PIC/S
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

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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

PRESS RELEASE: PIC/S MEETINGS IN NUSA DUA (INDONESIA)

From 5 to 9 October 2015, the Indonesian National Agency for Drug and Food Control (NADFC) hosted the following events in Nusa Dua (Indonesia): PIC/S Committee meeting, PIC/S Executive Bureau meeting, PIC/S Annual Seminar and 3rd PIC/S – ASEAN (Association of Southeast Asian Nations) Forum.

PIC/S Committee Meeting, Nusa Dua, Indonesia

PIC/S COMMITTEE

The PIC/S Committee met on 5-6 October 2015 under the chairpersonship of Dr Joey Gouws (South Africa's Medicines Control Council / MCC). The meeting was attended by 30 out of 46 PIC/S Participating Authorities (PA) as well as by a number of Applicants, Pre-Applicants and Associated Partners.

NEW PIC/S CHAIRMAN

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 4th PIC/S Chairman from the United Kingdom.

The incoming Chairman thanked the Committee and paid tribute to the outgoing Chairperson Dr Joey Gouws, Acting Head of South Africa's Medicines Control Council / MCC. Dr Gouws was the first PIC/S Chairperson from Africa. Her chairpersonship was marked by the reorganisation of PIC/S and the successful implementation of the new PIC/S Sub-Committee structure, a significant development of PIC/S activities - in particular training activities - as well as an increase in membership during her term (2014-2015).

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

NEW PIC/S SUB-COMMITTEE OFFICE HOLDERS

The PIC/S Committee elected the Members, Deputy Chairs and Chairs of the PIC/S Sub-Committee structure for the period 2016-2017. Office holders were elected for the following seven Sub-Committees: Training (SCT); Expert Circles (SCEC); Strategic Development (SCSD); Compliance (SCC); GM(D)P Harmonisation (SCH); Budget, Risk and Audit (SCB) and Communication (SC COM). All Sub-Committee Chairs will be Members of the PIC/S Executive Bureau.

Out of the 52 newly appointed Sub-Committee office holders, all continents are represented and 29 are from non-EEA PIC/S Participating Authorities. This reflects the more participative and efficient organisation of PIC/S, at a global level, since the successful implementation of the new PIC/S Sub-Committee structure in 2014.

NEW PIC/S EXECUTIVE BUREAU

A new PIC/S Executive Bureau was elected by the Committee as from 1 January 2016. The Executive Bureau Members for the period 2016- 2017 are:

- 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).

CROATIA / HALMED JOINS PIC/S

From left to right: Ms Ana Boban, Head of Department for Licensing, GMP and GVP Inspection (Croatia/HALMED), Ms Anne Hayes, Chair of the PIC/S Sub-Committee on Compliance (Ireland/HPRA), Dr Joey Gouws, PIC/S Chairperson (South Africa/MCC) and Ms Togi Hutadjulu, Head of Inspectorate (Indonesia/NADFC).

The PIC/S Committee invited the Agency for Medicinal Products and Medical Devices of Croatia (HALMED) to join the Scheme from 1 January 2016. HALMED will become PIC/S' 48th Participating Authority. HALMED applied for membership on 5 September 2014. A paper assessment was conducted in view of its accession to PIC/S, followed by an on-site visit on 29 June – 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.

SEMINAR ON BIOPHARMACEUTICALS (BIOTECHNOLOGY AND BIOLOGICALS): HOW TO INSPECT

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 with a traditional gong 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.

The objectives of the Seminar were to discuss and update inspectors on GMP principles and requirements specific to the field of biopharmeucticals, 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. 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.

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).

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.

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.

Dr. Roy A. Sparringa

Excerpt of the Seminar opening speech by Dr Roy A. Sparringa, M.App. Sc, Chairman of Badan POM/ NADFC, Indonesia.

«Thirty years ago the first biotechnologically manufactured medicines were introduced to the market. The first such substance approved for therapeutic use was recombinant human insulin. Since then, the pharmaceutical R&D pipeline and industry have been witnessing greater degree of dependence on biopharmaceuticals.

Development of these products is being undertaken by a growing number of players in the pharmaceutical industry, which include the big pharma companies as generic drug manufacturers and engaged in developing biosimilar as well.

Future pharmaceutical products based on biotechnology and biosimilar will become more and more important. Biopharmaceuticals products and its manufacturing process are undergoing rapid development and constant change. In order to ensure the quality of these products, National Regulatory Authorities should develop strategic international regulatory guidance that could drive the entire pharmaceutical industry, including biologics to higher standard of performance.

Ensuring the quality of biopharmaceutical and biosimilar – through official inspections– is strictly in compliance with the marketing authorization and GMP standards is undoubtedly a challenge for inspectors, considering the various differences in GMP regulations for medicinal products including its various interpretation among participating authorities.

