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

July 2016

Press release: PIC/S Meetings in Manchester (United Kingdom)

From 4 to 8 July 2016, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) hosted the following events in Manchester (UK): PIC/S Committee meeting, PIC/S Executive Bureau meeting, and PIC/S Annual Seminar.

PIC/S COMMITTEE MEETING

PIC/S Chairman, Mr Paul Hargreaves (UK / MHRA)

The PIC/S Committee met on 4-5 July 2016, under the chairmanship of Mr Paul Hargreaves (United Kingdom's Medicines and Healthcare products Regulatory Agency / MHRA). The meeting was attended by 41 out of 48 PIC/S Participating Authorities (PA) as well as by a number of Applicants, Pre-Applicants, Associated Partners and Guests.

THAI FDA JOINS PIC/S

The PIC/S Committee invited Thailand's Food and Drug Administration (Thai FDA) to join the Scheme from 1 August 2016. Thai FDA will become PIC/S' 49th Participating Authority. Thai FDA applied for a second time for membership in March 2015. A paper assessment was conducted in view of its accession to PIC/S, followed by an on-site visit in March 2016.

The PIC/S assessment of Thai FDA covered both traditional and modern medicines. The Audit team recommended to the Committee to accept the PIC/S membership application of Thai FDA. The Thai FDA Delegation in Manchester was led by the Secretary General of Thai FDA, Dr Boonchai Somboonsook.

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

PIC/S INSPECTORATES' ACADEMY (PIA) IS NOW LIVE

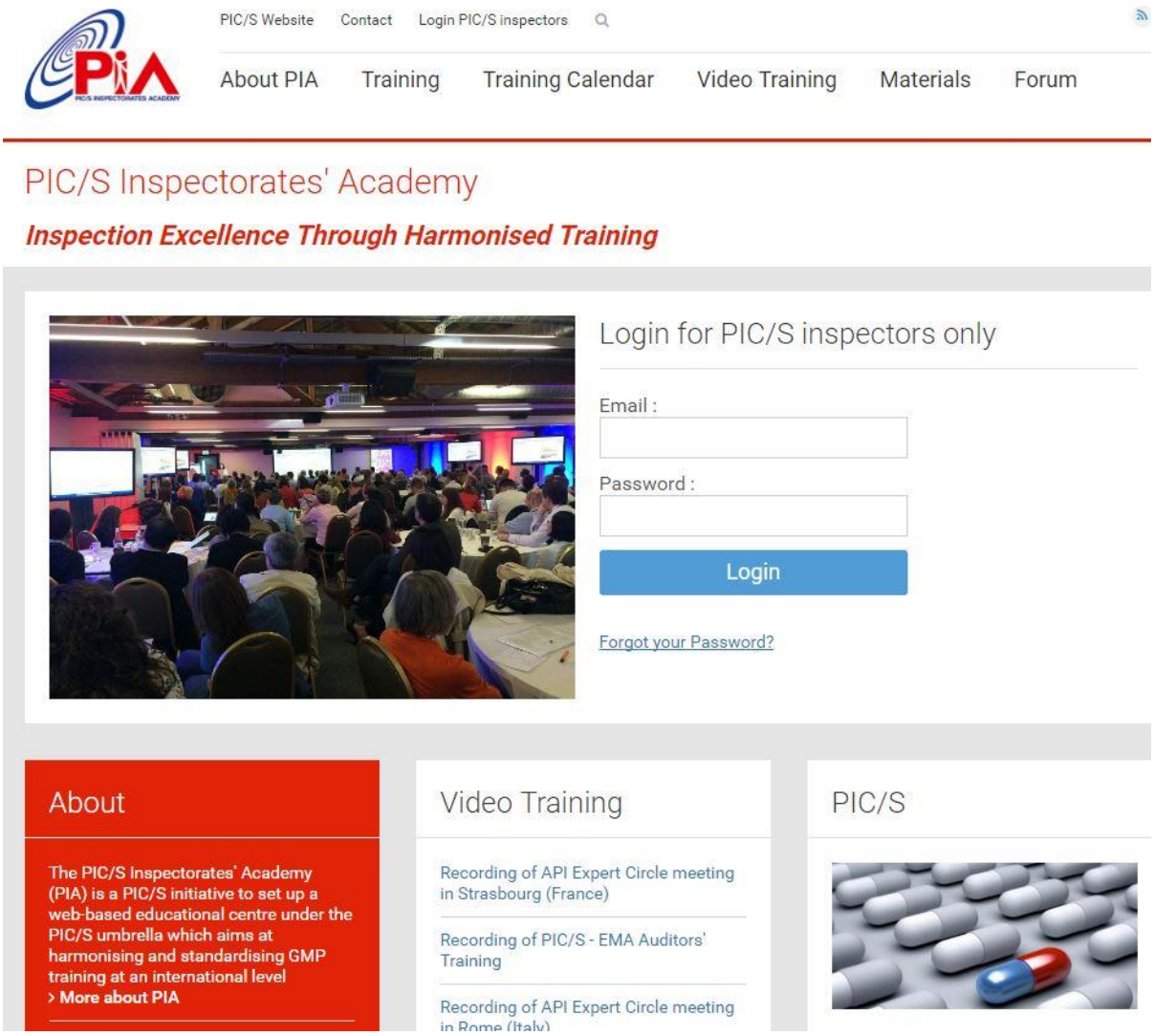
The PIC/S Inspectorates' Academy (PIA) is now up and running.

