



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

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ANNUAL REPORT 2016

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**

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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 an informal 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 2016, PIC/S comprised 49 Participating Authorities from all continents. For the list of PIC/S Participating Authorities, see Annex 2.

PIC/S aims at harmonising inspection procedures worldwide by developing common standards in the field of GMP and by providing training opportunities to inspectors. It also aims at facilitating co-operation and networking between competent authorities, regional and international organisations, thus increasing mutual confidence.

A Committee of the Participating Authorities' representatives (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 2016.

ANNUAL REPORT 2016

THE YEAR IN A NUTSHELL

The United Kingdom takes the lead

1. 2016 was a very important year for the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA), as it took over the PIC/S chairmanship and organised the annual training seminar in Manchester.



2. On 1st January 2016, Mr Paul Hargreaves (UK / MHRA) became the twenty-second Chairman of PIC/S. This is fourth time that the UK is providing a chairman to PIC/S. During his two-year term (2016-17), the PIC/S Chairman will be assisted in his task by Members of the Executive Bureau (for further details, see paragraph 5) as well as the Secretariat.

Photo: Mr Paul Hargreaves, PIC/S Chairman

3. In 2016 the PIC/S Committee met only once (instead of traditionally twice), as the annual training seminar took place in early July, thus making it difficult to organise another meeting either before or afterwards. The PIC/S Committee meeting was held in Manchester (UK) on 3-4 July 2016.

4. The activities of the PIC/S Committee over the year as well as the outcome of the Manchester meeting are summarised in this Annual Report.

New Executive Bureau for 2016-2017

5. On 1st January 2016, a new PIC/S Executive Bureau took over for a 2-year term (2016- 2017). It consists of:

- Mr Paul Hargreaves (United Kingdom / MHRA), PIC/S Chairman;
- Mr Boon Meow Hoe (Singapore / HSA), PIC/S Deputy Chairman and Chair of the Sub-Committee on Training (SCT);
- Dr Joey Gouws (South Africa / MCC), immediate former PIC/S Chairperson;
- Mr Jacques Morénas (France / ANSM), Chair of the Sub-Committee on Strategic Development (SCSD);
- Ms Anne Hayes (Ireland / HPRA), Chair of the Sub-Committee on Compliance (SCC);
- 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 / IGZ), Chair of the Sub-Committee on Budget, Risk and Audit (SCB); and
- Mr Mark Birse (United Kingdom / MHRA), Chair of the Sub-Committee on Communication (SC COM)

The Web Site of the PIC/S Inspectorates' Academy (PIA) is launched

6. The web site of the PIC/S Inspectorates' Academy (PIA) was launched on 18 July 2016. The launching of the PIA web site marks the completion of stage 1 of PIA, which is a dedicated, protected web-based platform incorporating PIC/S training material. PIA is accessible to all PIC/S Inspectorates, bringing together nearly 1,800 PIC/S inspectors. The PIA website is a sub-website of the PIC/S website which is available at <https://www.picscheme.org>.

7. PIA is a PIC/S initiative to set up a web-based educational centre under the PIC/S umbrella, which aims at harmonising and standardising GMP training at an international level through a certified qualification system. PIA delivers not only general or advanced training but also serves as a platform for discussion and sharing among regulators. It offers a single point of access to all PIC/S training activities and is being implemented in various stages.

8. The idea of the PIA was announced during the PIC/S 40th Anniversary in 2011. The concept was originally mooted by Mr Boon Meow Hoe (HSA / Singapore) that PIC/S should create a professional "Inspectors' Academy" delivering a variety of courses ranging from general training to highly specialised training for inspectors. The Academy was officially established at the PIC/S Committee meeting in Paris (France) on 20-21 October 2014.

9. With the completion of stage 1, stage 2 of PIA has now started. This second stage will focus on developing (e-learning) modules responding to specific training needs, which will have to be identified. It will also aim at co-operating with external stakeholders as well as developing PIC/S training recognition and certificates.

Planning ahead

10. In 2016 the PIC/S Executive Bureau (EB) met in Manchester (UK) on 2-3 July 2016. The second day of the meeting was traditionally devoted to the preparation of the Committee's meeting as well as to discussions on financial, administrative and staff related issues.

11. As the year before, the EB also met for an extraordinary "Strategy Meeting". This meeting took place on 2 July 2016. Based on the strategic orientations agreed by the EB during this Strategy Meeting as well as the previous Strategy Meeting in Nusa Dua (Indonesia) on 4 October 2015, the Secretariat prepared a strategic plan ("Road Map") for the period 2017-19. The draft Road Map was submitted to Members by written procedure on 30 November 2016. Based on Members' comments, the draft Road Map will be revised and presented at the next PIC/S Committee meeting.

PIC/S' expansion continues

12. The continuous expansion of PIC/S shows that the organisation is dynamic and attractive. Three new Competent Authorities joined PIC/S during the year.

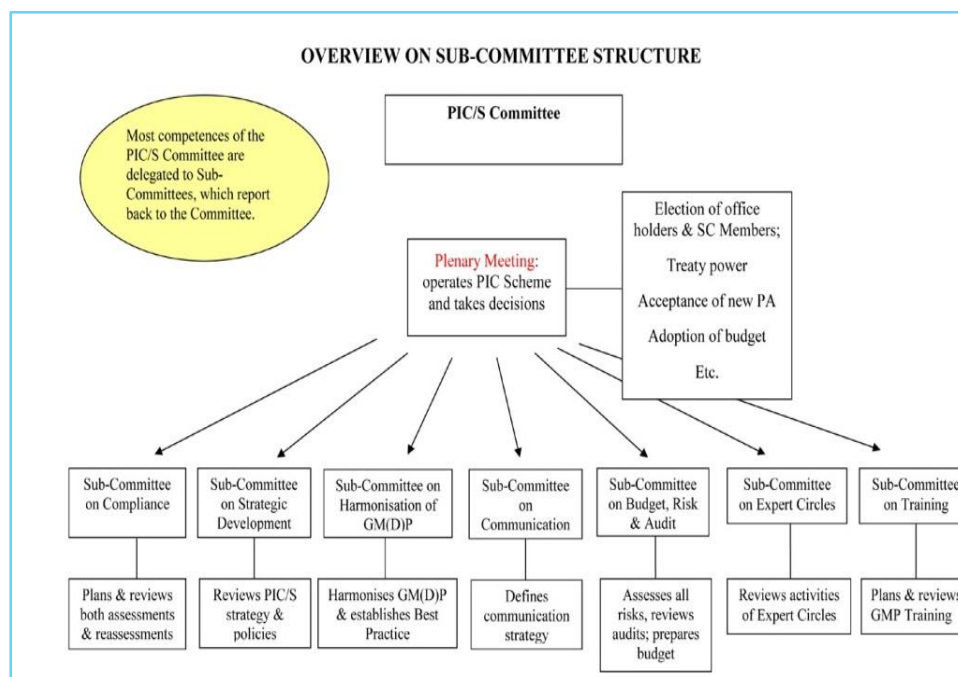
13. On 1st January 2016, two following Competent Authorities joined PIC/S:

- The Pharmacy and Poisons Board of Hong Kong (PPBHK) / Hong Kong SAR, which applied on 30 August 2013, became PIC/S' 47th Participating Authority.
- The Croatian Agency for Medicinal Products and Medical Devices (HALMED), which applied on 5 September 2014, became PIC/S' 48th Participating Authority.

