



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

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**ANNUAL REPORT 2015**

*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 2015, PIC/S comprised 46 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 2015.

# ANNUAL REPORT 2015

## THE YEAR IN A NUTSHELL

### Successful chairmanship for South Africa

1. 2015 was the second year of the chairmanship of Dr Joey Gouws (South Africa / Medicines Control Council), the first PIC/S Chairperson from the African continent. This coincided with Dr Gouws becoming the Registrar at the South African Medicines Control Council. It was thus a very busy year for the PIC/S Chairperson and for PIC/S!



**Dr Joey Gouws**  
PIC/S Chairperson

The PIC/S Chairperson is assisted in her task by:

- A Deputy Chairman in the person of Mr Paul Hargreaves (United Kingdom / MHRA);
- The immediate former Chairperson, Ms Helena Paula Baião (Portugal / INFARMED IP);
- Members of the Executive Bureau; and
- The Secretariat.

2. In 2015 the PIC/S Committee met twice: first in Geneva (Switzerland) on 11-12 May 2015, and then in Nusa Dua (Indonesia), on 5-6 October 2015.

3. The activities of the PIC/S Committee and the outcome of the two above mentioned meetings are summarised in this Annual Report.

### PIC/S' expansion continues

4. The continuous expansion of PIC/S shows that the organisation is dynamic and attractive. In 2015, PIC/S accepted the membership application of two new Competent Authorities (as from 1<sup>st</sup> January 2016):

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

5. One new application for PIC/S membership was received during the year: the Thai Food and Drug Administration, Ministry of Public Health (Thailand / Thai FDA), applied on 20 March 2015.

6. Side-meetings also took place with China / CFDA and Indian Authorities, which both expressed an interest to join PIC/S in the future:

- A Delegation from the China Food and Drug Administration met with the PIC/S EB in Geneva (Switzerland) on 13 May 2015 and in Nusa Dua (Indonesia) on 8 October 2015.
- The Heads of the Drug Control Authorities of the States of Gujarat and Telangana met with a PIC/S Delegation on 15 and 17 September 2015.

### **International Training Programme on APIs (Q7) unfolds**

7. The API International Training Programme (API ITP) is an initiative by PIC/S run by its Expert Circle on API with the support of the PIC/S Secretariat. It consists of three segments, of which the most important is the Q7 Training Course, open to regulators and industry, which focuses on familiarisation with ICH Q7 and which is organised jointly by PIC/S and the Parenteral Drug Association (PDA).

8. In 2015, four Q7 Training courses were successfully organised with the financial support of the European Commission. The courses took place in:

- Korea (Republic of) on 22-23 January 2015;
- Brazil on 10-12 February 2015;
- India on 14-18 September 2015;
- China on 23-24 November 2015.

9. The success and impact of the trainings largely exceeded expectations, particularly in terms of participants: 642 participants in total against a maximum of 400 expected (+60%).

10. The training courses in India and China, two key regions for API manufacturing, provided a unique opportunity to establish better contacts and for PIC/S to engage with these authorities. The training course in Brazil, a PIC/S Applicant, provided the occasion to further engage with inspectors from other non-PIC/S Member Latin American authorities including Colombia, Costa Rica, Cuba, Ecuador, Panama, Paraguay, Uruguay and Venezuela. The training course in Korea (Republic of), a PIC/S Participating Authority, allowed inspectors and industry from this region of Asia to improve knowledge and compliance of regulators and industry with ICH Q7.

### **Web Site of PIC/S Inspectorates' Academy (PIA) under construction**

11. The PIC/S Inspectorates' Academy (PIA) was officially established at the PIC/S Committee meeting in Paris (France) on 20-21 October 2014. PIA is a PIC/S initiative to set up a web-based educational centre. The idea of the PIA was announced during the PIC/S 40<sup>th</sup> 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.

12. PIA will be implemented in various stages. It attracts a lot of interest from Non-Members, Partner Organisations, Industry and Professional Organisations. It will become operational in 2016.

13. In 2015, the PIC/S Secretariat worked on a complete overhaul of the PIC/S web site, which will include a sub-site dedicated to PIA.

### **Strategy Meeting of the EB**

14. In 2015 the PIC/S Executive Bureau (EB) met twice: first in Geneva (Switzerland) on 11 May 2015, and then in Nusa Dua (Indonesia), on 5 October 2015. The EB always meets in the morning before the Committee's meeting. These meetings are usually dedicated (i) to discussing financial, administrative and staff related issues; (ii) to assisting the Chairperson in the execution of his/her mandate; and (iii) to preparing the meetings of the Committee.

15. In Nusa Dua, the EB also met for an extraordinary "Strategy Meeting". Strategy meetings are organised every 10-15 years in order to discuss the future of PIC/S and develop a strategy on how to achieve future goals. The "Strategy Meeting" in Nusa Dua was mainly devoted to the financing and staffing of the PIC/S Secretariat. A follow-up meeting is scheduled to take place in 2016 in Manchester in order to finalise the strategic orientation of PIC/S.

### **New EB for 2016-2017**

16. At its meeting in Nusa Dua in October 2015, the PIC/S Committee elected Mr Paul Hargreaves (United Kingdom / MHRA) as Chairman for the period 2016-2017. Mr Hargreaves is a long standing Member of the Committee with extensive experience (12 years with industry and 28 years as an inspector). He will be the 4<sup>th</sup> PIC/S Chairman from the United Kingdom.

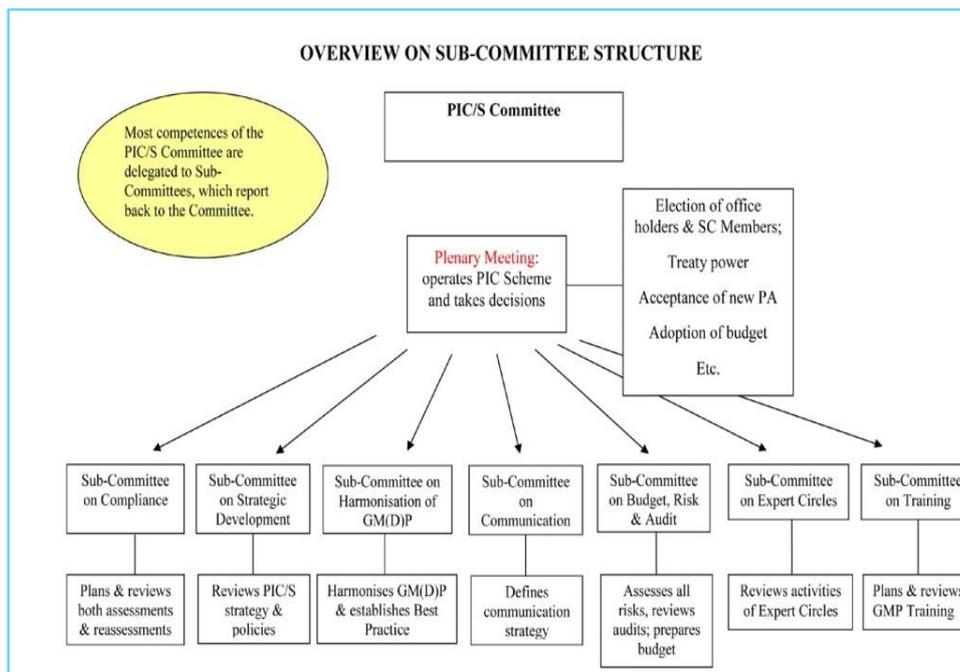
17. In addition, the PIC/S Committee renewed the composition of the PIC/S Executive Bureau, which will assist the Chairman in his task as from 1 January 2016. The Executive Bureau Members for the period 2016- 2017 will be:

