committee on Budget, Risk and Audit (SCB) is chaired by Ger Jan van Ringen (Netherlands / IGJ). It held two teleconferences on 5 March and 3 July 2018, during which it reviewed the PIC/S accounts and prepared the budget, as detailed below.

2017 Accounts

178.   The SCB reviewed the audit report on the 2017 accounts by the external auditor, Moore Stephens Refidar S.A. The accounts were closed with a small surplus.

179.   The Committee approved the Statement of Accounts for the Financial Year 2017 and agreed to transfer the 2017 balance to the PIC/S Reserve Fund. It discharged the Secretary of his responsibility for the 2017 accounts.

68.   The SCB also reviewed the financial part of the report on the 2017 annual seminar, which was found to be in line with those of previous seminar reports. The PIC/S Chairman thanked the 2017 Seminar Organiser, Chinese Taipei / TFDA, for the generous donation of the seminar surplus to PIC/S, which was used to further develop PIA.

2018 Accounts

180.   The SCB reviewed the status of income and expenditures of the 2018 accounts during the year.

181.   Based on a recommendation by the SCB, the Committee adopted an increase of the PIC/S annual fee for both Members and Applicants as from 2019. A revision of the related documents, i.e. the Financial Rules and the list of PIC/S fees, was also approved. As part of this revision, the annual fee for Pre-Applicants, which has been voluntary so far, was made compulsory.

182.   The Committee also appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2018 accounts.

2019 Budget and beyond

183.   As recommended by the SCB, the Committee approved the 2018 Budget for an amount of CHF 711,800 as well as a revised 3-year budget plan for the period 2019-2021.

184.   The Committee adopted Guidelines on Donation and discussed the establishment of a PIC/S Working Group on Third-Party Funding, which will be under the responsibility of the Executive Bureau.

COMMUNICATION

185.   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.

186.   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

187.   The Sub-Committee on Communication (SC COM) held one teleconference on 27 July 2018 under the chairmanship of Mark Birse (MHRA / UK). The Committee also discussed a number of communication-related topics, as listed below.

2019 Annual Work Plan

188.   The Committee adopted an Annual Work Plan for 2019.

PIC/S Working Group on Quality Defects Procedures

189.   The Committee decided in principle to establish 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. A call for volunteers was issued.

Foreign Inspections

190.   The list of foreign inspections planned in 2018 underwent three updates in the course of the year. The list includes around 1,200 planned foreign inspections by over 40 Inspectorates (including EDQM, UNICEF and WHO).

Single Contact Points (SCP)

55.   Members were encouraged to provide Single Contact Points (SCP) for the new PIC/S List of Committee Representatives.

List of GM(D)P Inspectors

191.   The list of GM(D)P Inspectors, employed by PIC/S PA and Partner Organisations, was revised by the Secretariat in the course of the year.

Communications from Participating Authorities

192.   A number of PA took advantage of PIC/S Committee meetings in Geneva and Chicago to inform the Committee on important changes or projects concerning their Agencies / Inspectorates.

193.   South Africa / SAHPRA reported that the Medicines Control Council (MCC) had ceased to exist on 31 January 2018 and was replaced by the South African Health Products Regulatory Authority (SAHPRA).

PIC/S Committee meeting in Chicago

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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 2018)

(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 Regions Branch (Santé Canada - Direction générale des opérations réglementaires et des régions)	RORB
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	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.