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

The PIC/S Deputy Chairman and visionary of the PIA, Mr Boon Meow Hoe (Singapore / HSA), also serving as Chair of the PIA Project Management Steering Committee (PMSC), announced the completion of stage 1 of the PIA, i.e. a dedicated web-based platform internal to PIC/S incorporating all PIC/S training materials, which will be accessible to all PIC/S Inspectorates, bringing together today 1789 PIC/S inspectors. The site is presently live at https://www.picscheme.org/en/pia-home. Login is required for the PIC/S inspector-only area.

With the completion of stage 1, stage 2 of the PIA will now start and focus on developing modules (e-learning) responding to specific training needs, to be identified, including possible co-operation with external stakeholders, as well as the development of PIC/S training recognition and certificates.

The PIA website is a sub-website of the new PIC/S website which is available at https://www.picscheme.org



2016 PIC/S SEMINAR ON INSPECTORATES OF THE FUTURE

A PIC/S Seminar was organised by the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) in Manchester (UK) on 6-8 July 2016. The topic of the Seminar was "Inspectorates of the Future". The Seminar was opened by the Chief Executive of MHRA, Dr Ian Hudson, and the PIC/S Chairman, Mr Paul Hargreaves.

The Seminar, which was the 5th organised in the UK since MHRA joined PIC/S as a Founding Member in 1971, was attended by more than 180 participants from 53 countries. All continents were represented. It was held at the Museum of Science and Industry in Manchester, which is the European City of Science 2016.

The objectives of the Seminar were to exchange and discuss on GMP topics affecting the work that Inspectorates do and what factors will drive them to do things differently in the future. This Seminar provided a unique opportunity to explore the current landscape with regard to inspection findings and trendings, with a particular focus on data integrity issues. It also looked to see what changes Industry have on the horizon. The Seminar discussed how various Inspectorates are collaborating on a number of topics and looking to establish best practice for risk based inspections and compliance management. Finally, participants were invited to look to what PIC/S will be doing in the future to support inspector education through the PIA (PIC/S Inspectorates' Academy) as well as reflect on PIC/S vision to 2020.

For more information on the Seminar, see **below.**

PIC/S WORKING GROUPS

The PIC/S Committee was updated on the work being carried out by the following Working Groups:

- the **PIC/S Working Group (WG) on Data Integrity** has completed a first draft guidance document on *Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments*. The priority of this WG has shifted from the development of Industry-facing guidance regarding data integrity to the development of Inspectorate guidance. The area of data integrity is complex and has a broad scope across GMP and GDP. A significant period of time will be required to prepare comprehensive PIC/S guidance, aide memoires and training material for Inspectorates which fully address the data integrity challenges faced by PIC/S inspectors during inspection. In order to respond to the need among Inspectorates to have initial guidance which facilitates a harmonised approach - considering the impact to public health - this first draft guidance has been developed in order to provide an interpretation of existing GMP / GDP data integrity requirements. It sets out basic expectations for good data governance and refers to the influence of organisational behaviour and global supply chain

challenges. It is foreseen that this guidance will be published as a draft in the course of August 2016 - for implementation on a trial-basis - as work continues to revise and expand the draft guidance, in particular relating to computerised systems.