- 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/HPFBI), 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);
- Mr Mark Birse (United Kingdom/MHRA), Chair of the Sub-Committee on Communication (SC COM)

### PIC/S Sub-Committee Structure

18. 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

19. 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.

20. 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 at next page.

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

21. The SCC held five teleconferences on 3 February, 9 April, 5 June, 24 September and 18 December 2015, 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**

22. A Note on the main principles for travelling related to on-site assessment visits (PIC/S Travel Guidance) was approved by the Committee and entered into force on 1 November 2015.

23. The SCC further discussed the drafting of a guideline for interpreting the Audit Checklist in co-operation with the EMA Compliance Group on the Joint Audit Programme (JAP). On the basis of a paper prepared by Canada / HPFBI, both the SCC and the EU JAP Compliance Group have agreed to develop guidance for indicators in several phases based on risk-level with 47 critical indicators to be dealt with in the 1<sup>st</sup> phase.

24. The SCC also discussed the revision of the PIC/S Joint Re-assessment Programme (JRP), including a desktop review along the lines of the desktop review in the EU JAP audit procedure. The desktop review will allow to assess whether an on-site audit is necessary or not; if yes, whether it should be a full on-site audit or a less detailed audit. The SCC has agreed on the essential criteria which must be fulfilled in order for a desk top re-assessment to be undertaken. The PIC/S Committee has also agreed in principle to the re-assessment interval.

25. Following the joint EMA and PIC/S training of auditors in London (UK) on 27-28 October 2014, the video-taped training was put on-line on the PIC/S' and EMA's password-protected web site for JRP and JAP auditors. Regarding the latter, the SCC has proposed to the PIC/S Committee to maintain a registry of trained auditors, which will contribute to the consistency of JRP assessments.

26. The SCC also proposed to revise the PIC/S Accession & Pre-Accession Guidelines. The aim is to have separate guidelines on pre-Accession.

### **Membership Applications**

27. In the course of 2015, 8 membership applications were in the process of being assessed.

28. The Applicants are the following: (*in alphabetical order*)

#### **Brazil / ANVISA**

29. The membership application of Brazil's Agência Nacional de Vigilância Sanitária (ANVISA), which was initially lodged in 2010, was completed by the end of 2014. In 2015, Brazil / ANVISA underwent an assessment process by the European Commission in order to be added to the EU White List of third countries with a regulatory framework for API equivalent to that of the EU.

30. The Rapporteur for the assessment of ANVSA's membership application to PIC/S, Mark Birse (UK / MHRA), informed the Committee that an on-site assessment visit would hopefully take place in the course of 2016. In this perspective the Committee nominated Ana-Rita Martins (Portugal / INFARMED I.P.) as Co-Rapporteur and Audit Team members from Argentina / INAME, Italy / AIFA and South Africa / MCC.

#### Croatia / HALMED

31. The Croatian Agency for Medicinal Products and Medical Devices (HALMED) applied for PIC/S membership on 5 September 2014. Following a paper assessment, an on-site assessment visit was carried out in Croatia from 29 June to 3 July 2015. The PIC/S assessment of HALMED was part of a tripartite assessment carried out jointly with the EU under the Joint Audits Programme (JAP) as well as jointly by Health Canada under the EU Canada Mutual Recognition Agreement (MRA). The Audit team recommended to the Committee to accept the PIC/S membership application of Croatia / HALMED.

32. At its meeting in Nusa Dua (Indonesia), the Committee endorsed the Team's recommendation and invited Croatia / HALMED to join PIC/S as of 1<sup>st</sup> January 2016. HALMED will become PIC/S' 48<sup>th</sup> Participating Authority.



Ms Ana Boban (Croatia/HALMED) and Ms Anne Hayes, Chair of the PIC/S Sub-Committee on Compliance (Ireland/HPRA),

The representatives of Hong Kong SAR / PPBHK, Mr Lot Chan and Ms Linda Woo, with the Rapporteur, Mr Tor Gråberg (Sweden / MPA) and the PIC/S Chairperson, Dr Joey Gouws (South Africa / MCC)

#### Hong Kong SAR / Pharmacy and Poisons Board of Hong Kong

33. At its meeting in Geneva in May 2015, the PIC/S Committee invited the Pharmacy and Poisons Board of Hong Kong (PPBHK), Hong Kong SAR, to join the Scheme as from 1 January 2016. PPBHK will become PIC/S' 47<sup>th</sup> Participating Authority.

34. PPBHK applied for membership on 30 August 2013. A paper assessment was conducted in view of its accession to PIC/S, followed by an on-site visit on 19-23 January 2015. The Audit team, led by Tor Gråberg (Sweden / MPA), recommended to the Committee to accept the PIC/S membership application of PPBHK.

## 香港藥劑業及毒藥管理局

Pharmacy and Poisons Board of Hong Kong

### **Hong Kong joins PIC/S –Mr Lot Chan, (Hong Kong SAR / PPBHK) highlights benefits & impact of the accession to PIC/S**

Accession to PIC/S has raised the standard and widened the exposure of both the Pharmacy and Poisons Board of Hong Kong (PPBHK) and the manufacturing industry of Hong Kong SAR. Inspectors of the Hong Kong Department of Health, i.e. inspectors who conduct GMP inspections for PPBHK, have gained much experience and knowledge in the past years through the enhancement of our quality system, participation in PIC/S meetings and training, and exchanging ideas and experience with inspectors around the globe.

The manufacturing industry of Hong Kong also took this opportunity to upgrade the manufacturing standards and strengthen training. The biggest impact is that Hong Kong has now a more robust system to ensure the quality of drugs available in the market, which directly benefits the Hong Kong community.

