Pharmaceutical Inspection Co-operation Scheme (PIC/S)

Presentation to

6th APAC

5th April 2017

Tokyo Japan

Boon Meow Hoe

PIC/S Deputy Chairman

PIC/S Executive Bureau Member

PIC/S Sub-Committee on Training Chairman

PIA Project Management Steering Committee Chairman

Agenda

1. Overview of PIC/S

- What is PIC/S?
  - PIC/S Membership
  - GMP Standard
  - Training

2. International Harmonization

- PIC/S Partners & Other Organisations
- PIC/S Working Groups
- PIC/S Expert Circles

3. Other

- PIA
- Last PIC/S Committee Meetings (Geneva, Feb 2017 and Manchester July 2016)

4. Q&A

What is PIC/S?

PIC : **Pharmaceutical Inspection Convention**

PIC Scheme : **Pharmaceutical Inspection Cooperation Scheme**

PIC	PIC Scheme
Established 1970	Established 1995
Convention	Scheme
Between 18 countries	Between 49 Agencies (NDRA) in the field of GMP for human or vet. use
Formal Treaty	An informal arrangement (purely technical, non-political, & not6-for-profit Association under Swiss law)
Legal status	Has no legal status (Not legally binding)
Focus on inspection	Focus on training & developing guidelines
Mutual recognition of inspections	Exchange of information

Both operate in parallel under the logo/abbreviation: "PIC/S"

PIC/S: PIC and PIC Scheme

PIC

A formal Convention between Countries

Since 1970 – 47 years old (a matured person)

PIC Scheme

A Cooperation Scheme between Authorities

Since 1995 – 22 years old (a thriving young lady!)

Then “married” together as **PIC/S**!

PIC/S' Goal

"To **lead** the international development, implementation and maintenance of **harmonised** **GMP standards** and **quality systems of inspectorates** in the field of medicinal products".

Achievement of PIC/S Goal

PIC/S Goal to be achieved by:

- ✓ Developing and promoting harmonised GMP standards and guidance documents.
- ✓ Training competent authorities, in particular GMP inspectors.
- ✓ Assessing (and reassessing) GMP Inspectorates.
- ✓ Facilitating the co-operation and networking for competent authorities and international organisations.

THAILAND / FDA JOINS PIC/S as from 1 August 2016 (49th Member)

Accession dates (1/3)

		Accession to PIC	Accession to PIC/S
1)	Austria	May 1971	Nov 1999
2)	Denmark	May 1971	Nov 1995
3)	Finland	May 1971	Jan 1996
4)	Iceland	May 1971	Nov 1995
5)	Liechtenstein	May 1971	Nov 1995
6)	Norway	May 1971	Nov 1995
7)	Portugal	May 1971	Jan 1999
8)	Sweden	May 1971	Feb 1996
9)	Switzerland	May 1971	Feb 1996
10)	UK	May 1971	Jun 1999
11)	Hungary	Aug 1976	Dec 1995
12)	Ireland	Dec 1977	Feb 1996
13)	Romania	May 1982	Nov 1995
14)	Germany	Sep 1983	Dec 2000
15)	Italy	Aug 1990	Feb 2000
16)	Belgium	Sep 1991	Feb 1997
17)	France	Dec 1992	Feb 1997
18)	Australia	Jan 1993	Nov 1995
19)	Netherlands	-	Nov 1995
20)	Czech Republic	-	Jan 1997
21)	Slovak Republic	-	Jan 1997

Accessions dates (2/3)