- the **PIC/S Working Group (WG) on Harmonisation of Classification of Deficiencies** has further refined its draft guidance following the outcome of an internal consultation carried out with PIC/S Members and Partners earlier this year. The workshop on **"**Inspection trends and inspection strategies for the future", which took place during the 2016 PIC/S Seminar, also provided valuable input, particularly with regard to the tool for Inspectorates to improve harmonised risk classification of GMP deficiencies. A second internal consultation consolidating recent developments will be carried out within PIC/S.
- the **EMA (European Medicines Agency) – PIC/S Joint Drafting Group on the revision of Annex 1 (sterile manufacturing)** of the PIC/S-EU GMP Guide is in the process of revising Annex 1 and a first draft will be issued shortly for PIC/S and EMA internal consultations. A joint public consultation with the EMA will be organised at a later stage.
- the **PIC/S Working Group (WG) on Controlling Cross-Contamination in Shared Facilities** has drafted 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. An internal consultation will shortly be carried out within PIC/S.
- the **PIC/S Working Group (WG) on Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP)**, whose primary purpose is to facilitate technical co-operation and harmonisation of practices (including the development of guidance and training material), capacity building and information sharing, is currently contemplating becoming an Expert Circle.
- the **PIC/S Working Group (WG) on Veterinary Medicinal Products** aims to better take into account the needs and specificities of Veterinary Agencies within PIC/S.
- the **EMA Drafting Group** aims amending the **Site Master File (SMF)** in view of mitigating drug shortages.
- the **PIC/S Working Group (WG) on Advance Therapy Medicinal Products (ATMPs)** remains on hold while awaiting the outcome of discussions on GMP for ATMPs in the EU.

The PIC/S Committee decided on the establishment of:

- a new **PIC/S Working Group on the revision of PIC/S Recommendations on Validation Master Plan; Installation and Operational Qualification; Non-Sterile Process Validation; and Cleaning Validation** (PI 006-3), in connection with the transposition and adoption by PIC/S of the EMA Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities.
- a new **PIC/S Working Group on the API Q&A** developed by PIC/S, which were not transferred to ICH, for the development of training material part of the PIC/S API International Training Programme.

PIC/S MEMBERSHIP APPLICATIONS

Overview of PIC/S 49 Members (blue) including Thai FDA which will become PIC/S 49th Member as of 1 August 2016; and 5 Applicants (yellow) and 3 (Pre-) Applicants (red)

Applicants (5)	**Pre-Applicants (3)**
Brazil / ANVISA	
Iran / IFDA	Belarus / MoH
Mexico / COFEPRIS	Chile / ISP
Philippines / PFDA	Kazakhstan / CCMPA
Turkey / TMMDA	

(in alphabetical order, starting with Applicants and then Pre-Applicants):

- **Brazil / ANVISA** reported on a major re-organisation, which may impact on its current membership application.
- An on-site assessment visit took place in September 2015 to **Iran / IFDA** (previously Iran / MoH) and a preliminary draft report was presented to the Committee, which recommended that a follow-up visit be undertaken to finalise the assessment of legislative requirements and the GMP compliance of IFDA in the field of herbal medicine.
- An on-site assessment visit took place to **Mexico / COFEPRIS** in January 2016 and a preliminary draft report was reviewed by the Committee, which invited the Rapporteur to finalise the report and submit it to the Sub-Committee on Compliance (SCC). It also invited Mexico / COFEPRIS to update the Rapporteur on the progress regarding outstanding issues, which need to be addressed. The

PIC/S Committee will review the situation at the next meeting and decide on a follow-up visit to Mexico / COFEPRIS. A Special Delegation from Mexico / COFEPRIS, led by the Commissioner of COFEPRIS, Mr Julio Sánchez y Tépoz, attended the meeting and reported on the measures taken by COFEPRIS to meet PICS/ requirements.

- The Committee decided to close the application process of **Philippines / PFDA** due to the lapse of the 6-year timeframe. As the Philippines have requested to be listed under the ASEAN Sectoral Agreement on GMP, the Committee invited PFDA to re-apply, once the ASEAN process had been successfully completed.
- Additional Audit Team members were appointed for the on-site assessment visit of **Turkey / TMMDA** to be planned in Q4 2016;
- The Committee noted the status of the pre-accession gap-analysis currently ongoing for **Kazakhstan / CCMPA** and closed the pre-accession processes of **Belarus / MoH** and **Chile / ISP**, which are finalising their CAPA, further to the completion of their respective pre-accession gap-analysis.
- **Russia / SID&GP** as well as **Vietnam / DAV**, which were invited to attend the Committee meeting as special Guests, updated the Committee on their respective GMP systems. Vietnam / DAV reported on its intent to lodge a PIC/S pre-accession application in the near future.
- A side-meeting took place between a Delegation of the PIC/S Executive Bureau and a Delegation of **China / CFDA** regarding the latter's intention to apply for PIC/S membership. An application is currently on hold due to some issues to be resolved by CFDA.