14. On 1st August 2016, the Thai Food and Drug Administration (Thailand / Thai FDA), which applied in March 2015, became PIC/S' 49th Participating Authority.

PIC/S Sub-Committee Structure

15. 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). The present report is structured along the same lines and provides an overview of activities in the above-mentioned fields.



COMPLIANCE

16. 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 compliance to the PIC Scheme is one of PIC/S’ most important and critical areas, which needs to be constantly monitored.

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

18. The SCC held three teleconferences on 19 May, 8 June and 14 October 2016, during which it discussed membership applications, pre-applications, contacts with non-Members, assessment and reassessment procedures and other topics, detailed below.

Evaluation and Re-evaluation Procedures

19. The SCC continued its discussions on the revision of the PIC/S Accession and Pre-Accession Guidelines as well as on the PIC/S Joint Reassessment Programme (JRP). Regarding the JRP, a new risk-based re-assessment process, in line with the proposed changes to the EMA Joint Audit Programme (JAP), and a new JRP evaluation template will be included.

20. The Working Group on the guideline and interpretation of the Audit Checklist, which is run in co-operation with the EMA Compliance Group on the Joint Audit Programme (JAP), is currently reviewing the 48 critical indicators. The Working Group is led by Louise Kane (Health Canada).

Membership Applications

21. In the course of 2016, PIC/S continued the assessment of the following six membership applications:

Brazil / ANVISA

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

23. In 2016, Brazil / ANVISA reported on an important, internal reorganisation and expressed the wish to request a clock-stop. The Committee invited ANVISA to submit a request in writing. As a result of ANVISA's reorganisation, the PIC/S on-site assessment visit could not be arranged.

Iran / FDA

24. The Division of Pharmaceutical and Narcotic Affairs (DPNA) of the Food and Drug Organisation (FDO) applied for PIC/S membership in 2009. FDO later on became the Iranian Food and Drug Administration (FDA). Due to two subsequent changes of the PIC/S Rapporteur, the Committee granted FDA a one-year clock-stop for the period 1 January – 31 December 2014. The new Rapporteur, Mr Paul Sexton (Ireland / HPRA), restarted the assessment process in 2015. A Co-Rapporteur and additional Audit Team members were also appointed for the on-site assessment visit, which took place on 12-16 September 2015.

25. A draft report was tabled to the PIC/S Committee at its meeting in Manchester. The Committee first clarified the issue related to the scope of the membership application and whether traditional medicine was included. DPNA is not in charge of traditional medicine and as a result this has not been assessed during the on-site assessment visit. However, the Committee agreed in Manchester that since there is a section of FDA, responsible for herbal products, this should be also assessed in line with past practice. As a result, a follow-up visit will be organised in 2017 in order to

assess the inspection of herbal medicine. The Rapporteur was invited to finalise his report after completion of the follow-up visit.

Mexico / COFEPRIS

26. After having successfully completed its pre-accession process, Mexico's Federal Commission for the Protection from Sanitary Risks – Ministry of Health (COFEPRIS) submitted a full membership application on 18 December 2014. The Committee appointed an Audit Team consisting of the Rapporteur, Manuel Ibarra (Spain / AEMPS), and inspectors from Italy / AIFA, Germany / ZLG, Israel / ISCP, and US FDA. The on-site assessment visit took place on 25-29 January 2016.

27. The Committee discussed the draft report in Manchester and noted that in line with a recommendation given during the pre-accession, Mexico / COFEPRIS had ended the practice of sub-contracting inspections to a third party. As a result, the number of inspections to be carried out had increased substantially and a number of corrective actions needed to be implemented.

28. The Committee agreed in principle on the need of a follow-up visit. The Rapporteur was invited to finalise his report after completion of the follow-up visit.

29. COFEPRIS Commissioner Julio Sánchez y Tépoz, who attended the meeting in Manchester, said that accession to PIC/S was an important objective of the Mexican Government and rapid accession was desirable.

Philippines / PFDA

30. The Philippines' Food and Drug Administration (PFDA) applied for PIC/S membership on 1st June 2009. The on-site assessment visit took place on 10-14 September 2012. Following a reorganisation, the PIC/S Committee granted PFDA a clock stop for the period 1 January 2015 – 31 December 2015, subject to the provision of a progress report on the implementation status of the corrective and preventive action plan (CAPA).

31. At its meeting in Manchester, the Committee discussed a Note on the accession process of Philippines / FDA, which concluded that the CAPA had not been successfully completed. Since PFDA had applied to be listed as an ASEAN Competent Authority under the ASEAN Sectoral MRA on GMP Inspection, PFDA was invited to reapply for PIC/S membership, once it had completed the ASEAN assessment process.

Turkey / TMMDA

32. The Turkey's Medicines and Medical Devices Agency (TMMDA) applied for PIC/S membership on 3 May 2013. Following the paper assessment of the application by the Rapporteur, Anne Hayes (Ireland / HPRA), and Co-Rapporteur, Michel Keller (Switzerland / Swissmedic), the Committee decided in Manchester to appoint additional Audit Team Members from Argentina / ANMAT, Chinese Taipei / TFDA, Malaysia / NPRA, and New Zealand / Medsafe and to proceed with the on-site assessment visit.

Thailand / Thai FDA

33. A membership application was received on 20 March 2015 from the Thai Food and Drug Administration, Ministry of Public Health (Thailand / Thai FDA). The on-site

assessment visit took place on 14-18 March 2016 under the leadership of the Rapporteur, Jacques Morénas (France / ANSM), and the Co-Rapporteur, Boon Meow Hoe (Singapore / HSA). Australia / TGA and Indonesia / NADFC provided each one Team Member for the on-site assessment visit.

