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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March 2017

# Press release: PIC/S Meetings in Geneva (Switzerland)

From 8 to 10 February 2017, the following meetings took place in Geneva (Switzerland): PIC/S Committee and PIC/S Executive Bureau.

## HEADLINES

- **NEW PIC/S STRATEGIC PLAN (ROAD MAP) FOR 2017-2019**
- **STRONG STANCE TAKEN BY PIC/S ON EUROPEAN COMMISSION'S PROPOSED STAND-ALONE ADVANCED THERAPY MEDICINAL PRODUCTS (ATMP) GMP GUIDELINES, WHICH WILL NOT ONLY LOWER GMP STANDARDS FOR ATMP AT THE RISK OF PATIENTS BUT LEAD TO INTERNATIONAL DIS-HARMONISATION**
- **NEW PIC/S APPLICATION LODGED IN AUGUST 2016 BY ITALY (VET) / DGSAF**
- **ARMENIA / SCDMTE AND SAUDI ARABIA / SFDA TO APPLY TO PIC/S**
- **LATEST PIC/S DEVELOPMENTS IN THE FIELD OF GM(D)P HARMONISATION, IN PARTICULAR DATA INTEGRITY, REVISION OF ANNEX 1, CONTROLLING CROSS-CONTAMINATION IN SHARED FACILITIES, CLASSIFICATION OF DEFICIENCIES, GDP, …**
- **NEW STAGE OF DEVELOPMENT PLANNED FOR PIC/S INSPECTORATES' ACADEMY: WEBINARS TO BE PRIORITISED**
- **NEW PIC/S WORKING GROUPS ESTABLISHED ON UNIQUE FACILITY IDENTIFIERS (UFI) AND ON MANAGING TRAVEL SAFETY OF INSPECTORS**

## PIC/S COMMITTEE MEETING

The PIC/S Committee met on 9-10 February 2017, under the chairmanship of Mr Paul Hargreaves (United Kingdom's Medicines and Healthcare products Regulatory Agency / MHRA). The meeting was attended by 37 out of 49 PIC/S Participating Authorities (PA) as well as by a number of Applicants, Pre-Applicants, Associated Partners and Guests.

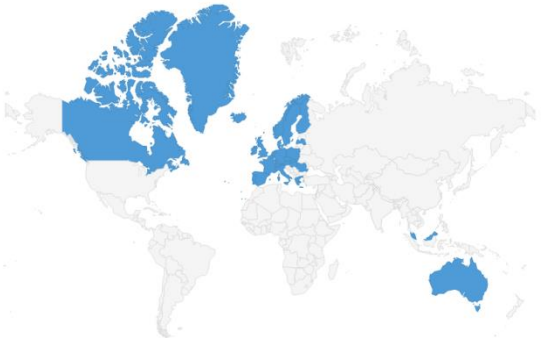
## PIC/S ROAD-MAP FOR 2017-2019

The PIC/S Committee reviewed a strategic plan (Road Map) for 2017-2019, based on discussions by the PIC/S Executive Bureau (EB) on PIC/S' future. The objectives are to:

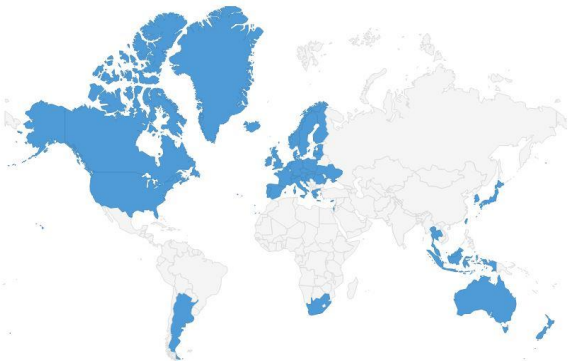
- enhance PIC/S' Sub-Committee (SC) structure and ensure the full implementation of the PIC/S Inspectorates' Academy (PIA) (www.picscheme.org/en/pia-home);
- identify PIC/S' next challenges and prepare to respond on how to address them;
- strengthen the PIC/S Secretariat by implementing an effective human resourcing strategy; and
- identify new income streams which will yield the required funding necessary to finance PIC/S' projects.