OTHER NEWS

The PIC/S Committee:

- welcomed the signing of a Letter of agreement between PIC/S and EU/EEA Heads of Medicines Agencies (HMA), by which PIC/S and HMA agree to co-operate in exchanging information in the context of the EEA Joint Audit Programme (JAP) of GMP Inspectorates and the PIC/S Joint Reassessment Programme (JRP) of Participating Authorities, which ensures that both new and current PIC/S Participating Authorities meet the same requirements. Through this agreement, PIC/S and HMA recognise that in the EEA context the EEA JAP and the PIC/S JRP are deemed equivalent. Furthermore, PIC/S and HMA agree to exchange auditing schedules with a view to avoid any duplication and foster mutual acceptance and recognition of audits as well as maintain equivalent auditing tools and programmes, including joint training of auditors;
- was updated on the PIC/S re-assessment of Malaysia / NPRA, for which an on-site re-assessment visit took place in October 2015 and discussed the planning of future re-assessments in accordance with the PIC/S JRP and EU JAP Audit schedules. Re-assessment Team Members volunteered for the PIC/S re-assessment of Australia / TGA and Singapore / HSA in 2017;
- was updated on revisions currently underway for Chapters 1, 2, 3, 5, 6, 7 and 8 of the PIC/S GMP Guide as well as of revisions of Annexes 13 and 17;

- discussed the recent developments on ATMPs in the EU further to the outcome of the EU Consultation Document on GMP for ATMPs developed by the EMA Committee for Advanced Therapies (CAT) and agreed to carry out a PIC/S-internal survey on ATMP requirements;
- reviewed the outcome of surveys carried out within PIC/S on Unique Facility Identifiers (UFI) and Voluntary Acceptance of Same Scope Inspection Results. The first aims at allowing UFIs to identify a manufacturing site as well as maintain the site's records of operations and products; the latter intends to reduce same scope inspections by encouraging PIC/S Participating Authorities to accept inspection findings on a voluntary basis;
- adopted new Terms of Reference for PIC/S Working Groups and discussed a proposal to amend the PIC Scheme to allow Inspection Units of Partner Organisations to join PIC/S as "Participating Authorities" in order to allow for increased co-operation;
- discussed co-operation with Professional Organisations such as ISPE and PDA;
- discussed how to enhance internal PIC/S communication through single contact points;
- adopted the revised mandate of the Expert Circle on Human Blood, Tissues, Cells & ATMPs, further to its revision which was discussed during the 21st Expert Circle Meeting, hosted by AIFA, in Rome (Italy), on 26-30 October 2015;

- adopted a revision to the PIC/S Financial Rules and approved the 2015 accounts;
- enhanced its future international co-operation with Partners and other Organisations, in particular with:
    - **WHO** (World Health Organization). The revised Memorandum of Understanding (MoU) between PIC/S and WHO entered into force on 29 February 2016. A side-meeting between a WHO Delegation and the PIC/S Executive Bureau took place in the margins of the Committee meeting in Manchester in order to discuss in which areas co-operation and synergies could be explored in the future;
    - **ICH** (International Conference on Harmonisation). The PIC/S Committee agreed that PIC/S apply to become an Observer to ICH following the recent ICH reform. This will allow PIC/S to monitor and contribute to GMP-related developments at ICH and avoid unnecessary duplication of activities. The Committee was updated on work currently carried out by ICH, in particular on Q12 and Q3D;
    - **ICMRA** (International Coalition of Medicines Regulatory Authorities). The Committee agreed to a proposal by ICMRA that a PICS/ representative be appointed on the ICMRA GMP project and that PIC/S become involved in some specific GMP activities.

RECENT TRAINING ACTIVITIES

A Training by PIC/S Expert Circle on API was hosted by China / CFDA in Beijing on 23-24 November 2015. This Training was part of the PIC/S International API Training Programme and was organised with the support of the EU Commission and China Chamber of commerce of Medicines & Health Products Importers & Exporters (CCCMPHIE). More than 140 participants from industry and CFDA central and provincial authorities participated. The focus was on ICH Q7 as well as more advanced API current topics.