34. Based on the assessment visit report, the Committee agreed to invite Thai FDA to join PIC/S on 1st August 2016.



From left to right: Dr Suchart Chongprasert (Thai FDA), Dr Boonchai Somboonsook, Secretary General of Thai FDA, Mr Jacques Morénas, Rapporteur for the application of Thai FDA (France / ANSM), Ms Prapassorn Thanaphollert (Thai FDA), Mr Daniel Brunner, Secretary of PIC/S.

Pre-Applications

35. PIC/S' Accession Guidelines provide for the possibility for a Competent Authority to ask PIC/S to carry out a pre-assessment by a PIC/S auditor. 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.

36. In the course of 2016, the following 3 pre-applications were under review:

Belarus / MoH

37. Belarus' Ministry of Health (MoH) applied for pre-application on 30 September 2012. The Rapporteur, Iveta Vilcane (Latvia / ZVA), presented her gap analysis report at the Committee meeting in Geneva in 2015. Belarus / MoH provided an official reply to the gap analysis report as well as a CAPA the same year.

38. At its meeting in Manchester, the Committee appointed Unine Felix (South Africa / MCC) to review the CAPA provided by Belarus / MoH. However, as the latter is not part of the pre-accession process, the Committee decided to close the pre-accession and to invite Belarus / MoH to apply for membership, once the CAPA had been implemented.

Chile / ISP

39. Chile's "Instituto de Salud Pública" (Public Health Institute) applied for pre-application on 30 December 2013. The Committee endorsed the gap analysis report

prepared by the Rapporteur, Rachel Shimonovitz (Israel / ISCP) and the Co-Rapporteur, Raquel San José (Spain / AEMPS). It invited ISP / Chile to submit a Corrective and Preventive Action Plan (CAPA).

40. At its meeting in Manchester, the Committee decided to close the pre-accession and to invite Chile / ISP to apply for membership, once the CAPA had been implemented.

Kazakhstan / CCMPA

41. Kazakhstan's Committee for the Control of Medical and Pharmaceutical Activities (CCMPA) applied for pre-application on 1 November 2013. The Committee agreed to prolong the pre-assessment period until the submission of the gap analysis by the Rapporteur, Rosmarie Neeser Zaugg (Switzerland / Swissmedic), which was expected by the end of the year.

Reassessment of Participating Authorities

42. 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 also reassessed for equivalence on a regular basis. The JRP is run in parallel with the EU's Joint Audit Programme (JAP) and uses basically the same tools. JAP assessments and JRP reassessments are deemed equivalent.

43. Malaysia / NPRA was re-assessed in 2015 and the on-site re-assessment visit took place on 12-13 & 15-16 October 2015. At the Manchester meeting, the Rapporteur, Anne Hayes (Ireland / HPRA), and the Co-Rapporteur, Michel Keller (Switzerland / Swissmedic), presented the outcome of the visit. Once reviewed by the SCC, the report will be tabled at the next meeting.

44. US FDA was assessed by the EU and the on-site assessment visit took place on 14-18 September 2015, using the harmonised PIC/S-EMA JAP/JRP assessment procedure as a basis. The report, drafted by the Team Leader, Mark Birse (UK / MHRA), was tabled to the SCC for review. At its meeting in Manchester, the Committee invites the EU leader to perform one observed inspection in order for the EU assessment process to be deemed equivalent to a PIC/S re-assessment in line with PIC/S JRP criteria.

45. The Committee also agreed to reassess Australia / TGA and Singapore / HSA in 2017.

Corrective Action by recently acceded PIC/S PA

46. The Committee agreed to close the process of corrective actions by Hong Kong / PPBHK, which had been successfully completed following its accession to PIC/S on 1st January 2016.

Non-Members

47. Close contacts were kept with a number of non-Members. A meeting between the PIC/S Executive Bureau and a Delegation from the China Food and Drug Administration (CFDA) took place in Manchester on 7 July 2016 while both Russian and Vietnamese representatives were invited to attend the PIC/S Committee meeting as guests. The Russian inspectorate was represented by the "State Institute of Drugs and Good Practices" (SID&GP) of the Ministry of Industry and Trade of the Russian Federation (Minpromtorg) while Vietnamese inspectorate was represented by the Drug Administration of Vietnam (DAV).

GMDP

48. 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.

49. 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.

50. 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

51. The SCH held three teleconferences 23 February, 7 June and 8 December 2016, 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 Working Groups, detailed below.

52. In Manchester, the Committee elected Luisa Stoppa (Italy / AIFA) as SCH Deputy Chairperson (in replacement of Marisa Delbò, Italy / AIFA) and as “PIC/S-EMA Liaison Officer”.

Working Groups under SCH

53. Four Working Groups are operating under the SCH.

Working Group on Data Integrity

54. 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. A first draft was completed by the Working Group. In Manchester, the Committee agreed to publish the draft “PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments” (PI 041-1 (Draft 1)) and to implement it on a trial-basis for a period of 6 months. Participating Authorities were invited to report back on the implementation of the guidance document by the end of February 2017. The draft will then be revised and submitted for adoption.

Working Group on Harmonisation of the Classification of Deficiencies

55. The Working Group on Harmonisation of the Classification of Deficiencies, led by Jenny Hantzinikolas (TGA / Australia), 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 will also be included. These efforts are hoped to facilitate more consistent responses among

international regulatory authorities when responding to GMP deficiencies and GMP non-compliance.

56. The first draft of the Guidance on the Classification of Deficiencies was submitted to PIC/S Members and Partner Organisations on 7 January 2016. Comments were due by 31 January 2016. The WG then shared a revised draft with inspectors at the occasion of the 2016 Annual Seminar in Manchester, during which a tool to improve the risk classification of GMP deficiencies was tested on the basis of case studies. A second, written consultation will be organised at a later stage.

Working Group on Annex 1 / Sterile Manufacturing

57. 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. The joint PIC/S-EMA Drafting Group is led by Andrew Hopkins (UK / MHRA) and includes representatives of the Competent Authorities of PIC/S and EEA.

58. The joint Drafting Group has prepared a revision of Annex 1. Two drafts were submitted to PIC/S and EEA Competent Authorities for comments on 4 August (first draft) and 13 December 2016 (second draft). Once Step 1 will have been successfully completed, a joint public consultation with the EMA will be organised (Step 2).

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

59. 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.