With a population of over 250 million people –the fourth most populous country in the world–, Indonesia healthcare market is worth $24 billion, and this could reach $31 billion in 2016. At the same time, Indonesians are forecasted to spend almost $150 per person on healthcare in 2015, up from $35 in 2005. There are approximately 10,000 primary care centres and over 2,200 hospitals. Three percent of Indonesia's GDP is spent on healthcare. Henceforward, as the government commitment, this should increase soon to 5%. Our pharma market is expanding quickly with the growth 85% during the 2007–2013. It is valued at $6.5 billion with an annual growth rate of 12.5%. This growth is expected to continue through 2018.»

3rd PIC/S - ASEAN FORUM

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.

The purpose of this half-day meeting, which took place in Nusa Dua on 8 October 2015, 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).

In short

Current PIC/S Working Groups:

The Committee was updated on the work being carried out by:

• **the PIC/S Working Group (WG) on Harmonisation of Classification of Deficiencies.** A preliminary guidance document has been drafted which includes a tool for Inspectorates to improve harmonised risk classification of GMP deficiencies. Recommendations to facilitate harmonised compliance and enforcement approaches to address GMP non-compliance will also be included. These efforts are hoped to facilitate more consistent responses among international regulatory authorities when responding to GMP deficiencies and GMP non-compliance;

• **the PIC/S Working Group (WG) on Advance Therapy Medicinal Products (ATMPs)**. A draft Aide-Memoire to support the inspection of ATMPs facilities has been drafted and will be further discussed at the PIC/S Expert Circle on Blood, Tissues, Cells and ATMPs in Rome (Italy) on 26-30 October 2015;

• **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**. A joint consultation on the draft revision is planned for 2016;

• **the PIC/S Project Management Steering Committee in charge of the PIC/S Inspectorates' Academy (PIA)**. The first stage of the PIA consisting in a web-based platform internal to PIC/S is close to completion. The Committee adopted the visual identity of the PIA;

• **the PIC/S Working Group (WG) on Data Integrity**. The priority of this WG will be the development of 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; a secondary priority will later consist in the development of inspectorate guidance to equip inspectors with the basic skills for performing data integrity inspections;

• **the PIC/S Working Group (WG) on Controlling Cross-Contamination in Shared Facilities**. The goal of this WG 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;

• **the PIC/S Working Group (WG) on Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP)**. This WG 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;

• **the PIC/S Working Group (WG) on Veterinary Medicinal Products**, for which the mandate is yet to be finalised;

• the participation of PIC/S in (i) the EMA Drafting Group to amend the Site Master File (SMF) in view of mitigating drug shortages as well as (ii) the EMA Drafting Group on ICH Q12.

PIC/S Chairperson with PIC/S Sub-Committee on GM(D)P Harmonisation Chair, Mr Paul Gustafson (Canada / HPFBI).

Inspection Excellence Through Harmonised Training

Ongoing activities

The Committee:

- noted that the PIC/S and the EU revised Annex 15 entered into force on 1 October 2015 and that as a result the PIC/S GMP Guide has been revised and published with reference (PE-009-12);

- was updated on revisions currently underway for Chapters 1, 2, 6 and 7 of the PIC/S GMP Guide as well as of revisions of Annexes 13 and 17;

- 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);

- noted the status of surveys being carried out within PIC/S on Unique Facility Identifiers (UFI) and Voluntary Acceptance of Same Scope Inspection Results. The latter is intended to reduce same scope inspections by encouraging PIC/S Participating Authorities to accept inspection findings on a voluntary basis;

- noted that the new procedure adopted for informing foreign regulatory authorities of inspections to be conducted in their jurisdiction (PI-039-1) will enter into force as from 1 November 2015. This procedure is intended to allow increased possibilities of joint or observed inspections, in addition to the PIC/S list of planned foreign inspections.

- discussed further developments and conditions to international co-operation with Partners and other Organisations, in particular with:

• ICMRA (International Coalition of Medicines Regulatory Authorities), with a view to strengthening synergies and co-operation between PIC/S and ICMRA;

• WHO (World Health Organisation), with a view to renewing the Memorandum of Understanding between PIC/S and WHO in order to further expand co-operation;

• ICH (International Conference on Harmonisation), for which the Committee was updated on work carried out by ICH (Q12 and Q3D) and agreed to make a link to the ICH Q&A on Q7 to which PIC/S contributed.

• was updated on joint training endeavours with Professional and Other Organisations such as ISPE and PDA.