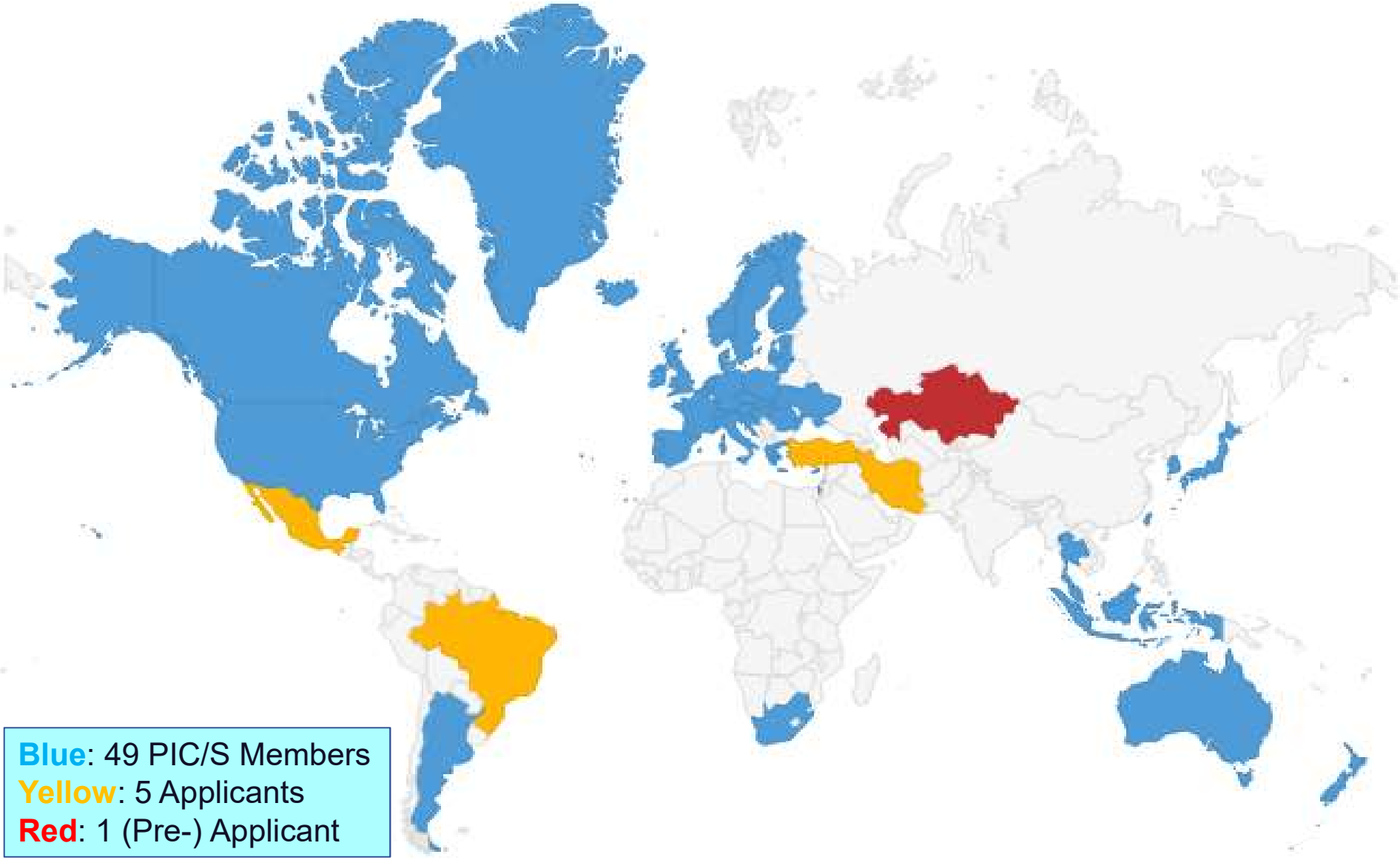
		Accession to PIC	Accession to PIC/S
22)	Spain	-	Jan 1998
23)	Canada	-	Jan 1999
24)	Singapore	-	Jan 2000
25)	Greece	-	Jan 2002
26)	Malaysia	-	Jan 2002
27)	Latvia	-	Jan 2003
28)	Czech Rep (Vet)	-	Jul 2005
29)	Poland	-	Jan 2006
30)	Estonia	-	Jan 2007
31)	South Africa	-	Jul 2007
32)	Argentina	-	Jan 2008
33)	Malta	-	Jan 2008
34)	Cyprus	-	Jul 2008
35)	France (Vet)	-	Jan 2009
36)	Israel	-	Jan 2009
37)	Lithuania	-	Jul 2009
38)	USA	-	Jan 2011
39)	Ukraine	-	Jan 2011
40)	Slovenia	-	Jan 2012
41)	Indonesia	-	Jul 2012