The Road Map includes an action plan for which priorities have been set to ensure its successful implementation, in particular with regard to additional financial resources with a view to further increase the output of PIC/S.

The goals of the previous Road Map (Blueprint) for the period 2006-2015 have been successfully implemented and even surpassed in some cases. PIC/S membership expansion was notably stronger than anticipated. In 2004, it was estimated that PIC/S membership by the end of 2015 would reach around 40 Participating Authorities ("PA") whereas PIC/S comprised 46 PA at the end of 2015 and 49 PA on 1st August 2016.



*PIC/S 29 Members in 2006*



*PIC/S 49 Members in 2016*

**Key priorities for 2017 - 2019 as outlined in the Road Map**

Training remains PIC/S' most important field of activity. The PIC/S Inspectorates' Academy (PIA) was successfully launched in July 2016 but a lot of work remains to be done. Resources should be increased and the related financing considered. Considerations will be given on the training of inspectors on the revised Annex 1 (sterile manufacturing) of the PIC/S GMP Guide, once completed. Instruments to measure the efficacy of PIC/S training events will be introduced.

In terms of Strategic Development and Communication, PIC/S will strive to better communicate with Heads of Agencies (HoA) in order to get increased support. An annual Work Plan may be developed to present PIC/S' future goals and achievements as well as to increase PIC/S' visibility. PIC/S will work toward improved co-operation with the International Coalition of Medicines Regulatory Authorities (ICMRA), which is a strategically important organisation. This co-operation will focus on the ICMRA GMP Project and on the Unique Facility Identifier (UFI) as well as the PIC/S survey on the acceptance of "same scope inspection results".

Continued compliance of Participating Authorities to PIC/S requirements is a prerequisite in order to maintain equivalent GMP systems. PIC/S will focus on the Joint Reassessment Programme (JRP) and implement desktop assessments, where appropriate. For this, PIC/S needs more trained Rapporteurs. The possibility of having dedicated resource pool of auditors to undertake new assessments will be considered. An annual reporting system on key indicators of PIC/S Participating Authorities will possibly be introduced.

The harmonisation of GM(D)P is an essential mission of PIC/S, which should consider whether to strengthen its position in areas such as Advanced Therapy Medicinal Products (ATMPs), Veterinary Medicinal Products (VMPs), Investigational Medicinal Products (IMPs) or emerging technologies. Instruments to measure the use/implementation of guidance documents will be introduced and the project on a PIC/S Library providing an index of GMP guidance resources from PIC/S Participating Authorities completed.

PIC/S has several, very active Expert Circles in fields such as Active Pharmaceutical Ingredients (APIs), Quality Risk Management (QRM), Good Distribution Practice (GDP) or Blood, Tissues, Cells & ATMPs. These Expert Circles operate under different

organisational rules than Sub-Committees and Working Groups. To be consistent, the rules should be aligned. The size of Co-ordinating Committees will be increased in order to facilitate the running of Expert Circle meetings. Scientific Committees in charge of reviewing the scientific programme of Expert Circle meetings will be activated.

In terms of financing, considerations will be given on possible ways to reduce staff costs and office-related costs. At the same time, the feasibility for third party funding and a fee increase will be investigated. To facilitate long-term planning, a multi-annual budget plan will be prepared.

## RISK OF GMP DIS-HARMONISATION IN THE FIELD OF ADVANCED THERAPY MEDICINAL PRODUCTS (ATMP)

The Committee expressed its unanimous concern at the **European Commission's proposed stand-alone Advanced Therapy Medicinal Products (ATMP) GMP Guidelines**, which will not only lower GMP standards for ATMP at the risk of patients but lead to an internationally non harmonised approach to the implementation of GMP for ATMP.