60. The WG is chaired by Graeme McKilligan (UK / MHRA). A face-to-face meeting took place on 16 February 2016 in London (UK), during which the WG drafted the Aide-Memoire. The draft PIC/S Aide-Memoire on Cross-Contamination in Shared Facilities will be submitted to the comments of Members in early 2017 after its review by the SCH.

61. The WG has proposed to become an Expert Circle and to develop some training material (including case studies) in the form of webinars, which could be shared through the PIA. The mandate of the Expert Circle will be submitted to the PIC/S Committee in 2017.

Working Group on Advance Therapy Medicinal Products (ATMPs)

62. The Working Group on Advance Therapy Medicinal Products (ATMPs) was established in 2015 in order to draft an Aide-Memoire to support the inspection of ATMPs facilities. It is chaired by Annie Rietveld (Netherlands / IGZ). The draft Aide-Memoire was discussed at the PIC/S Expert Circle on Blood, Tissues, Cells and ATMPs in Rome (Italy) on 26-30 October 2015. However, due to developments in the EU (see below), it was put on hold.

63. The PIC/S Committee has taken position against the European Commission's stand-alone GMP Guide for ATMPs developed by a Joint Drafting Group including Members from the EMA Committee for Advanced Therapies (CAT) and the Inspectors

Working Party on GMDP (IWP). There are a number of concerns, which are also shared by the EMA IWG on GMPD, regarding this guide, in particular the fact that the proposed GMP requirements are lower than those contained in the PIC/S GMP Guide.

64. In Manchester, the Committee noted that the EC has ignored concerns from Competent Authorities of EU MS as well as those expressed by PIC/S during the consultation. It expressed concerns that the safety of patients could no longer be guaranteed due to the inevitable impact on the quality of medicines. In addition, due to the introduction of lower GMP standards for ATMPs in the EU, the EU and PIC/S GMP Guides will cease to be equivalent. The Committee agreed to conduct a PIC/S-internal survey on current ATMP GMP requirements and prepare a response to the EC, which was sent on 7 October 2016. An ad hoc Working Group on ATMPs was established to prepare the questionnaire and assess the replies.

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

65. 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.

66. In connection with the transposition of the revised EU GMP Guide for PIC/S purpose, the SCH discussed the issue of “gender neutral language” in the PIC/S GMP Guide as well as in PIC/S guidance documents. In Manchester, the Committee discussed agreed in principle to use the gender-neutral term “he/she”.

67. In 2016, the SCH actively continued to harmonise and transpose GM(D)P guidance documents.

68. The revised Chapters 1 (Pharmaceutical Quality Systems), 2 (Personnel), 6 (Quality Control), and 7 (Outsourced Activities) reached Step 3 (adoption) and entered into force on 1 January 2017.

69. Revisions to Chapters 3 (Premise and Equipment), 5 (Production), & 8 (Complaints and Recalls) reached Step 1 (consultation of PA) in 2016.

70. PIC/S experts are also involved in EMA Drafting Groups on the revision of Annex 1, 13 and 17 of the EU-PIC/S GMP Guide.

- Annex 1 (Sterile Manufacturing): See paragraphs 56-57.
- Annex 13 (Investigational Medicinal Products): The EC intends to publish a standalone guide on IMPs, which will replace Annex 13. The public consultation on the ATMP Guide, which includes ATMP-IMPs, has just started. The European Commission aims to publish the new GMP for IMPs guidelines in April 2017.
- Annex 17 (Real Time Release Testing, previously Parametric Release): the revision was submitted to public consultation by the EU and PIC/S on 15 September 2015 (with comments by 11 December 2015). The EMA Drafting Group is reviewing the comments and preparing a revised draft.

71. PIC/S also follows the work on the drafting of the EU Annex 21 (GMP Obligations for Importation to the EU). It may decide to develop a PIC/S-specific Annex.

Guidance Documents

72. All PIC/S guidance documents are available on the PIC/S website <http://www.picscheme.org>.

GMP Guidance Documents

Revision of PIC/S Recommendations on Validation Master Plan; Installation and Operational Qualification; Non-Sterile Process Validation; and Cleaning Validation

73. In Manchester, the Committee decided to establish a Working Group on the revision of PIC/S Recommendations on Validation Master Plan; Installation and Operational Qualification; Non-Sterile Process Validation; and Cleaning Validation (PI 006-3), in connection with the transposition and adoption by PIC/S of the EMA Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities. The UK / MHRA volunteered to chair this WG.

74. An interim revision of the above-mentioned recommendations (PI 006-4 (Draft 1)) was prepared by the SCH and submitted to Members for comments on 27 October 2016. The period of consultation ended on 31 December 2016.

GDP guidance documents

75. In 2016, the SCH reviewed a draft Aide-Memoire for GDP inspections as well as a draft Q&A document for GDP, which have been developed by the Expert Circle on GDP. These GDP-related documents will be submitted to Members for comments in 2017.

EMA guidance documents

76. Following their review and adaptation for PIC/S purpose, the following EMA documents were submitted to Members for comments on 27 October 2016:

- Guidelines on the formalised risk assessment for ascertaining the appropriate Good Manufacturing Practice for excipients of medicinal products for human use (PI 041-1);
- Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (PI 042-1) (to be read in relation with the revised Chapters 3 & 5 of the EU-PIC/S GMP Guide);
- Guidelines on the principles of Good Distribution Practices for active substances for medicinal products for human use (PI 043-1).

PIC/S Library

77. 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).

TRAINING

78. 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) and Good Clinical Practices (GCP).

79. The Sub-Committee on Training (SCT), led by Boon Meow Hoe (Singapore / HSA), is the oldest Sub-Committee and was initially established as a Working Group under the PIC/S Committee. It met twice in 2016: on 4 May and 8 July. Its mandate has remained by and large the same over the past decades – see box at next page.

The mandate of the SCT is to:

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

80. The following PIC/S training activities were held in 2016 (in chronological order):

Date	Place	Activity	Organised by
12-14 April	Pretoria (South Africa)	PIC/S Expert Circle meeting on GDP	South Africa / MCC
6-8 July	Manchester (UK)	PIC/S Seminar 2016 on "Inspectorates of the Future"	UK / MHRA
8-9 August	San Juan (Puerto Rico)	PIC/S – PDA Q7 Training	PDA and PIC/S

26-28 September	EMA, London (UK)	PIC/S Advanced QRM Training Course	Hosted by EMA, organised by PIC/S
24-28 October	Hong Kong (China)	PIC/S Expert Circle meeting on Human Blood, Tissues, Cells and ATMPs	Hong Kong SAR / PPBHK
5-9 December	Toyama (Japan)	PMDA-ATC GMP Inspection Seminar	Japan / PMDA (with the support of PIC/S)

Annual Training Seminar

81. 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 Participating Authority. 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.