Accessions dates (3/3)

	Accession to PIC	Accession to PIC/S
42) New Zealand	-	Jan 2013
43) Chinese Taipei	-	Jan 2013
44) United Kingdom (Vet)	-	Jan 2014
45) Japan	-	Jul 2014
46) Korea (Republic of)	-	Jul 2014
47) Hong Kong SAR	-	Jan 2016
48) Croatia/HALMED	-	Jan 2016
49) Thailand FDA	-	Aug 2016

49 PIC/S Members (as at 4 April 2017)

5 PIC/S Applicants & 1 Pre-Applicant



Blue: 49 PIC/S Members
Yellow: 5 Applicants
Red: 1 (Pre-) Applicant

5 PIC/S Applicants & 1 Pre-Applicant

5 Applicants

Brazil/ANVISA
IRAN / IFDA
Mexico / COFEPRIS
Turkey/TMMDA
Italy (Vet) / DGSAF

1 Pre-Applicant

Kazakhstan / CCMPA

Agencies showing interest in joining PIC/S

- **Armenia / SCDMTE**
- **Saudi Arabia / SFDA**
- **Vietnam / DAV**
- Bulgaria / BDA
- China / CFDA
- Nigeria / NAFDAC
- Russia / SID&GP
- Uganda / NDA
- Zimbabwe / MCAZ

1. Pre-accession procedure

- As some of the new applicants may have notable differences or are not familiar to PIC/S standards, a new “period” offers a “softer” approach and more time to adjust.
- It is a kind of pre-assessment and gap analysis of the Applicant Authority to the PIC/S requirements and a possible on site visit of an “auditor” appointed by the Committee
- Time frame up to 2 years
- Then, time to decide for the application. Is the Applicant ready?

  The Committee will decide on the next steps (invitation to apply or further delay to prepare)

2. Membership Accession procedure

Steps to Accession

- General interest & commitment, eg. attend Seminars
- Written application to Secretary + supporting documents
- PIC/S Committee appoints Rapporteur to evaluate
- Applicant invited to Committee meeting to answer questions of Rapporteur and Committee
- PIC/S delegation undertakes assessment visit (Inspectorate's procedures; observe 3 or 4 inspections)
- Delegation report issued (to applicant & Committee)
- Committee decides on membership.

Benefits of PIC/S Membership (1/2)

(For NDRA, National Drug Regulatory Authorities)

- ✓ Training opportunities(seminars, Joint Inspections, etc.)
- ✓ International GMP harmonisation (Involvement with developing international GMPs)
- ✓ Networking with other Inspectors (for calibration of GMP expectations and facilitate information sharing)
- ✓ High standards (Accession forced improvements – i.e. discipline)
- ✓ Exchange / Sharing of information
- ✓ Rapid Alert System
- ✓ Facilitate the conclusion of other Agreements (Facilitate Government to Government MRA: E.g. Australia/TGA MRA, ASEAN MRA)

Benefits of PIC/S Membership (2/2)

For Industry)

- ✓ Reduced duplication of inspections
- ✓ Cost saving
- ✓ Export facilitation
- ✓ Enhanced market access

How PIC/S operates?