Hong Kong SAR has a drug regulatory framework comparable to that in other PIC/S countries and the GMP Inspectorate has established a quality system since 2009. The manufacturing industry of Hong Kong has also been very supportive to the accession of PPBHK to PIC/S. Probably the biggest challenge is capacity building, in both the GMP Inspectorate and the manufacturing industry.

### Iran / MoH

35. The Iranian Ministry of Health (MoH) applied for PIC/S membership in 2009. Due to two subsequent changes of the PIC/S Rapporteur, the Committee granted Iran / MoH 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. The report will be tabled to the PIC/S Committee in 2016.

### Mexico / COFEPRIS

36. 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 will take place in the first quarter of 2016.

### Philippines / PFDA

37. A clock stop was granted to the Philippines' Food and Drug Administration (PFDA) for the period 1 January 2015 – 31 December 2015, subject to the provision of a progress report for Q3 2015 on the implementation status of the corrective and preventive action plan (CAPA). The report was, however, received with some delay. As a result, the Committee was unable to take a decision on a follow-up on-site visit, which was agreed in principle following the initial on-site assessment visit in 2012.

### Thailand / Thai FDA

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

Morénas (France / ANSM) and Boon Meow Hoe (Singapore / HSA) were nominated as Rapporteur and Co-Rapporteur, respectively. Australia / TGA and Indonesia / NADFC agreed to provide each one Team Member for the on-site assessment visit. Following the successful completion of the paper assessment, which covered both traditional and modern medicines, the Committee agreed to proceed with the on-site assessment visit in the first half of 2016.

#### Turkey / TMMDA

38. The Committee endorsed the paper assessment of the membership application by the Turkey's Medicines and Medical Devices Agency (TMMDA), which was prepared by the Rapporteur, Anne Hayes (Ireland / HPRA), and Co-Rapporteur, Michel Keller (Switzerland / Swissmedic). It also endorsed the Rapporteur's recommendation to carry out an on-site assessment visit in 2016.

#### **Pre-Applications**

39. 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.

40. In the course of 2015, 3 pre-applications were under review.

41. The Pre-Applicants are: (*in alphabetical order*)

#### Belarus / MoH

42. The Rapporteur, Iveta Vilcane (Latvia / ZVA), presented her gap analysis report on Belarus' Ministry of Health (MoH), which highlighted a number of organisational issues and potential conflict of interests in the Belarus' GMP inspection system. The required organisational changes at the Ministry will not be possible without the necessary political will. The Committee prolonged the pre-assessment period until the end of 2015. Belarus / MoH reported that on 21 May 2015, a new law came into force, which made GMP inspections compulsory for all products (including export-only). The Ministry was also working on updating the GMP Guide and approving all SOPs. Belarus MoH provided an official reply to the gap analysis report on 27 August 2015.

#### Chile / ISP

43. The Committee endorsed the gap analysis report on Chile's "Instituto de Salud Pública" (Public Health Institute), which was 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).

## Kazakhstan / CCMPA

44. The Committee agreed to prolong the pre-assessment period of Kazakhstan's Committee for the Control of Medical and Pharmaceutical Activities (CCMPA) until September 2016 due to the change in Rapporteur. The new Rapporteur, Rosmarie Neeser Zaugg (Switzerland / Swissmedic), continued to request and assess additional information by CCMPA. Her gap analysis report will be tabled to the PIC/S Committee in 2016.

## **Reassessment of Participating Authorities**

45. In order to ensure that both new applicants and older 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.

46. Malaysia / NPCB was re-assessed in 2015 and the on-site re-assessment visit took place on 12-13 & 15-16 October 2015.

47. 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. The Committee agreed in principle that the assessment of US FDA be recognised as a PIC/S re-assessment.

## **Non-Members**

48. Close contacts were kept with a number of non-Members of which China's Food and Drug Administration (CFDA) and India (the Central Drugs Standard Control Organization and some State Drug Control Authorities).

49. A meeting between the PIC/S Executive Bureau and a Delegation from the China Food and Drug Administration (CFDA) took place on 13 May 2015 in Geneva (Switzerland). Discussions focused on the planning of a roadmap for a future accession of CFDA to PIC/S as well as opportunities for cooperation between CFDA and PIC/S prior to accession, in particular in the field of training and gap analysis. CFDA received funds from the Gates Foundation to carry out a feasibility study on acceding to PIC/S, which was completed in 2015. The outcome of the study was presented to PIC/S and Gates Foundation at a meeting in Beijing (China) on 20 November 2015. PIC/S was represented by Mr Boon Meow Hoe (Singapore / HSA).

50. For India, a PIC/S Delegation, which participated in the PIC/S-PDA API Q7 Training in India from 14-18 September 2015, met with the Heads of the Drug Control Authorities of the States of Gujarat and Telangana. The meetings were the first ever between PIC/S and Indian authorities, which expressed a keen interest in joining PIC/S in the future.

## **Corrective Action or updates by recently acceded PIC/S PA**

51. Following an update provided by Korea (Republic of) / MFDS on corrective actions following its recent assessment and accession to the Scheme, the Committee agreed that no further update is required from MFDS.

## **GMDP**

52. The harmonisation of Good Manufacturing Practice (GMP) and – more recently – of Good Distribution Practice (GDP) is at the very heart of PIC/S. As mentioned in the PIC/S Blueprint, 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.

53. 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.

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

55. The SCH held four teleconferences 17 March, 4 June, 17 September and 19 November 2015, 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.

### **Working Groups under SCH**

56. Four Working Groups are operating under the SCH.

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

57. The Working Group on Harmonisation of the Classification of Deficiencies, led by Jenny Hantzinikolas (TGA / Australia), has drafted a preliminary 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 noncompliance.

#### Working Group on Annex 1 / Sterile Manufacturing

58. The PIC/S Committee adopted a mandate for the Working Group on Annex 1 / Sterile Manufacturing at the Rome meeting and asked it to conduct preliminary discussions on whether Annex 1 should be completely rewritten or whether its Technical Interpretation should be updated. The WG came to the conclusion that Annex 1 should be completely revised. At the Paris PIC/S Committee meeting the WG was merged in order to establish a joint PIC/S-EMA Drafting Group in view revising Annex 1 jointly with the EMA. The Drafting Group is led by Andrew Hopkins (UK / MHRA) and includes representatives of the Competent Authorities of PIC/S and EEA.

### Working Group on Data Integrity

59. 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 initially aimed at developing an industry-facing guidance regarding data integrity so that industry can more quickly and effectively manage data integrity vulnerabilities and raise basic compliance in this area.