82. In 2015, the Seminar was organised by the Indonesian National Agency for Drug and Food Control / NADFC in Nusa Dua, Indonesia, on 7-9 October 2015. The topic of the seminar was “Biopharmaceuticals (Biotechnology and Biologicals): How To Inspect”. For more details, see the Annual Report for 2015. The evaluation report, which was reviewed by the SCT, was presented at the occasion of the PIC/S Committee meeting in Manchester on 4-5 July 2016.

83. In 2016, the Seminar was organised by the United Kingdom’s Medicines and Healthcare products Regulatory Agency (MHRA) in Manchester (UK) on 6-8 July 2016. The topic of the Seminar was “Inspectorates of the Future”.



84. The Seminar was opened by the Chief Executive of MHRA, Dr Ian Hudson (photo), and the PIC/S Chairman, Mr Paul Hargreaves. The Seminar was the 5th organised in the UK since MHRA joined PIC/S as a Founding Member in 1971. It was attended by more than 180 participants from 53 countries. All continents were represented. The objectives of the Seminar were to exchange and discuss on GMP topics affecting the work that Inspectorates do and what factors will drive them to do things differently in the future.

85. The 2.5 day Seminar took place in an innovative format consisting of mixed presentations and parallel workshops. The workshops, which were larger than usual, were supported by a range of technology including live surveys capturing feedback for instant review. Participants were also able to take advantage of a specific PIC/S Seminar application developed for the occasion.



86. The lectures and presentations focused on inspection trends & GMP deficiencies; GMP evolution, in particular data integrity inspections in the supply chain; global developments in the pharmaceutical industry; co-operation between Regulatory

Agencies; risk-based inspection models; whistle-blower cases; compliance management; and shortages and supply chain issues.

87. Four workshops for inspectors followed on:
- Inspection trends and inspection strategies for the future (Workshop leader: Health Canada).
 - Data Integrity: tools and techniques (Workshop leader: UK / MHRA & Australia / TGA).
 - Shortages (Workshop leaders: European Medicines Agency (EMA) and UK / MHRA).
 - Compliance Management (Workshop leader: US FDA).

88. The last day of the Seminar was mainly devoted to the outcome of the workshops and the presentation of the next seminar, which will be hosted by Chinese Taipei / TFDA in Taipei on 13-15 September 2017. The topic of the seminar is the inspection of “Quality Control Laboratories”.



2016 Seminar - Official photo with participants

Joint Visits Programme / Coached Inspection Programme

89. At the end of 2016, there were approximately 15 active 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).

90. The JVP 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.

91. The participation in the JVP has been progressively extended from GMP inspectors to GDP, GCP¹ and GVP² inspectors. At the end of 2016, there were 8 Joint Visits Groups for GCP/GVP co-ordinated by the PIC/S Working Group on GCP/GVP (see paragraph 113).

PIC/S International Training Programme on API

92. The API International Training Programme (API ITP) is run by the Expert Circle on API (see paragraph 111). It consists of three segments: the PIC/S-PDA Q7 Training, open to regulators and industry; the Advanced Training for regulators; and the Q&A.

- The Q7 training, which focuses on familiarisation with ICH Q7, is for both industry and regulators; it is organised jointly by PIC/S and the Parenteral Drug Association (PDA);
- The advanced training on API inspection, focusing on improving the skills of inspectors and sharing approaches for addressing contemporary issues, is for regulators only;
- The Q&A on ICH Q7 is on the interpretation of the requirements of ICH Q7 and is open to both industry and regulators.

93. The Q7 training and the advanced training on API have been recorded in view of the development of e-learning modules, which are integrated into the PIA (see paragraph 97ff).

94. The bulk of the Q7 training was organised in 2015: four Q7 Training courses were successfully organised and co-financed by the European Commission in Korea (Republic of); Brazil; India; and China. In 2016, one course took place in Puerto Rico on 8-9 August 2016.

95. With regard to Q&A on ICH Q7, the PIC/S Committee established a new PIC/S Working Group on “API Q&A developed by PIC/S but not transferred to ICH”. The aim is to use these Q&A to develop training material part for the PIC/S API International Training Programme.

1 Good Clinical Practice

2 Good Vigilance Practice / Pharmacovigilance

PIC/S New Inspector Training Course

96. 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 extremely popular and well attended. In 2014, a “Train the Trainer” course was also organised to complement the NITC.

97. The SCT discussed the possibility of organising another NITC in conjunction with the 2016 Seminar in Manchester. However, due to limited resources, the organisation of the course has been rescheduled to 2017.

PIC/S Inspectorates’ Academy (PIA)

98. The PIC/S Inspectorates’ Academy (PIA) is a project run by the PIA Management Steering Committee (PMSC) and the SCT, both placed under the chairmanship of Boon Meow Hoe (Singapore / HSA).

99. PIA is a PIC/S initiative to set up a web-based educational centre under the PIC/S umbrella and to provide harmonized, standardised GMP training 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. 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 will be implemented in three independent stages.

100. The first stage consists in the launching of the PIA. A PIA Project Management Steering Committee (“PMSC”) monitors the progress and discusses issues in relation with the development and implementation of the PIA project. The PMSC held one teleconference on 17 May 2016. The PIA will first be developed within PIC/S before being opened up to external organisations.



101. 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 logo³ and its motto, which is “**Inspection Excellence through Harmonised Training**”. Initially planned for Q3 2015, the PIA website was launched on 18 July 2016. This marks the end of Stage 1 and the beginning of Stage 2 of PIA. Stage 2 will focus on identifying training needs, developing e-learning modules, seeking funding, etc.

102. The PIA website is a sub-site of the PIC/S website, which went through a complete overhaul in 2016. The new web site is accessible on tablets and smartphones and provides higher visibility on SC activities. The PIA sub-site contains training material, mainly taped video training, as well as a forum for inspectors to interact. Its access is password-restricted. Around 1,800 PIC/S inspectors have access to PIA, provided that they register first on-line.

³ The PIA logo is registered with the Swiss Office of Intellectual Property.

PMDA Training Course supported by PIC/S

103. Japan / PMDA organised with the support of PIC/S a GMP Training Course on 5-9 December 2016 in Toyama (Japan). The course included a mock inspection at an active manufacturing site for solid dosage forms. 19 participants attended the training, which will be repeated on an annual basis.