The 4th meeting of the PIC/S Expert Circle on GDP was hosted by South Africa / MCC on 12-14 April 2016 in Pretoria. This Expert Circle meeting, which was attended by close to 60 inspectors from 23 countries allowed for the successful development of a draft PIC/S Aide-Memoire for GDP inspections as well as a draft Q&A document for GDP.

COMING UP...

- 8-9 August 2016: PIC/S – PDA (Parenteral Drug Association) ICH Q7 Training in San Juan (Puerto Rico);
- 26 – 28 September 2016: PIC/S Advanced QRM Training, in London (United Kingdom), hosted by the European Medicines Agency (EMA);
- 24-28 October 2016: PIC/S Expert Circle on Blood, Tissue, Cells and ATMPs, in Hong Kong (Hong Kong SAR), hosted by Hong Kong SAR / PPBHK;
- 5-9 December 2016: Japan / PMDA GMP Training Course with the support of PIC/S, in Toyama, Japan;

- 5-7 April 2017: PIC/S Expert Circle on APIs meeting and Advanced Training, in Melbourne (Australia), hosted by Australia / TGA;

- 13-15 September 2017: Annual PIC/S Seminar on "Quality Control Laboratories: How to Inspect", in Taipei, Chinese Taipei, hosted by Chinese Taipei / TFDA.

2016 PIC/S SEMINAR ON INSPECTORATES OF THE FUTURE

Dr Ian Hudson, Chief Executive (UK / MHRA)

Seminar Opening Address by
Dr Ian Hudson, Chief Executive of UK / MHRA

Dr Ian Hudson welcomed all Seminar participants to Manchester. He gave an overview on MHRA as well as its range of responsibilities and international engagement. MHRA continued to be fully committed to work together with global regulators such as PIC/S. Over the past 20 years significant changes occurred across the pharmaceutical manufacturing arena: new products, ATMP, biosimilars complex biologicals, new process, new supply chains, new facilities, new GMPs. PIC/S played a key role and facilitated the knowledge and education of inspectors across the world. MHRA was honoured to be able to contribute this year to PIC/S' training through the hosting of this Seminar. In terms of international co-operation, MHRA highly valued the interactions between regulators that bring patient benefits. This approach also benefited industry with having clearer international recognised standards to follow. It is with this in mind, that the MHRA chose the topic of "Inspectorates of the Future". The association between PIC/S and PIC/S Associated Partners such as EMA, EDQM, WHO & UNICEF helped ensure globally the manufacture and distribution of safe and effective medicines.

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

The first day started with a series of lectures and presentations on inspection trends & GMP deficiencies deriving from a recent survey conducted among PIC/S Participating Authorities and Applicants; GMP evolution, in particular data integrity inspections in the supply chain; and a presentation by an invited industry speaker on global developments.

Two parallel workshops for inspectors followed on:

- **Inspection trends and inspection strategies for the future**, which included a review and comparison of trends globally, deficiency classification harmonisation and the use of the PIC/S deficiency tool currently in development by the PIC/S Working Group on Harmonisation of Classification of Deficiencies (Workshop leader: Health Canada).
- **Data Integrity: tools and techniques**, which included a focus on the trustworthiness of paper, data audits and navigating chromatography systems (Workshop leader: UK / MHRA & Australia / TGA).

Lectures and presentations followed on the morning of the second day dealing with Regulatory Agencies working together, in particular through PIC/S or the International Coalition for Medicines Regulatory Authorities (ICMRA); risk-based inspection models and implementation as well as a focus on whistle-blower cases; compliance management, including what is done beyond inspections to drive compliance; and finally a presentation on shortages and complex supply chain issues by an invited industry speaker.

Two parallel workshops for inspectors followed on:

- **Shortages**, which included a series of practical examples and discussions on what inspectors can do, their "role" in reducing shortages and how PIC/S can promote work in this area (Workshop leaders: European Medicines Agency (EMA) and UK / MHRA).

- **Compliance Management**, which allowed for a review of what inspectors/agencies are doing now and what more could be done in the future, in particular via PIC/S. Participants also exchanged views on strategies for inspections and how to handle whistle blowers (Workshop leader: US FDA).

During the last day of the Seminar, a summary of the outcome of the workshops was presented followed by a presentation on the PIC/S Inspectorates' Academy (PIA).

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