This initiative by the European Commission in the field of ATMP, which will lead to a revision of **EU GMP Guide Annex 2 (Biological Products)**, will also result in the PIC/S GMP Guide and the EU GMP Guide no longer being equivalent. Since 1989, both Guides have been developed in parallel and systematically kept aligned on the basis of a harmonised consultation procedure between PIC/S and the European Medicines Agency (EMA).

Since the launch of the EU stakeholder consultation back in 2015, PIC/S has repeatedly tried to engage with the European Commission to draw attention on the detrimental effects of this initiative, whether in terms of risks to public health or in terms of non harmonisation of international GMP requirements for ATMP.

Such efforts have so far proved fruitless. The Commission has ignored all requests for co-operation, including a proposal by PIC/S to form a joint working party with the EMA Inspectors Working Group in order to produce an internationally harmonised, fully integrated GMP Guidance for ATMP, which would serve to both fulfil the European Union's objectives and the PIC/S harmonisation needs. This would in turn benefit patient access to such innovative treatments.

This disappointing situation has led to a complete absence of co-operation in this field despite high-level exchanges voicing PIC/S' concerns, among which: loss of harmonisation, lack of integration with GMP Guidelines, risk of confusion and double-standards and most importantly an increased risk to patients.

It is also perceived that the lack of international harmonisation will potentially impact in the availability of ATMP across regions regulated by PIC/S Participating Authorities as well as cause regulatory burden for manufacturers which will have to comply with different codes, of which one will be of lower standards.

The PIC/S Committee reviewed various contingency options and agreed that PIC/S standards must be up-kept. As it has not been possible for PIC/S to be involved in the EU drafting process, the PIC/S Committee concluded that all PIC/S can do is draw the Commission's attention on its responsibilities. A new letter to this effect has been addressed to the Director General for Health and Food Security of the European Commission, published on the PIC/S website for reasons of transparency.

In order to ensure future GMP harmonisation in this field and guarantee the safety of patients, it is hoped that the Commission will reconsider its draft guidelines, prior to publishing them, and that the drafting process will be restarted in order to ensure a more inclusive and international approach, if not now, at least in the near future.

## ITALY (VET) / DGSAF APPLIES TO PIC/S

The **Directorate General for Animal Health and Veterinary Medicinal Products (DGSAF) - Ministry of Health of Italy** applied for PIC/S membership on 26 August 2016. The PIC/S assessment process for Italy (Vet) / DGSAF will be facilitated through the recognition of the EMA Joint Audit Programme (JAP) audit conducted in October 2015, in line with the Letter of agreement between PIC/S and EU/EEA Heads of Medicines Agencies (HMA).

## ARMENIA / SCDMTE & SAUDI ARABIA / SFDA TO APPLY TO PIC/S

The **Scientific Centre of Drug and Medical Technology Expertise (SCDMTE)** of Armenia officially announced to the Committee that it would presently be submitting a membership accession application to PIC/S, further to its pre-accession application completed in 2014.

The **Saudi Food and Drug Authority (SFDA)** was invited to attend the Committee meeting as guest and updated the Committee on its intent to lodge a PIC/S pre-accession or accession application in the near future.

## LATEST PIC/S DEVELOPMENTS IN GM(D)P HARMONISATION

Development and promotion of high and harmonised GM(D)P standards and guidance documents has been at the forefront of PIC/S activities since the very start. Under the impulse of the Sub-Committee on GM(D)P Harmonisation (SCH), led by Canada / RORB, a significant number of PIC/S initiatives in this field are currently under development.

The Committee noted that the revised GMP Guide (PE 009-13) entered into force on 1st January 2017. All non-EEA Participating Authorities of PIC/S (and Applicants) have been invited to transpose the **revised Chapters 1, 2, 6 & 7 of the PIC/S GMP Guide** into their own GMP Guides.

The revision of **Chapter 3, 5, and 8 of the PIC/S GMP Guide** are ongoing as well as the **transposition by PIC/S of the EMA Guidelines** on:

- the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use;
- the principles of good distribution practice for active substances of medicinal products for human use;
- setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities.