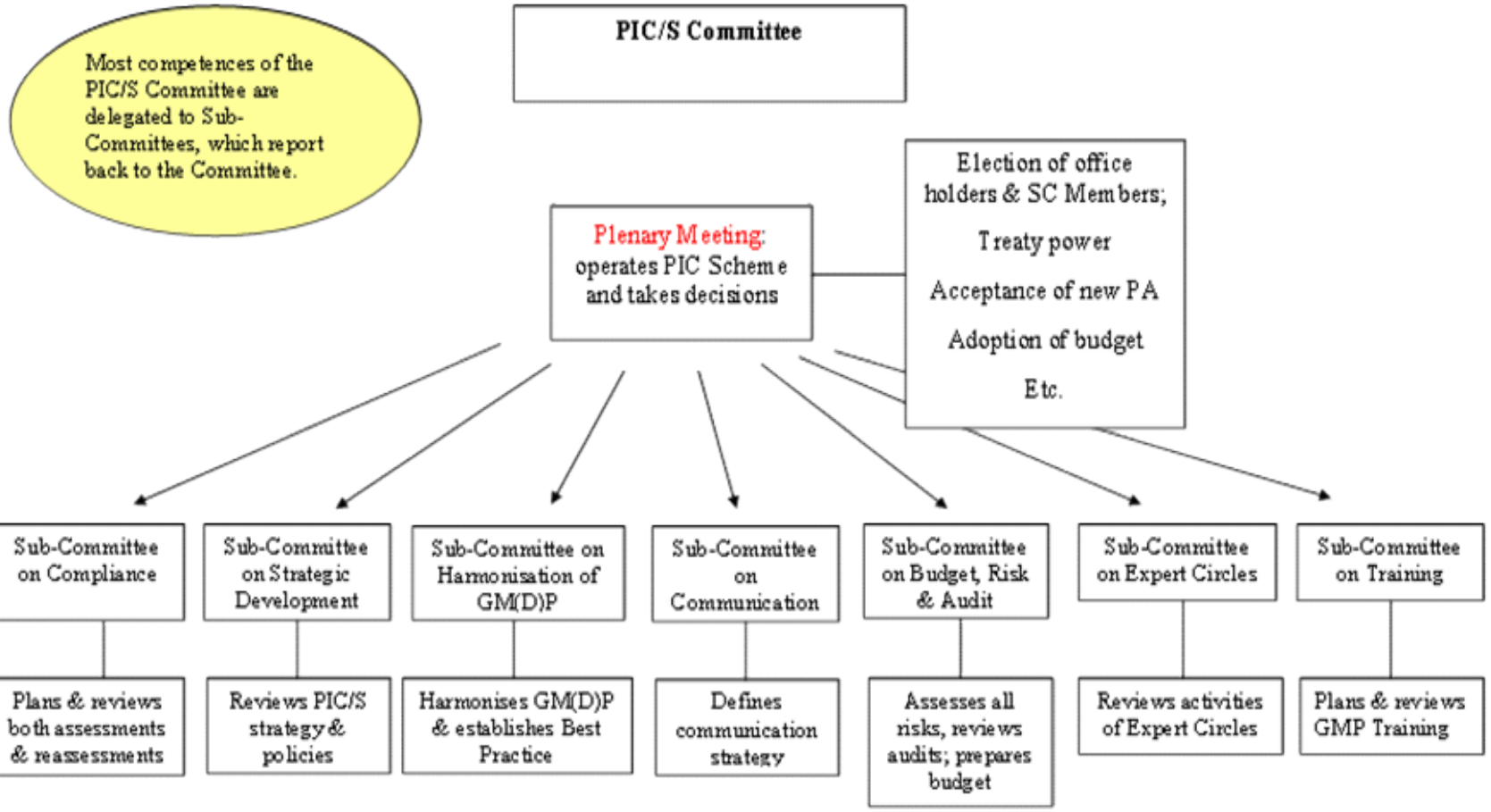
- PIC/S Committee
- Secretariat
- Executive Bureau: Chair, Deputy Chair, immediate past Chair, seven Chairs of Sub-Committees
- Small Budget
- Good relationship and co-operation
- Training opportunities
- Exchange of information, rapid alerts
- Development of GMP guidelines

New PIC/S Organisational Sub-Committee Structure

To reply to PIC/S's growing membership, a new Sub-Committee structure has been developed and come in force on 1st January 2014, in order to:

- Favour the participation of all PIC/S Participating Authorities
- Establish a more participative and efficient organisation of PIC/S, where each Sub-Committee will be responsible for its respective core areas and will take the lead in developing policies.