60. However, when discussing its Terms of Reference, the Working Group suggested changing the order of priority and developing first a PIC/S data integrity guidance document for inspectors to provide them with the basic skills for performing data integrity inspections. Another priority will be to develop advanced training to inspectors. The Terms of Reference will be discussed by the PIC/S Committee in 2016.

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

61. The goal of the Working Group on Controlling Cross-Contamination in Shared Facilities is to draft an Aide Memoire which will focus on harmonising /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.

62. The WG is chaired by Graeme McKilligan (UK / MHRA) and held two teleconferences in 2015. A face-to-face meeting was expected to take place in January 2016 in London (UK) in order for the WG to draft an Aide-Memoire. The purpose of this guidance document would be to assist GMP inspectors in the assessment of the risks of cross contamination in shared facilities.

### Working Group on Advance Therapy Medicinal Products (ATMPs)

63. 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 recent developments in the EU (see below), it was put on hold.

64. The PIC/S Committee discussed a PIC/S position with regards to the EU Consultation Document on GMP for ATMPs developed by the EMA Committee for Advanced Therapies (CAT). There are two main concerns, which are also shared by the IWG on GMPD: the guidance is in a separate guide and the proposed GMP requirements are lower than those contained in the PIC/S GMP Guide, in particular Annex 2. No PIC/S or EU Competent Authority is supporting the European Commission's proposal. Consequently, an official letter was sent by the SCH Chairman to the European Commission on 12 November 2015.

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

65. The SCH actively continued to harmonise GM(D)P guidance documents with the EU, in particular the PIC/S and EU GMP Guides and Annexes, and to submit revisions for adoption to the PIC/S Committee.

66. This was notably the case of the revised Annex 15 of the PIC/S GMP Guide, which entered into force on 1 October 2015 simultaneously as the revised Annex 15 of the EU GMP Guide. For the revised PIC/S GMP Guide, see PE 009-12.

67. Comments received the consultation of non-EEA PA of PIC/S on to Chapters 1 (Pharmaceutical Quality Systems), 2 (Personnel), 6 (Quality Control), and 7 (Outsourced Activities), which ended on 30 September 2014, were reviewed by the SCH.

68. Revisions to Chapters 3 (Premise and Equipment), 5 (Production), & 8 (Complaints & Recalls) have been almost completed by the SCH and will be submitted for internal consultation to PIC/S PA in 2016 (stage 1 of the adoption process).

69. 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): PIC/S and EMA work jointly on the revision of Annex 1. The EMA-PIC/S Joint Drafting Group on Annex 1, chaired by Andrew Hopkins (UK / MHRA), is working on a draft which should be submitted to the PIC/S Committee in the 2<sup>nd</sup> quarter of 2016.
- Annex 13 (Investigational Medicinal Products (IMP)): The EC wishes to delete this Annex from EU EudraLex Volume 4 and replace it by new EU guidelines on GMP for IMP for human use and related inspection procedures.
- 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. The public consultation will close on 11 December 2015.
- Annex 21 (GMP Obligations for Importation to the EU): PIC/S follows the work on the drafting of this new EU Annex and may decide to develop in parallel a PIC/S-specific Annex.

## **Guidance Documents**

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

### Site Master File

71. Goh Choon Wee (Singapore / HSA) has been nominated as representative from a non-EEA PIC/S PA for the EMA Drafting Group to amend the Site Master File (SMF) in view of mitigating drug shortages. The SMF is originally a PIC/S guidance

document, which has been adopted by the EU and which is now included in Part III of EU GMP Guide.

#### Guidance on “foreign inspections”

72. The Committee adopted a new procedure for informing foreign regulatory authorities of inspections to be conducted in their jurisdiction (PI 039-1). The procedure, which was drafted by the SCH, entered into force on 1 November 2015. This procedure will help facilitate promotion of co-operation and effective exchange of information between PIC/S Participating Authorities and will increase possibilities of joint or observed inspections, in addition to the PIC/S list of planned foreign inspections.

#### EMA guidance documents

73. The SCH continued its work to review and adapt the following EMA documents:

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

#### **PIC/S Library**

74. 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).

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

75. The Committee was updated on the outcome of a PIC/S-internal survey, carried out by US FDA, on the identification of companies through a Unique Facility Identifiers (UFI) such as a Data Universal Number System (D-U-N-S).

#### **TRAINING**

76. 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 tools to inspectors active in other areas such as Good Distribution (GDP) and Good Clinical Practices (GCP).

77. 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 five times in 2015: on 11 February, 31 March, 12 May, 8 September and 9 October 2015. Its mandate has remained by and large the same over the past decades – see box below.

The mandate of the SCT is to:

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

78. The following PIC/S training activities were held in 2015 (in chronological order):

Date	Place	Activity	Organised by
22-23 January	Seoul (Korea, Republic of)	PIC/S - PDA ICH API (Q7) Training	PIC/S and PDA in co-operation with MFDS
10-12 February	Brasilia (Brazil)	PIC/S - PDA ICH API (Q7) Training	PIC/S and PDA in co-operation with ANVISA
23-26 March	Taipei (Chinese Taipei)	PIC/S Expert Circle on Good Distribution Practices (GDP)	TFDA (Chinese Taipei)
14-15 September	Hyderabad (India)	PIC/S - PDA ICH API (Q7) Training	PIC/S and PDA in co-operation with DIA

17-18 September	Ahmedabad (India)	PIC/S - PDA ICH API (Q7) Training	PIC/S and PDA in co-operation with DIA
7-9 October	Nusa Dua (Indonesia)	PIC/S Seminar on “Biopharmaceuticals (Biologicals and Biotech): How to inspect”	NADFC (Indonesia)
5-7 October	Los Angeles (USA)	PIC/S Advanced QRM Training Course	US FDA
20-22 October	Strasbourg (France)	PIC/S Expert Circle on APIs and Advanced Training on APIs	EDQM
26-30 October	Rome (Italy)	PIC/S Expert Circle on Blood, Tissue and Cells	AIFA (Italy)
23-24 November	Beijing (China)	PIC/S API (Q7) Training	PIC/S and CFDA (China)

### Annual Training Seminar

79. 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 organization and outcome of annual seminars in line with the PIC/S Aide Memoire on the Organisation of Seminars.

#### 2014 Seminar

80. The evaluation report on the 2014 Seminar, organized by the French National Agency for Medicines and Health Products Safety (Agence nationale de sécurité du médicament et des produits de santé – ANSM) in Paris, France, on 22-24 October 2014, was reviewed by the SCT and the PIC/S Committee. The seminar’s topic was the management of “dedicated facilities”. For more details, see the Annual Report for 2014.