A PIC/S Working Group will be established for the revision of the **PIC/S Recommendations on Validation Master Plan; Installation and Operational Qualification; Non-Sterile Process Validation; and Cleaning Validation (PI 006-3)**.

Regarding the **draft revision of Annex 1** (sterile manufacturing) to the PIC/S and EU GMP Guide by the PIC/S – EMA Working Group on Annex 1, chaired by UK / MHRA, a joint public consultation will be launched with the EMA. The Committee agreed to involve WHO in the joint publication of this document, as well as in several other future PIC/S guidance documents.

The Committee was informed of a proposal by the SCH to develop in the future some minimum requirements in PIC/S **equivalent to Annex 16** to the EU GMP Guide (certification by a Qualified Person (QP) and batch release).

An update on the status of the work of the EMA drafting groups in which PIC/S is represented for the revision of **Annex 13** (Investigational Medicinal Products), **Annex 17** (Real time release testing) and for (new) **Annex 21** (Imports) was also provided.

The 6-month trial implementation period for the **draft PIC/S guidance on Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments** (PI 041-1 (Draft 2)) developed by the PIC/S Working Group on Data Integrity, chaired by Australia / TGA and UK / MHRA, ended on 28 February 2017. Feedback from PIC/S Participating Authorities will be assessed prior to the adoption process being initiated.

The PIC/S Working Group on Controlling Cross-Contamination in Shared Facilities (CCCISF), chaired by UK / MHRA, has finalised a **draft PIC/S Aide-Memoire on Cross-Contamination in Shared Facilities**, currently under internal consultation. The Committee also endorsed a new mandate for this Working Group for it to become an Expert Circle in order to develop specific training for inspectors in this field.

The Committee was updated on the status of development of the **draft PIC/S guidance on Classification of Deficiencies** by the PIC/S Working Group, chaired by Australia / TGA, further to input from the PIC/S Seminar in July 2016 and the PIC/S Expert Circle on QRM Advanced Training in September 2016.

The PIC/S Expert Circle on GDP, led by UK / MHRA, has finalised a **draft Aide-Memoire on Inspection of Manufacturers and Wholesale Distributors for Compliance with GDP** and **draft Q&A for the PIC/S GDP Guide**. An internal consultation will shortly be launched.

## PIC/S INSPECTORATES' ACADEMY

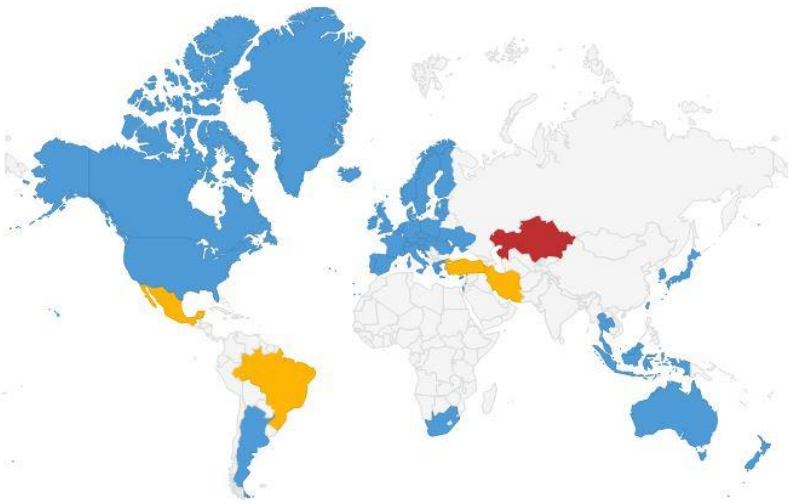
The PIC/S Executive Bureau reviewed and discussed priorities in the implementation of the PIC/S Inspectorates' Academy (PIA) for which the web platform was launched in July 2016. The purpose of the PIA is to harmonise and calibrate the training of inspectors by offering a common training platform to PIC/S inspectors, thus ensuring a greater consistency in the interpretation of GMP. It also aims at making training materials more readily accessible to close to 1,800 PIC/S inspectors.