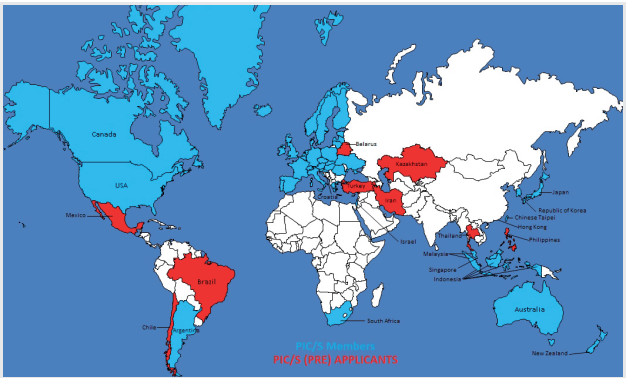
• was updated on the recent activities of PIC/S Expert Circles.

PIC/S QRM Advanced Training, hosted by US FDA, Los Angeles (USA), October 2015

PIC/S Applicants

Overview of PIC/S 48 Members (blue) including Hong Kong SAR/PPBHK and Croatia / HALMED which will become PIC/S 47th and 48th Members as of 1 January 2016;

and 9 (Pre-) Applicants (red)



APPLICANTS (6)

Brazil / ANVISA
Iran / MoH
Mexico / COFEPRIS
Philippines / PFDA
Thailand / Thai FDA
Turkey / TMMDA

PRE-APPLICANTS (3)

Belarus / MoH
Chile / ISP
Kazakhstan / CCMPA

- The paper assessments of Thailand / Thai FDA and Turkey / TMMDA were reviewed by the Committee which appointed additional Audit Team members and agreed on-site assessment visits in 2016;
- The status of Mexico / COFEPRIS was discussed and an on-site visit in 2016 agreed;
- The on-site visit of Iran / MoH took place in September 2015;
- Philippines / PFDA provided an update on the implementation of its CAPA;
- The pre-accession gap analysis for Chile / ISP has been completed;
- a revision of the PIC/S accession and pre-accession guidelines was proposed;
- an update on prospective future applicants was given, in particular on recent exchanges with China / CFDA with regards to their interest in applying to PIC/S in the near future.

Re-Assessment of PIC/S Members

- an update was provided on the revision of the PIC/S Joint Re-assessment Programme (JRP), intended to ensure that current PIC/S Members continue to meet the same standards as new PIC/S Members, including a new risk-based re-assessment process, in line with proposed changes to the EMA (European Medicines Agency)'s Joint Audit Programme (JAP).
- The re-assessment of Malaysia / NPCB took place in October 2015;
- The re-assessment of US FDA is to be recognised within the frame of the EU assessment of US FDA which took place in September 2015, using the current harmonised PIC/S-EMA JAP/JRP assessment procedure.

Recent Training Activities

PIC/S - PDA ICH Q7 Training by PIC/S Expert Circle on API and PDA, with the support of the European Commission, in Hyderabad and Ahmedabad (India) on 14-18 September 2015. More than 240 participants from industry and regulatory authorities participated including the Heads of the Indian Drug Regulatory Authorities of the States of Andhra Pradesh, Telangana and Gujarat.

PIC/S QRM Advanced Training by PIC/S Expert Circle on QRM, hosted by US FDA, in Los Angeles (USA) on 5-7 October 2015. This training event attracted 60 inspectors and was part of cycle of three PIC/S Advanced QRM Training courses for which the first one took place in Japan in December 2014, hosted by PMDA, and the next one will take place in Europe in the course of the second half of 2016.

7th PIC/S Expert Circle Meeting on API, hosted by EDQM, in Strasbourg (France), on 20-22 October 2015. This meeting which provided for advanced API training attracted more than 90 inspectors from 40 countries. The overall objective was to strengthen international co-operation and share experiences in the field of API inspections. A focus was made on current data integrity issues.

21st PIC/S Expert Circle Meeting on Human Blood, Tissues, Cells and ATMPs, hosted by 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).

COMING UP…

- 23-24 November 2015: **PIC/S - CFDA API** Training by PIC/S Expert Circle on API in Beijing (China), hosted by China/CFDA, with the support of the EU Commission;
- 12-14 April 2016: **PIC/S Expert Circle on GDP**, in Pretoria, Gauteng Province, South Africa, hosted by MCC/South Africa;
- 6-8 July 2016: **PIC/S Annual Seminar** on Inspectorates of the Future in Manchester (UK), hosted by MHRA http://www.pics2016.co.uk

MHRA hosts PIC/S 2016 Manchester / UK

This seminar will explore the current landscape with regard to inspection findings and trendings, with a particular focus on data integrity issues and then look to see what changes Industry have on the horizon. It will then also explore how various Inspectorates are collaborating on a number of topics and look to establish best practice for risk based inspections and compliance management. Finally, the seminar will look to what in the future PIC/S will be doing to support Inspector education through the PIA and also the PIC/S vision to 2020.