#### 2015 Seminar



81. A PIC/S Seminar was organised by the Indonesian National Agency for Drug and Food Control / NADFC (Badan Pengawas Obat dan Makanan Republik Indonesia) in Nusa Dua, Indonesia, on 7-9 October 2015. The topic of the seminar was “Biopharmaceuticals (Biotechnology and Biologicals): How To Inspect”. The Seminar was opened by the Chairman of NADFC, Dr Roy A. Sparringa. The Seminar, which was the first organised in Indonesia since the accession of NADFC to PIC/S in 2012, was attended by more than 130 participants from 44 countries. All continents were represented.

Photo: Dr Joey Gouws, PIC/S Chairperson (South Africa/MCC) and Ms Togi Hutadjulu, Head of Inspectorate, (Indonesia/NADFC)

82. The objectives of the Seminar were to discuss and update inspectors on GMP principles and requirements specific to the field of biopharmaceuticals, in particular in order to ensure a better understanding of biotech manufacturing processes and relevant current regulatory requirements, including laboratory testing and risk-based inspections of biopharmaceuticals facilities.

PIC/S 2015 Seminar Logo



83. The Seminar also aimed at providing input for a revision of the current PIC/S Aide Memoire on Inspection of Biotechnology Manufacturer (PI 024-2), which entered into force on 1 January 2006.

84. The 2.5 day Seminar started with a series of lectures and presentations, including invited industry speakers, followed by four parallel workshops for inspectors on the 2nd day of the Seminar, on:

- Viral Reduction/Inactivation (Workshop leader: Switzerland/Swissmedic & Netherlands/IGZ)
- Inspecting Biopharmaceutical QC Laboratories (Workshop leader: Finland / FIMEA)
- Process Transfer from development to commercial production (Workshop leader: US FDA & Poland/MPI)
- Discussion on the revisions of the Aide Memoire on Inspection of Biotechnology Manufacturer (Workshop leader: Australia / TGA, Singapore / HSA & UK / MHRA).

85. During the last day of the Seminar, a summary of the outcome of the workshops was presented followed by a discussion on the follow-up to be given to the Seminar. A number of PIC/S Participating Authorities volunteered to contribute to the revision of the PIC/S Aide-Memoire, taking into account the valuable feedback resulting from the Seminar.

86. A presentation of industry perspectives on present and future challenges, followed by a presentation on the Single Use Technology Assessment Program (SUTAP) ended the Seminar.



Chairman of NADFC, Dr Roy A. Sparringa, opens 2015 Seminar in Nusa Dua (Indonesia)



2015 Seminar - Official photo with participants

## Future seminars

87. The SCT reviewed the preparations of the 2016 and 2017 seminars:
- UK / MHRA will host the 2016 Seminar on 6-8 July 2016 in Manchester (UK) on “Inspectorates of the Future”.
  - Chinese Taipei / TFDA will host the 2017 Seminar in Taipei in September 2017.

## **Joint Visits Programme / Coached Inspection Programme**

88. At the end of 2015, there were approximately 17 active Joint Visit Groups involving around 50 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 harmonization (see box below).

89. The SCT aimed to further improve participation in the JVP and CIP, notably by promoting the respective programmes in all Expert Circles.

### ***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.*

90. The participation in the JVP has been progressively extended from GMP inspectors to GDP, GCP and GVP<sup>1</sup> inspectors. At the end of 2015, there were 10 Joint Visits Groups for GCP/GVP co-ordinated by the PIC/S Working Group on GCP/GVP (see paragraph 116).

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<sup>1</sup> Good Vigilance Practice / Pharmacovigilance

## **PIC/S International Training Programme on API**

91. The API International Training Programme (API ITP) is run by the Expert Circle on API under the chairmanship of Carmelo Rosa (US FDA) with the active support of the PIC/S Secretariat. 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.

92. One of the priorities of the API Expert Circle is to have the Q7 training recorded in view of the development of e-learning modules, to be later integrated into the PIA project (see paragraph 99ff).

93. In 2015, four Q7 Training courses were successfully organised and co-financed by the European Commission. The courses took place in:

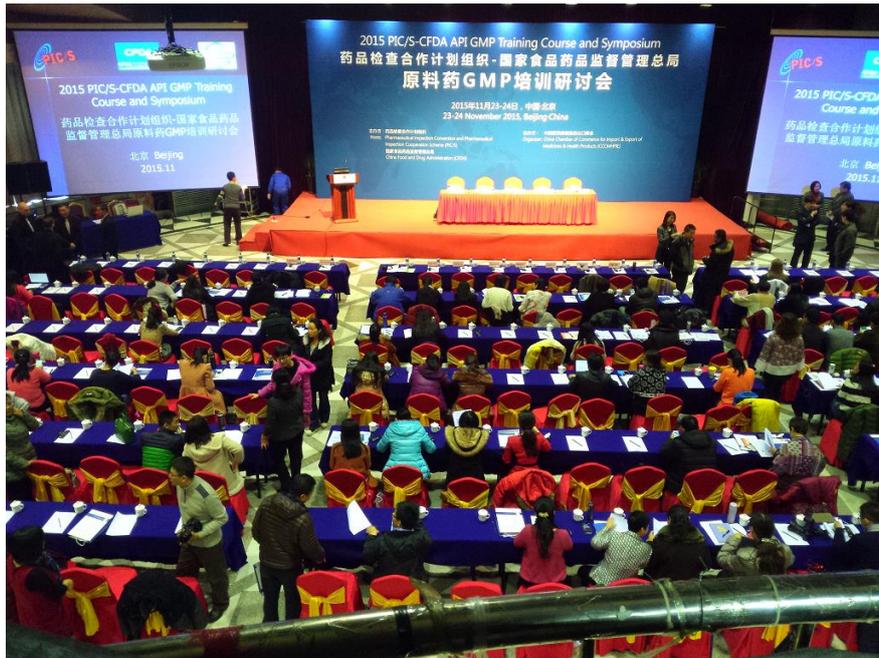
- Korea (Republic of);
- Brazil;
- India.
- China.

94. In Korea (Republic of), the Q7 training took place on 22-23 January 2015 with the support of Korea / MFDS. It attracted 127 participants. PIC/S speakers were provided by UK / MHRA and US FDA.

95. In Brazil, the Q7 event was held on 10-12 February 2015 with the support of Brazil / ANVISA. 123 participants took part in the training event. PIC/S speakers were provided by Spain / AEMPS and US FDA.

96. In India, the Q7 training course was held in Hyderabad and Ahmedabad (India) on 14-18 September 2015. 246 participants from industry and regulatory authorities took part in the events, including the Heads of the Indian Drug Regulatory Authorities of the States of Andhra Pradesh, Telangana and Gujarat. PIC/S speakers were provided by Australia / TGA, Portugal / INFARMED I.P. and US FDA.