US FDA Webinar on Data Integrity

104. A US FDA webinar training on data integrity took place on 22-23 March 2016, in which interested PIC/S inspectors were invited to participate.

EXPERT CIRCLES

105. 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.

106. 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

107. The SCEC is chaired by Andreas Krassnigg (Austria / AGES). In 2016, it held two teleconferences: the first on 15 March and the second on 7 June.

Expert Circle on Human Blood, Tissues, Cells & ATMP

108. 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). The revised draft mandate of the Expert Circle was adopted in Manchester.

109. The 22nd meeting of this Expert Circle was hosted by Hong Kong SAR / PPBHK on 24-28 October 2016 in Hong Kong, China. It attracted 114 participants from 32 countries. At this meeting, experts discussed issues related to the inspection of blood, blood components, plasma derivatives, cells and tissues. As at the previous meeting in Rome (Italy), discussions also focused on ATMPs as well as a on a PIC/S survey (mapping of competences) in the field of blood, tissues, cells & ATMPs.

Expert Circle on QRM

110. The Expert Circle on Quality Risk Management (QRM) is chaired by Kevin O'Donnell (Ireland / HPRA) and has been mandated to organise three Advanced QRM Training Courses between 2014 and 2016. The first course took place in Tokyo (Japan) on 8-10 December 2014. The second course was hosted by US FDA, in Los Angeles (USA) on 5-7 October 2015. The third and last course was held at the EMA on 26-28 September 2016 in London (UK). It attracted 74 inspectors from 29 countries.

Expert Circle on GDP

111. The Expert Circle on Good Distribution Practice (GDP) was established in 2013. It is chaired by Steve Todd (UK / MHRA). The 4th meeting of the Expert Circle on GDP was organised by South Africa/MCC on 12-14 April 2016 in Pretoria. It was attended by 54 delegates from 23 countries. The meeting focused on the training of GDP Inspectors, in particular on the PIC/S Guide to GDP.



4th meeting of the PIC/S Expert Circle on GDP IN Pretoria (South Africa)

Expert Circle on API

112. The Expert Circle on Active Pharmaceutical Ingredients (API) is chaired by Carmelo Rosa⁴ (US FDA) and has been actively involved in the planning and organisation of:

- Q7 events (including identification of PIC/S speakers); and
- The 8th Meeting of Expert Circle Meeting (including Advanced Training) in Melbourne (Australia), to be hosted by TGA on 5-7 April 2017.

Working Group on Medicinal Products for Veterinary Use

113. Following a survey on veterinary competencies of PIC/S PA, the Committee agreed in principle to set up an Expert Circle on medicinal products for veterinary use. An Ad Hoc Working Group consisting of France / ANSES, Ireland / HPRA and UK / VMD, has been established to draft a mandate. Discussions on this mandate continued in 2016.

Working Group on GCP / GVP

114. The aim of the Working Group on Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP) is 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, led by Mandeep Rai (UK / MHRA), continues to be very active in the field of training through the PIC/S Joint Visits Programme, 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.

STRATEGIC DEVELOPMENT & CO-OPERATION

115. 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.

116. 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

⁴ Mr Rosa stepped down as Chairman in December 2016.

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

117. 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.

118. The SCSD is chaired by Jacques Morénas (France / ANSM). It held teleconferences on 28 April and 14 December 2016.

International Coalition of Medicines Regulatory Authorities (ICMRA)

119. In 2014, the Committee agreed in principle to further strengthen its co-operation with the International Coalition of Medicines Regulatory Authorities (ICMRA). ICMRA is involved in exploring the better sharing and reliance of GMP information between its Members. Through closer co-operation with ICMRA, some PIC/S goals and initiatives can be further advanced such as facilitating the acceptance of same scope inspection results.

120. In 2016, the ICMRA GMP Project dealing with the issue of “equivalence” invited PIC/S to be formally represented in the ICMRA “GMP reliance framework on equivalency”. This project looks at possible ways to assess information using inspection reports from other authorities. During phase 2 of the project, an increased number of desk-top reviews of inspection reports will be made. The PIC/S Committee accepted the invitation by the ICMRA GMP Project to be represented and nominated Anne Hayes (Ireland/HPRA) as its representative.

Voluntary Acceptance of Same Scope Inspection Results

121. In the context of increased foreign inspections and multiple initiatives in the field of cooperation between drug regulatory authorities, 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 2016 included around 1,500 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).

122. More recently, the SCSD has carried out a survey with the aim of reducing the number of “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.

123. All PAs provided an input to the survey, which covered both domestic and foreign inspections. The survey shows clear limitations regarding the voluntary acceptance of same scope inspection results mainly due to legal obstacles. Addressing these obstacles may be possible through the ICMRA GMP reliance framework on “equivalency” (see above). This will be further discussed in 2017.

Advantages and Privileges of PIC/S Membership

124. Based on an SCSD paper, the Committee discussed in 2015 whether to extend the advantages and privileges of Members to Applicants and Partner Organisations. Members agreed in principle on the following:

- Membership benefits needed to be more clearly defined with respect to training activities as well as to financial aspects;
- Participation in PIC/S Working Groups was a Member-only privilege;
- The PIC Scheme should be amended to allow Partner Organisations to apply as Members.

125. The above decisions and their implementation were further discussed in 2016:

- With regard to membership benefits, the Committee endorsed a proposal by the SCSD that the ratio of Members’ fees to non-Members fees should be 1:2 (e.g. for Seminars or Expert Circle meetings).
- With regard to the participation of Partner Organisations in PIC/S Working Groups (WGs) as well as in PIC/S Sub-Committees (SCs), this will remain possible but as “guests” only. The Committee adopted in Manchester revised Terms of Reference for both SCs and WGs.
- With regard to the proposal to allow the Inspectorates of Partner Organisations to join PIC/S, the SCSD discussed an amendment of the Scheme while the Committee agreed in principle to allow the Inspectorates of Partner Organisations to join PIC/S as full Members, subject to the clarification of accession criteria – in particular the compliance to the PIC/S checklist of indicators.

Unique Facility Identifiers (UFI)

126. At its meeting in Manchester, the Committee agreed in principle to establish a PIC/S Working Group on the Unique Facility Identifiers (UFI) for drug establishments. The identification of companies through a UFI will allow PIC/S to have a harmonised and consistent system to localise a manufacturing site. A survey by US FDA has

shown that PIC/S PAs use different systems; however, different systems will also give different locations. Moreover, it increases the risk of “shadow factories”.