PIC/S new structure as of 1 January 2014



PIC/S GMP Guide (1/2)

Virtually identical to EC GMP Guide
(main difference = "Qualified Person" vs. "authorised person")

Basic GMP Guide (Part I)

GMP Guide for APIs (Part II)

Plus Annexes, covering:

- Sterile Medicinal Products
- Sampling of Starting Materials & Packaging Materials
- Pressurised Metered Dose Aerosols
- Liquids, Creams & Ointments
- Computerised Systems
- Radiopharmaceuticals

PIC/S GMP Guide (22)

Plus Annexes, covering:

- Biologicals
- Herbals
- Medicinal gases
- Use of Ionising Radiation
- Investigational Medicinal Products
- Products Derived from Human Blood & Plasma
- Qualification and Validation
- Parametric release
- Reference and Retention Samples

Training - A Key Feature of PIC/S (1/4)

The training of GMP inspectors has been one of PIC/S' main features since the very beginning. Training Competent Authorities, in particular inspectors, is an integral and key activity of PIC/S in achieving its mission.

Training - A Key Feature of PIC/S (2/4)

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 a key 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).

Training - A Key Feature of PIC/S (3/4)

The various PIC/S training tools have been put in place progressively. At the beginning, there was only one annual Seminar. Then, a Joint Visits Programme (JVP) was added to train inspectors and harmonise both GMP standards and inspection procedures. In the 1990s, Expert Circles in specialised areas were established. New Inspector Training Courses and Train the Trainer Courses were developed as from 2011 and 2014 respectively. The **PIC/S Inspectorates' Academy (PIA)** was established in 2014 and officially launched in 2016.

A Summary of PIC/S Training Tools (4/4)

Currently PIC/S boasts various training and harmonisation tools, which have proved to be effective and are constantly being further developed and improved. These include:

- ✓ **Seminars**
- ✓ **Expert Circles**
- ✓ **Joint Visits Programme**
- ✓ **Coached Inspections Programme**
- ✓ **Training Courses for New Inspectors**
- ✓ **Train the Trainer Courses**
- ✓ **Training for Auditors**
- ✓ **API International Training Programme**
- ✓ **Other Non-PIC/S Training Events & Tools**

More information about all PIC/S training activities and tools is available at the **PIC/S Inspectorates' Academy.**

Development of GMP Guidance Documents

- Usually initiated at end of PIC/S Seminars
- PIC/S Working Group formed
- Author prepares draft
- Comments from Working Group
- Comments from PIC/S Inspectorates
- Comments from Industry
- Endorsed by PIC/S Committee for general distribution
- Simultaneous distribution by EMA (& vice versa)

PIC/S Seminars (1/5)

- Packaging & Labelling	Switzerland, 1971
- Contamination	Sweden, 1972
- Quality	France, 1972
- Sampling & Analytical Control	UK, 1973
- Contract Manufacture & QC	Switzerland, 1974
- QC Department	Denmark, 1975
- Stability	Austria, 1976
- Isolation/ID/Quantification of Drugs	Sweden, 1977
- Tablet Manufacture	UK, 1978
- Large Volume Parenterals	Norway, 1978
- PIC Basic GMP Guide	
- (Need for Revision?)	Finland, 1979
- Tablet Manufacture	Denmark, 1980
- Manufacture of Active Ingredients	Switzerland, 1980
- Inspection & Testing in Relation to the Marketing Authorisation	Belgium, 1993

PIC/S Seminars (2/5)

- Control Laboratory	Hungary, 1981
- Validation	Ireland, 1982
- Packaging	Portugal, 1983
- Production of Biological Products	Germany, 1984
- Premises	Norway, 1985
- Plastics	Sweden, 1986
- Inspection	UK, 1987
- Water	Switzerland, 1988
- Contamination Risk in the Manufacture of Parenterals	Austria, 1989
- Blood & Blood Products	Denmark, 1990
- Audit - Pharmaceutical Inspection	Hungary, 1991
- Products Derived from Biotechnology	Italy, 1992
- Qualification & Validation	Ireland, 1994
- Manufacture of Sterile Products	Iceland, 1995

PIC/S Seminars (3/5)