The Executive Bureau decided on the need to prioritise the development of webinars over video recording of PIC/S training activities. This will allow for a more interactive and cost-effective delivery of e-learning training in the future. Such webinars are to be developed by PIC/S PA and may involve possible co-operation with external stakeholders, including Professional Associations (e.g. ISPE, PDA), other relevant Organisations (e.g. IFPMA), and consultants. Funding remains a key consideration.

## PIC/S EXECUTIVE BUREAU MEETING WITH ICH

A meeting between the PIC/S Executive Bureau and a Delegation from the Secretariat of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) took place on 9 February 2017. Discussions focused on areas of mutual interest where PIC/S and ICH could work jointly, in particular on PIC/S and ICH training activities including the PIC/S– PDA training programme on ICH Q7. ICH was invited to attend the PIC/S Committee meeting as special guest. PIC/S applied in December 2016 to become an ICH Observer.

## PIC/S MEMBERSHIP APPLICATIONS



*Overview of PIC/S current 49 Members (blue); 5 Applicants (yellow); and 1 (Pre-) Applicants (red)*

| Applicants (5) | Pre-Applicants (1) |
|---|---|
| Brazil / ANVISA | |
| Iran / IFDA | |
| Italy (Vet) / DGSAF | Kazakhstan / CCMPA |
| Mexico / COFEPRIS | |
| Turkey / TMMDA | |

- **Brazil / ANVISA** provided an update on a major re-organisation and the impact on its current membership application, which may have to be re-lodged.
- A follow-up visit to **Iran / IFDA** will take place in Q2-Q3 2017 further to the on-site assessment visit in September 2015. The follow-up visit will aim to review the implementation of the CAPA and finalise the assessment of legislative requirements and the GMP compliance of IFDA in the field of herbal medicine.
- A follow-up visit to **Mexico / COFEPRIS** will take place in Q2-Q3 2017 further to the on-site assessment visit in January 2016. The follow-up visit will aim to review the implementation of the CAPA.
- An on-site assessment visit to **Turkey / TMMDA** took take place after the PIC/S Committee meeting.
- A Rapporteur and Co-Rapporteur were appointed for the assessment of **Italy (Vet) / DGSAF**.
- The Committee noted the status of the pre-accession gap-analysis currently ongoing for **Kazakhstan / CCMPA**.

## OTHER NEWS

### The PIC/S Committee:

- established a new **Working Group on Unique Facility Identifiers (UFI)**, led by US FDA, to respond to the need for an internationally recognised UFI to be selected for use by international regulators;
- established a new **Working Group on Inspector Travel Safety** with the objective of developing guidance for inspectors on managing travel risks;
- discussed the outcome and conclusions drawn from the findings of the PIC/S survey on **Voluntary Acceptance of Same Scope Inspection Results** and how to reduce same scope inspections by encouraging PIC/S Participating Authorities to accept inspection findings on a voluntary basis;
- was updated by the newly appointed PIC/S representative in the **International Coalition of Medicines Regulatory Authorities (ICMRA) GMP Project** on discussions with regard to strengthening co-operation between PIC/S and the ICMRA GMP project;