Co-operation with Associated Partners and other Organisations

Associated Partners (EDQM, EMA, UNICEF and WHO)

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

128. Close co-operation was maintained with the European Medicines Agency (EMA), in particular in the field of harmonisation of GMP guides and guidance documents.

129. The Memorandum of Understanding between PIC/S and the European Directorate for the Quality of Medicines & Healthcare (EDQM) on the one hand and the Memorandum of Understanding between PIC/S and UNICEF on the other hand were renewed by written procedure in the course of the year. Both EDQM and UNICEF also actively co-operate with PIC/S Participating Authorities in the field of foreign inspections exchange information on planned GMP inspections.

130. A new Co-operation Agreement was signed with the World Health Organization (WHO) and entered into force on 29 February 2016. The new agreement allows for the exchange of confidential information between the two Organisations. A side-meeting between a WHO Delegation and the PIC/S Executive Bureau took place in the margins of the Committee meeting in Manchester in order to discuss in which areas co-operation and synergies could be explored in the future such as on publishing joint guidance documents.

131. The former PIC/S Chairperson, Dr Joey Gouws (South Africa / MCC), participated in the 51st WHO Expert Committee on Specifications for Pharmaceutical Preparations, which was held in Geneva (Switzerland) on 17-21 October 2016. She also represented PIC/S at the occasion of the 17th International Conference of Drug Regulatory Authorities (ICDRA), which took place in Cape Town (South Africa) from 28 November to 2 December 2016.

Other organisations

ASEAN

132. Following its accession to PIC/S, Thailand / Thai FDA succeeded to Indonesia / NADFC as PIC/S – ASEAN Liaison Authority and provided an update on activities in ASEAN, which are of interest to PIC/S. This was notably the case of the discussions on the request by Philippines / PFDA to be listed under the ASEAN Sectoral Mutual Recognition Arrangement (MRA) on Good Manufacturing Practice (GMP). This issue was discussed at the 5th meeting of the Joint Sectoral Committee (JSC) on GMP Inspection of Manufacturers of Medicinal Products (JSC GMP MRA) and the 23rd meeting of the Pharmaceutical Product Working Group (PPWG) of ASEAN Member States, which were held in Siem Reap (Cambodia) on 16-17 May and 19-20 May 2016, respectively.

133. Thailand / Thai FDA also reported on the special PPWG-HOD meeting held on 18-19 August 2016 in Singapore, which discussed – amongst other matters – the expansion of the MRA on GMP Inspection for medicinal products, both geographically

(Vietnam expressed an interest) and in terms of scope (possible inclusion of APIs and biological products).

134. Following the third PIC/S – ASEAN Forum, held in Nusa Dua (Indonesia) on 8 October 2015, discussions between PIC/S and ASEAN continued by written procedure on ways to institutionalise co-operation. PIC/S made a proposal for the signing of a Memorandum of Understanding while ASEAN suggested establishing Terms of Reference (ToR) for a joint ASEAN PPWG-PIC/S Consultative Meeting.

Heads of EEA Medicines' Agencies

135. A letter of agreement was signed between PIC/S and EU/EEA Heads of Medicines Agencies (HMA) and entered into force on 15 August 2016. The letter has been published on the PIC/S and HMA websites. Under this agreement, PIC/S and HMA agree 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 Participating Authorities, which ensures that both new and current PIC/S Participating Authorities 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. Furthermore, PIC/S and HMA agree to exchange auditing schedules 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

136. The Committee agreed that PIC/S should apply to become an Observer to the International Conference on Harmonisation (ICH) following the recent ICH reform. The official application was submitted on 22 December 2016.

137. The Committee was also updated on work currently carried out by ICH, in particular on Q12 and Q3D;

ICMRA

138. PIC/S continued to co-operate with the International Coalition of Medicines Regulatory Authorities (ICMRA). For more details, see paragraphs 118-119.

ISPE

139. PIC/S was invited to the ISPE Singapore Affiliate's Annual Conference on 24-27 August 2016, where it was represented by the PIC/S Deputy Chairman, Boon Meow Hoe (Singapore / HSA). The SCH Chair, Paul Gustafson (Canada / RORB), represented PIC/S at the ISPE 2016 Annual Meeting in Atlanta (USA) on 18-21 September 2016.

OECD

140. The Organisation for Economic Co-operation and Development (OECD) launched its report on International Regulatory Co-operation, which also covers PIC/S, at the occasion of an OECD meeting in Paris (France) on 2 November 2016. The SC COM Chairman, Mr Mark Birse (UK / MHRA), represented PIC/S at this occasion.

PDA

141. The PIC/S Chairman was invited to attend two conferences by PDA:
- The 1st Europe Annual Meeting of PDA held on 28-29 June 2016 in Berlin (Germany);
 - The PDA-FDA Joint Regulatory Conference held on 12-14 September 2016 in Washington DC (USA).

BUDGET, RISK & AUDIT

142. 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

143. The Sub-Committee on Budget, Risk and Audit (SCB) is chaired by Ger Jan van Ringen (Netherlands / IGZ). It held two teleconferences on 21 March and 5 October 2016, during which it reviewed the accounts, prepared the budget and made a proposal for a revision of the PIC/S Financial Rules, which was adopted by the PIC/S Committee in Manchester. The revision introduces a number of changes, including the possibility for Participating Authorities to make use of the PIC/S Reserve Fund in order to organise the annual PIC/S training seminar.

2015 Accounts

144. As recommended by the SCB, the Committee approved the Statement of Accounts for the Financial Year 2015 and agreed to transfer the 2015 balance to the PIC/S Reserve Fund. It reviewed the financial audit of the 2015 accounts by the external auditor, Moores Refidar S.A., and discharged the Secretary of his responsibility for the financial year 2015 in line with PIC/S' Financial Rules.

145. The Committee also noted the separate audit report on income and expenses under the PIC/S International Training Programme on APIs (Q7), which was subject to an EC grant. The audit report has been prepared by the external auditor, Moore Stephens, and reviewed by the SCB.

146. The financial part of the report of the 2015 Seminar has also been reviewed by the SCB.

2016 Accounts

147. The Committee appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2016 accounts. It agreed that in addition to the regular annual audit of the 2016 accounts, a special audit on accounting processes and the internal control system should be carried out by the External Auditor.

2017 Budget

148. The Committee approved the 2017 Budget for an amount of CHF 650,750.

COMMUNICATION

149. PIC/S regularly communicates on its activities through press releases, annual reports and its web site. Good communication between Participating Authorities 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.

150. 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 below.