97. In China, PIC/S successfully delivered a Q7 Training with the support of CFDA. The training was held in Beijing (China) on 23-24 November 2015. 146 participants took part in the event. PIC/S speakers were provided by US FDA and Portugal / INFARMED I.P.



Q7 Training in China

### **PIC/S New Inspector Training Course and Train the Trainer Course**

98. The SCT discussed the possibility of organising a PIC/S – HPRA (Ireland) New Inspector Training Course (“NITC”) in conjunction with the 2016 Seminar in Manchester. However, due to limited resources, the organisation of the course was postponed.

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

99. 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).

100. 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.

101. 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.



Inspection Excellence  
through Harmonised  
Training

102. Initially planned for Q3 2015, the launch of PIA was postponed to 2016. The completion of the web site and the review of the training material proved both to be very time-consuming. At its meeting in Nusa Dua (Indonesia), the PIC/S Committee adopted the official PIA logo and its motto, which is “Inspection Excellence through Harmonised Training”. As previously agreed, the PIA will first be developed within PIC/S before being opened up to external organisations.

### **Joint Training with Professional and Other Organisations**

103. The SCT and the PIC/S Committee continued to discuss proposals for joint training events with ISPE and PDA.

104. A conference on Quality & Regulations organised by PDA, in co-operation with PIC/S, took place in Brussels (Belgium) on 23-24 June 2015. Ireland / HPRA, South Africa / MCC and UK / MHRA provided speakers to this event.

### **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 2015, it held two teleconferences on 20 February and 7 May 2015.

### **Expert Circle on API**

108. The Expert Circle on Active Pharmaceutical Ingredients (API) is chaired by Carmelo Rosa (US FDA) and has been actively involved in the following activities:

- Planning and organisation of Q7 events (including identification of PIC/S speakers);
- Planning and organisation of the 7<sup>th</sup> Meeting of the Expert Circle Meeting (including Advanced Training) in Strasbourg (France), hosted by EDQM on 20-22 October 2015 (see box below), and the 8<sup>th</sup> Meeting of Expert Circle Meeting (including Advanced Training) in Australia, to be hosted by TGA in 2017;
- Contributing to the ICH Q7 Q&A which was published by ICH in June 2015.



Mr Carmelo Rosa (US FDA, CDER), Chairman of the PIC/S Expert Circle on APIs, and Dr Florence Benoit-Guyod (EDQM), host of the Strasbourg Expert Circle meeting

109. The 7<sup>th</sup> PIC/S Expert Circle Meeting on API took place in Strasbourg (France) on 20-22 October 2015. It was hosted by EDQM. As part of the PIC/S International API Training Programme, an advanced training for inspectors in APIs was delivered. The meeting was attended by more than 90 inspectors from regulatory agencies of 40 countries, including PIC/S Members and non-Members.

110. The overall objective of the meeting was to strengthen international co-operation and share experiences in the field of API inspections. A focus was made on current data integrity and falsification issues.

### **Expert Circle on GDP**

111. The Expert Circle on Good Distribution Practice (GDP) is one of the most recent Expert Circles and was established in 2013. It is chaired by Steve Todd (UK / MHRA). The 3<sup>rd</sup> meeting of the Expert Circle on GDP was hosted by Chinese Taipei / TFDA on 24-26 March 2015 in Taipei. It was attended by 47 delegates from 25 countries. The 4<sup>th</sup> meeting will be hosted by South Africa / MCC in 2016 in Pretoria.

### **Expert Circle on QRM**

112. The Expert Circle on Quality Risk Management (QRM) is chaired by Kevin O'Donnell (Ireland / HPRA) and 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. This training event attracted 67 inspectors. The third and last course will be held in Europe in 2016 and take place at the EMA in London.

### **Expert Circle on Human Blood, Tissues, Cells & ATMP**

113. The Expert Circle on Human Blood, Tissues and Cells is the oldest Expert Circle in PIC/S. The 21<sup>st</sup> meeting of this Expert Circle was hosted by Italy / AIFA in Rome (Italy), on 26-30 October 2015. This Meeting attracted more than 120 inspectors from 36 countries and allowed, among others, discussions on contemporary issues and mapping of competences of PIC/S Participating Authorities in the field of blood, blood components, plasma derivatives, cells and tissues with particular focus on Advanced Therapies Medicinal Products (ATMPs). Various workshops were organised related to blood inspections; inspections on tissue and cells for transplantation; gene therapy; and the PIC/S Aide-Memoire on ATMPs. During the meeting, Experts also agreed on their future mandate, which will be submitted to the SCEC and the Committee for adoption.

### **Working Group on Medicinal Products for Veterinary Use**

114. 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. In 2015, this Working Group continued its work, which it hopes to finalise in 2016.

### **Working Group on the revision of PI 011-3 (Computerised Systems)**

115. In 2015, the Expert Circle on Computerised Systems was deactivated in order to allow Experts on Computerised Systems to focus on the revision of the "PIC/S Guidance Document on Good Practices for Computerised Systems in regulated GxP environments" (PI 011-3). The Working Group is led by Karl-Heinz Menges (Germany / Regierungspräsidium Darmstadt) but due to its small size, it had not started with its work yet. The Committee agreed to make a call for additional volunteers.

### **WG on GCP / GVP**

116. With respect to the project of extending PIC/S' mandate from GMP to new fields such as Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP), the Working Group on GCP and GVP continued its discussion under the leadership of Mandeep Rai (UK / MHRA). This Working Group has been 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

117. 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.

118. 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
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

119. The SCSD is chaired by Jacques Moréas (France / ANSM). It held three teleconferences on 27 January, 28 April and 2 December 2015 and took 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 and to facilitate the mutual acceptance/ reliance of GMP information. Since its inception, PIC/S has offered a proactive frame for inspection sharing and has encouraged its Members to accept inspection findings on a voluntary basis, by relying on mutual trust and confidence building, based on the PIC/S accession process.

## **Voluntary Acceptance of Same Scope Inspection Results**

120. In the context of increased foreign inspections and multiple initiatives in the field of cooperation between drug regulatory authorities, the SCSD decided to carry out a survey with the aim of reducing the number of “same scope inspections”.

121. 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.

122. At its meeting of 11-12 May 2015, the Committee reviewed the preliminary outcome of a survey carried out among PIC/S Participating Authorities on the mutual acceptance / reliance of same scope inspection results for domestic as well as foreign inspections.

123. The survey must be seen in relation with already existing measures by PIC/S to reduce foreign inspections such as through the maintenance of a list of planned foreign inspections - which in 2015 included around 1,200 planned inspections globally – as well as the PIC/S procedure for team inspections (PI 031-1).