- agreed on the process for the revision of the **PIC/S Rapid Alert Procedure** (PI 010-4) in order to maintain its alignment with the current EMA rapid alert procedure and contribute to future revisions by the EMA;
- endorsed the **PIC/S re-assessments** of Malaysia / NPCB (presently NPRA), for which an on-site re-assessment visit took place in October 2015; as well as recognised as a PIC/S re-assessment, the on-site EU assessment of US FDA which took place in September 2015 using the harmonised PIC/S JRP and EMA JAP re-assessment process;
- noted the **PIC/S re-assessments** of Australia / TGA and Singapore / HSA planned in Q3 2017 and discussed the planning of future re-assessments in accordance with the PIC/S JRP and EU JAP Audit schedules;
- agreed to open up the **PIC/S Joint Visits Programme (JVP)** to non-PIC/S inspectors for Joint Visit groups active in the field of Good Clinical Practices (GCP) & Good Pharmacovigilance (GVP), which are co-ordinated by the PIC/S Working Group on GCP & GVP, led by UK / MHRA. The JVP allows 3 Inspectors from 3 different countries to team up to observe inspections in each country with a view to comparing inspection procedures and techniques and harmonising interpretation in their field of competence;
- was updated on the **PIC/S Working Group on the API Q&A** established for the development of training material part of the PIC/S API International Training Programme based on API Q&A which were not integrated into the ICH Q7 Q&A document;
- was updated on opportunities for **co-operation on training with Professional Associations** (e.g. ISPE, PDA) and **Other Organisations** (e.g. ICH). A side-meeting with PDA took place on 9 February 2017;
- was updated by the new PIC/S – ASEAN Liaison Authority, Thailand / Thai FDA, on recent activities within ASEAN. The Committee also agreed to consider a light instrument for **co-operation with ASEAN** in specific areas of mutual interest;
- was updated on the signing of the **EU – US Mutual Recognition Agreement (MRA)** and was updated on recent GMP-related developments by **EDQM, EMA** and **WHO** as PIC/S Associated Partner Organisations. The Committee noted that the Memorandum of Understanding (MoU) with **EDQM** had been renewed in June 2016 for the next 3 years, and the Co-operation Agreement with **UNICEF** has been renewed in November 2016 for the next 3 years;
- was informed of recent changes concerning PIC/S Participating Authorities and noted a planned survey on a **PIC/S' stakeholders' mapping**;
- noted the status of the **PIC/S Working Group (WG) on Veterinary Medicinal Products**.

## RECENT TRAINING ACTIVITIES

A **PIC/S Advanced QRM Training** was held, in London (United Kingdom), hosted by the EMA on 26 – 28 September 2016. This was the third of a cycle of 3 advanced trainings run by the PIC/S Expert Circle on QRM, for which the first took place in 2014, in Tokyo, hosted by Japan / PMDA and the second in 2015, in Los Angeles, hosted by US FDA. This advanced training aimed at enabling GMP inspectors to effectively inspect QRM activities on site at an advanced level and effectively use the 2012 PIC/S Recommendation in relation to risk-based GMP inspection planning as well as the 2012 PIC/S Aide Memoire on QRM. 74 participants from 29 countries attended.


The **22nd PIC/S Expert Circle on Human Blood, Tissues, Cells and ATMPs** was held in Hong Kong, on 24-28 October 2016, hosted by Hong Kong SAR / PPBHK. The meeting allowed for discussions on contemporary issues and mapping competences of PIC/S Participating Authorities in the field of blood, blood components, plasma derivatives, cells and tissues with particular focus on ATMPs. The meeting also allowed for a review of the different initiatives and current guidance documents on ATMPs and blood establishments as well as for the sharing of experiences between inspectors to improve consistency in the field of blood establishments and ATMP facilities inspections. It also provided an opportunity for exchanging ideas and fostering collaboration among inspectorates, academia and stakeholders. The meeting was attended by 114 participants from 32 countries.

A **GMP Training Seminar** organised by PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) was held on 5-9 December 2016 in Toyama, Japan. This training event was supported by PIC/S.

## COMING UP...

- 5-7 April 2017: **PIC/S Expert Circle on APIs meeting and Advanced Training**, in Melbourne, hosted by Australia / TGA;
- 26-28 June 2017: **PIC/S Expert Circle on Blood, Tissues, Cells and ATMPs meeting**, in Seoul, hosted by Korea (Republic of) / MFDS;
- 31 July - 4 August 2017: **Japan / PMDA - ATC GMP Inspection Seminar**, with the support of PIC/S, in Yamaguchi, Japan;


- 13-15 September 2017: **Annual PIC/S Seminar on "Quality Control Laboratories: How to Inspect"**, in Taipei, hosted by Chinese Taipei / TFDA;
- September 2017: **PIC/S New Inspector Training Course**, in Dublin, hosted by Ireland / HPRA.

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