The mandate of the SC COM is to:

1. Monitor PIC/S' public relations and the exchange of information
2. Define a communication strategy to better promote PIC/S
3. 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

151. The Sub-Committee on Communication (SC COM) held two teleconferences on 14 March and 20 December 2016 under the chairmanship of Mark Birse (MHRA / UK). During these two teleconferences, the SC COM identified the following priorities:

- To increase the visibility of PIC/S;
- To draft a stakeholders' map;
- To improve the standard presentation on PIC/S; and
- To contribute to the new PIC/S website.

Single Points of Contact

152. The Committee endorsed a proposal by the SC COM to introduce a Single Contact Point with a generic e-mail address for each PIC/S Participating Authority. The Single Contact Point will ensure that a reply is given to all queries.

Rapid Alert

153. The SC COM submitted a proposal for a revision of the PIC/S SOP on Rapid Alert to PIC/S Members with the purpose to align it with the recently revised EU RA. The deadline for comments was 16 December 2015.

PIC/S Web Site

154. The new PIC/S website (www.picscheme.org) and the sub-site on the Academy (PIA) were successfully launched on 18 July (see paragraph 100). The new web site includes new tools such as a Content Management System, a Data Management System as well as several modules (e.g. for directories, newsletters, etc.).

Foreign Inspections

155. The list of foreign inspections planned in 2016 was updated twice in the course of the year. The list includes around 1,500 planned foreign inspections by 38 Inspectorates (including EDQM, UNICEF and WHO).

List of GM(D)P Inspectors

156. 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

157. A number of PA took advantage of PIC/S Committee meeting in Manchester to inform the Committee on important changes or projects concerning their Agencies / Inspectorates.

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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.

LIST OF PIC/S PARTICIPATING AUTHORITIES
(as of 31 December 2016)

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

	PARTICIPATING AUTHORITY	ACRONYM
Argentina	Instituto Nacional de Medicamentos (<i>National Institute of Drugs</i>)	INAME
Australia	Therapeutic Goods Administration	TGA
Austria	Austrian Agency for Health and Food Safety	AGES
Belgium	Agence Fédérale des Médicaments et des Produits de Santé (<i>Federal Agency for Medicines and Health Products</i>)	AFMPS
Canada	Health Canada - Regulatory Operations and Regions Branch (<i>Santé Canada - Direction générale des opérations réglementaires et des régions</i>)	RORB
Chinese Taipei	Taiwan Food and Drug Administration	TFDA
Croatia	Agency for Medicinal Products and Medical Devices of Croatia (<i>Agencija za lijekove i medicinske proizvode</i>)	HALMED
Cyprus	Pharmaceutical Services	CyPHS
Czech Republic ⁵	Státní Ústav pro Kontrolu Léčiv (<i>State Institute for Drug Control</i>)	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv (<i>Czech Institute for State Control of Veterinary Biologicals and Medicines</i>)	ISCVBM
Denmark	Danish Medicines Agency	DKMA
Estonia	State Agency of Medicines	SAM
Finland	Finnish Medicines Agency	FIMEA
France ⁶	Agence nationale de sécurité du médicament et des produits de santé (<i>French National Agency for Medicines and Health Products Safety</i>)	ANSM
	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (<i>French Agency for Food, Environmental & Occupational Health Safety</i>)	ANSES

⁵ SÚKL and ÚSKVBL count as two distinct Participating Authorities.

⁶ ANSM and ANSES count as two distinct Participating Authorities.

Germany ⁷	Bundesministerium für Gesundheit (<i>Federal Ministry of Health</i>)	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten (<i>Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices</i>)	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων (<i>National Organization for Medicines</i>)	EOF
Hong Kong SAR	Pharmacy and Poisons Board of Hong Kong	PPBHK
Hungary	National Institute of Pharmacy and Nutrition (NIPN)	NIPN
Iceland	The Icelandic Medicines Agency	IMA
Indonesia	National Agency for Drug and Food Control	NADFC
Ireland	Health Products Regulatory Authority	HPRA
Israel	Institute for the Standardization and Control of Pharmaceuticals	ISCP
Italy	Agenzia Italiana del Farmaco	AIFA
Japan ⁸	Ministry of Health, Labour and Welfare	MHLW
	Pharmaceuticals and Medical Devices Agency	PMDA
	Japanese Prefectures	-
Korea (Republic of)	Ministry of Food and Drug Safety	MFDS
Latvia	Zāļu Valsts Aģentūra (<i>State Agency of Medicines</i>)	ZVA
Liechtenstein	Amt für Gesundheit (<i>Office of Healthcare</i>)	AG
Lithuania	State Medicines Control Agency	SMCA
Malaysia	National Pharmaceutical Regulatory Agency	NPRA
Malta	Medicines Authority Malta	MAM
Netherlands	Inspectie voor de Gezondheidszorg (<i>Dutch Health Care Inspectorate</i>) ⁹	IGZ
New Zealand	Medicines and Medical Devices Safety Authority	Medsafe
Norway	Norwegian Medicines Agency	NOMA
Poland	Main Pharmaceutical Inspectorate	MPI

⁷ 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.

⁸ MHLW, PMDA and the Japanese Prefectures count as one Participating Authority. The Japanese Prefectures are represented by MHLW.

⁹ The competence for GMP/GDP inspections in the Netherlands is allocated to the central authority, Dutch Healthcare Inspectorate (IGZ). IGZ is the PIC/S Participating Authority representing GMP/GDP for human as well as veterinary medicinal products. IGZ performs national and international GMP/GDP inspections representing the Health Care Inspectorate - Pharmaceutical Affairs and Medical Technology 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.

Portugal	Autoridade Nacional do Medicamento e Produtos de Saúde IP (<i>National Authority of Medicines and Health Products IP</i>)	INFARMED IP
Romania	National Agency for Medicines and Medical Devices	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	Medicines Control Council	MCC
Spain	Agencia Española de Medicamentos y Productos Sanitarios (<i>Spanish Agency for Medicines and Medical Devices</i>) ¹⁰	AEMPS
Sweden	Medical Products Agency	MPA
Switzerland	Swiss Agency for Therapeutic Products	Swissmedic
Thailand	Food and Drug Administration	Thai FDA
Ukraine	State Service of Ukraine on Medicines and Drugs Control	SMDC
United Kingdom ¹¹	Medicines and Healthcare Products Regulatory Agency	MHRA
	Veterinary Medicines Directorate	VMD
United States of America	United States Food and Drug Administration	US FDA

¹⁰ 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.

¹¹ MHRA and VMD count as two distinct Participating Authorities.