124. These measures already contribute in the avoidance of duplicate inspections as PIC/S Members are encouraged to either perform a joint inspection or rely on the inspection report from a PIC/S Participating Authority (or PIC/S Partner Organisation).

## **International Coalition of Medicines Regulatory Authorities (ICMRA)**

125. Back in 2014, the Committee agreed in principle to further strengthen its co-operation with other international initiatives such as the ICMRA (International Coalition of Medicines Regulatory Authorities). 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. By joining efforts, leveraging resources and sharing co-ordination around issues resulting from complex supply chains, international co-operation can be greatly strengthened in order to lead towards the global provision of safe and effective, quality medicines by rationalising inspections and allowing for more efficient deployment of global inspection resources, while avoiding duplication.

126. In 2015, the ICMRA Working Group dealing with equivalence focused its discussions on the sharing of data to foster mutual reliance; on how non-ICMRA members can fit within the ICMRA framework; and on how to reduce the number of inspections within the ICMRA framework. On its side, PIC/S discussed how to strengthen the visibility of PIC/S’ activities and ensure that that Heads of Agencies (HoA) are well aware of PIC/S activities.

## **Advantages and Privileges of PIC/S Membership**

127. The Committee discussed a paper by the SCSD on the advantages and privileges of Members and whether to extend them to Applicants and Partner Organisations. Members agreed in principle that participation in PIC/S Working

Groups was a Member-only privilege. However, Joint Working Groups with Partners can be established for the purpose of harmonisation. To harmonise the way that PIC/S in general and Working Groups in particular engage with Partner Organisations and Non-Members, the PIC/S Committee mandated the SCSD to draft Terms of Reference for Working Groups and to make a proposal on amending the PIC Scheme to allow Partner Organisations to apply as Members. There was a consensus that membership benefits needed to be more clearly defined with respect to training activities as well as to financial aspects.

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

### Associated Partners (EDQM, EMA, UNICEF and WHO)

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

129. Close co-operation was maintained with the European Medicines Agency (EMA), in particular in the field of harmonisation of GMP guides and guidance documents, as well as with the European Directorate for the Quality of Medicines & Healthcare (EDQM), which has been the first Associated Partner to ever organise a PIC/S Expert Circle meeting (see paragraph 109).

130. Both EDQM and UNICEF also actively co-operate with PIC/S Participating Authorities in the field of foreign inspections and exchange information on planned GMP inspections.

131. Co-operation was also intensified with the World Health Organization (WHO) in 2015. PIC/S' partnership agreement with WHO was successfully revised. One of the main amendments is the inclusion of a clause on confidentiality, which will allow for the exchange of confidential information between the two Organisations. The finalised agreement was endorsed by the PIC/S Committee and signed by the PIC/S Chairperson in December 2015. The agreement was then sent to WHO for signing.

132. The Committee also discussed a proposal by WHO aiming at sharing information and avoiding duplication in the field of strengthening regulatory systems. The Sub-Committee on Strategic Development (SCSD) and the Sub-Committee on Compliance (SCC) reviewed the proposal in 2015 and requested additional information from WHO.

133. Ms. Helena Baião (Portugal / INFARMED IP) in her capacity as EB Member attended the WHO consultation on “data management, bioequivalence, good manufacturing practices and medicines’ inspection”, which was held in Geneva (Switzerland) on 29 June – 1 July 2015.

### Other organisations

#### *ASEAN*

134. Indonesia / NADFC, acting as PIC/S – ASEAN Liaison Officer, provided regular updates on activities in ASEAN, which were of possible interest to PIC/S such as the work accomplished by the Task Force on ASEAN Regulatory Framework for Traditional Medicines and Health Supplements, the Pharmaceutical Product Working

Group (PPWG) of ASEAN Member States and the Joint Sectoral Committee (JSC) on GMP Inspection of Manufacturers of Medicinal Products (JSC GMP MRA).

135. Philippines / PFDA, which also applied for PIC/S membership, also applied to be listed under the ASEAN Sectoral Mutual Recognition Arrangement (MRA) on Good Manufacturing Practice (GMP).

136. A PIC/S - ASEAN Forum, the third of its kind, was organised in the framework of the 2015 Seminar in Nusa Dua (Indonesia) on 8 October 2015. A PIC/S delegation, led by the PIC/S Chairperson, met with a delegation from ASEAN (Association of Southeast Asian Nations), led by the Chair of the ASEAN Consultative Committee for Standards and Quality (ACCSQ) Pharmaceutical Product Working Group (PPWG), Dato' Eisah binti A. Rahman. The ASEAN Delegation comprised representatives of the ASEAN Secretariat as well as ASEAN Competent Authorities from Indonesia, Malaysia, Philippines, Singapore and Thailand.

137. The purpose of this meeting was to discuss how to institutionalise co-operation between PIC/S and ASEAN in order to reach a new level of co-operation, further to the two previous PIC/S – ASEAN Forums in Kuala Lumpur (2010) and Singapore (2007).

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

138. PIC/S continued to lobby, jointly with the EMA Compliance Group on the Joint Audit Programme (JAP), for the mutual recognition of audits between HMA (Joint Assessment Programme) and PIC/S (Assessment & Re-Assessment). At the end of the year, the matter was still with EEA Heads of Medicines' Agencies.

#### *ICH*

139. The Committee discussed whether PIC/S should adopt the ICH Q&A document on Q7, which is based on a PIC/S Q&A document on Q7 transferred to ICH in November 2013. It is agreed will make a cross-reference to the ICH Q7 Q&A but not adopt it as such. The Q&A not transferred to ICH will be developed as training material by the PIC/S API Expert Circle.

140. The Committee also discussed the impact of new ICH Guidance documents on the work of GMP inspectors. This is potentially the case of ICH Q12 (Lifecycle Management) and ICH Q3D (Elemental Impurities). The lack of consultation of GMP inspectorates in the drafting process is regretted.

#### *OECD*

141. The Organisation for Economic Co-operation and Development (OECD) invited PIC/S to participate in a survey on international regulatory co-operation, in which some PIC/S accomplishments, in particular in the field of training, were highlighted. The Chairman of the SCSD, Mr Jacques Morénas (France / ANSM), also took part in a OECD meeting on international regulatory co-operation, which was held in Paris (France) on 17 April 2015.

## **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.

143. The Sub-Committee on Budget, Risk and Audit (SCB) is chaired by Paul Hargreaves (UK / MHRA). It held two teleconferences on 29 April and 18 September 2015 during which it discussed mainly financial issues.

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

## **2014 Accounts**

144. As recommended by the SCB, the Committee approved the Statement of Accounts for the Financial Year 2014 and agreed to transfer the 2014 balance (CHF 10,956.31) to the PIC/S Reserve Fund. It reviewed the financial audit of the 2014 accounts by the external auditor, Moores Refidar S.A and discharged the Secretary of his responsibility for the financial year 2014 in line with PIC/S' Financial Rules.

145. The SCB reviewed the financial part of the report of the 2014 Seminar and found it to be very clear and detailed.

## **2015 Accounts**

146. The Committee appointed the external auditor, Moores Refidar S.A., for the financial audit of the 2015 accounts. It agreed that in addition to the regular annual audit of the 2015 accounts, a special audit on accounting processes and the internal control system should be carried out by the External Auditor

## **2016 Budget**

147. The Committee approved the 2016 Budget for an amount of CHF 619,600.

## **COMMUNICATION**

148. PIC/S regularly communicates on its activities through press releases, annual reports and – since the start of millennium – 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.

149. 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

150. The Sub-Committee on Communication (SC COM) held two teleconferences on 16 February and 16 April 2015 under the chairmanship of Tor Gråberg (Sweden / MPA), who resigned from his position in September 2015. The position was left vacant until the election, which took place at the PIC/S Committee in Nusa Dua. During the two teleconferences in the first half of 2015, the SC COM discussed the definition of a communication strategy for PIC/S, including the establishment of contact points for specific questions, and the outcome of a questionnaire on the PIC/S list of planned foreign inspections.

### **Foreign Inspections**

151. The list of foreign inspections planned in 2015 was updated twice in the course of the year. The list includes around 1,200 planned foreign inspections by 34 Inspectorates (including EDQM, UNICEF and WHO).

### **Rapid Alert**

152. The SC COM postponed the discussion on a proposal for a revision of the PIC/S SOP on Rapid Alert to align it with the recently revised EU RA.

### **Unique Facility Identifier (UFI) for Drug Establishments**

153. The US FDA updated the PIC/S Committee on the outcome of the questionnaire on UFI. 23 replies were received. Systems vary greatly between PA ranging from sophisticated (geocoding) to very simple (only addresses). Not all PA have a system to verify and validate the address of the manufacturer, thus increasing the risk of shadow factories. The matter will be further discussed at the next PIC/S Committee meeting.

### **PIC/S Web Site**

154. The Secretariat worked on the upgrade the PIC/S website ([www.picscheme.org](http://www.picscheme.org)) as well as on the sub-site on the Academy (PIA). The upgrade web site will include new tools such as a Content Management System, a Data Management System as well as several modules (e.g. for directories, newsletters, etc.).

### **Other issues**

#### List of GM(D)P Inspectors

155. The list of GM(D)P Inspectors, employed by PIC/S PA and Partner Organisations, was updated.

Communications from Participating Authorities

156. A number of PA took advantage of the two annual meetings to inform the Committee on important changes or projects concerning their Agencies / Inspectorates.

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Incoming PIC/S Chairperson (2016-2017)  
Mr Paul Hargreaves (UK / MHRA) with  
outgoing PIC/S Chairperson (2014-2015)  
Dr Joey Gouws (South Africa / MCC)

**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 2015)

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

	<b>PARTICIPATING AUTHORITY</b>	<b>ACRONYM</b>
Argentina	Instituto Nacional de Medicamentos <i>(National Institute of Drugs)</i>	INAME
Australia	Therapeutic Goods Administration	TGA
Austria	Austrian Agency for Health and Food Safety	AGES
Belgium	Agence Fédérale des Médicaments et des Produits de Santé <i>(Federal Agency for Medicines and Health Products)</i>	AFMPS
Canada	Health Products and Food Branch Inspectorate	HPFBI
Chinese Taipei	Taiwan Food and Drug Administration	TFDA
Cyprus	Pharmaceutical Services	CyPHS
Czech Republic <sup>2</sup>	Státní Ústav pro Kontrolu Léčiv <i>(State Institute for Drug Control)</i>	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv <i>(Czech Institute for State Control of Veterinary Biologicals and Medicines)</i>	ISCVBM
Denmark	Danish Medicines Agency	DKMA
Estonia	State Agency of Medicines	SAM
Finland	Finnish Medicines Agency	FIMEA
France <sup>3</sup>	Agence nationale de sécurité du médicament et des produits de santé <i>(French National Drug and Health Products Safety Agency)</i>	ANSM
	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail <i>(French Agency for Food, Environmental &amp; Occupational Health Safety)</i>	ANSES

<sup>2</sup> SÚKL and ÚSKVBL count as two distinct Participating Authorities.

<sup>3</sup> ANSM and ANSES count as two distinct Participating Authorities.

Germany <sup>4</sup>	Bundesministerium für Gesundheit ( <i>Federal Ministry of Health</i> )	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten ( <i>Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices</i> )	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων ( <i>National Organization for Medicines</i> )	EOF
Hungary	National Institute of Pharmacy and Nutrition	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 <sup>5</sup>	Ministry of Health, Labour and Welfare	MHLW
	Pharmaceuticals and Medical Devices Agency	PMDA
	Japanese Prefectures	-
Korea (Republic of)	Ministry of Food and Drug Safety	MFDS
Latvia	Zāļu Valsts Aģentūra ( <i>State Agency of Medicines</i> )	ZVA
Liechtenstein	Amt für Gesundheit ( <i>Office of Healthcare</i> )	AG
Lithuania	State Medicines Control Agency	SMCA
Malaysia	National Pharmaceutical Control Bureau	NPCB
Malta	Medicines Authority Malta	MAM
Netherlands	Inspectie voor de Gezondheidszorg ( <i>Inspectorate of Health Care</i> )	IGZ
New Zealand	Medicines and Medical Devices Safety Authority	Medsafe
Norway	Norwegian Medicines Agency	NOMA
Poland	Main Pharmaceutical Inspectorate	MPI

<sup>4</sup> BMG and ZLG count as one Participating Authority.

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

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	Medicines Control Council	MCC
Spain	Agencia Española del Medicamento y Productos Sanitarios <i>(Spanish Agency of Drugs and Health Products)</i>	AEMPS
Sweden	Medical Products Agency	MPA
Switzerland	Swiss Agency for Therapeutic Products	Swissmedic
Ukraine	State Administration of Ukraine on Medicinal Products	SAUMP
United Kingdom <sup>6</sup>	Medicines and Healthcare Products Regulatory Agency	MHRA
	Veterinary Medicines Directorate	VMD
United States of America	United States Food and Drug Administration	US FDA

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<sup>6</sup> MHRA and VMD count as two distinct Participating Authorities.