- Computer Systems	Australia, 1996
- GMP Standards for APIs	Australia, 1996
- Manufacture & Inspection of APIs	Finland, 1997
- Quality Systems for Inspectorates	Holland, 1998
- Non-technical Aspects of Inspection	UK, 1999
- Biotechnology	France, 2000
- Inspection of Utilities	Czech Rep, 2001
- Interface between GCP and GMP	Canada, 2002
- Inspection of QC laboratories	Slovak Rep, 2003
- Inspection of APIs	Spain, 2004
- Primary packaging, labelling and prevention of mix-up	Romania, 2005
- Risk Management	Germany, 2006
- Solid Dosage Form Manufacturers	Singapore, 2007
- Good Distribution Practices	Poland, 2008

PIC/S Seminars (4/5)

- Sterile Aseptic Manufacturing	Sweden, 2009
- Herbal / Traditional Medicines	Malaysia, 2010
- Good Inspection Practices	South Africa, 2011
- Qualification and Validation	Ukraine, 2012
- Global Supply Chains and GMP compliance	Canada, 2013
- Dedicated Facilities or Not	France, 2014
- Biopharmaceuticals (biotechnology and biologicals): how to inspect	Indonesia, 2015
- Inspectorates of the Future 2016	UK/Manchester

Future PIC/S Seminar (5/5)

- ✓ QC Laboratory: How to inspect — Chinese Taipei 2017

- ➢ PIC/S Annual Seminar 2018 — US/FDA
- ➢ PIC/S Annual Seminar 2019:
  Japan/PMDA? Korea/MFDS? Thailand/FDA?
  Hong Kong SAR/PPBHK?

PIC/S Seminar 2016

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".

Attended by more than 180 participants from 53 countries.

PIC/S Committee Meeting & Seminar 2016

34

Manchester / UK, 4 to 8 July 2016

PIC/S Committee Meeting

Switzerland / Geneva, 9 to 10 February 2017

PIC/S Joint Visits programme(JVP)

- Started in 1987
- Around 25 groups of 3 inspectors from 3 countries
- 1 inspection per 6 months per country
- for training purposes
- for uniform GMP interpretation
- for uniform inspection procedures
- for mutual confidence

Typical PIC/S Inspection of a Medicine Manufacturer

Before the inspection *(**Pre**-inspection activities):*

- Lead inspector assigned.
- Inspection team selected.
  - Technical specialist sometimes included on team
- Company notified.
  - Company requested to provide Site Master File (SMF)
- Inspection team reviews documentation.
  - SMF, complaints, recalls, testing failures, marketing authorisations.
- Lead inspector prepares inspection plan & sends to company.
- Inspection conducted. *(**On-site**-inspection activities):*

Typical PIC/S Inspection of a Medicine Manufacturer (cont'd)

*After the inspection (**Post**-inspection activities):*

- Caucus of inspection team.
- Interim inspection report prepared (deficiencies only).
- Exit interview with company:
  - Attendance sheet completed.
  - Interim inspection report provided (discussion encouraged).
  - Written response requested within 4 weeks.
- Objective evidence assessed by lead inspector.
- If response judged OK, inspection closed out.
- Final inspection report sent to company
- If response not OK, refer to Independent Committee for appropriate action.

PIC/S Inspection Report

- Identical to the EU Inspection Report format
- SOP for PIC/S Inspection Report format is available on PIC/S web site (document PI 013-3)
- This format used by PIC/S and EU Inspectorates to prepare GMP inspection reports
- Uniform system of classifying GMP deficiencies
  - "critical", "major" & "other"

Quality system requirements for pharmaceuticals inspectorates

- Reference document : PI 002-3
- Purpose : adopting a common standard for quality system requirements in order to achieve consistency in inspection standards between National Pharmaceutical Inspectorates and thus to facilitate mutual recognition of those Inspectorates

Joint Reassessment programme (JRP)

Goals

- To verify that PIC/S member authorities maintain compliance with the requirements of the Scheme (as described in paragraph 8 of the Scheme [PIC/S 1/95 modified]).
- To verify the implementation of quality system requirements for pharmaceutical inspectorates.
- To help maintain consistency among PIC/S member authorities

PIC/S Blueprint

- PIC/S Blueprint for the period 2006-2015 (A 10-year master plan adopted in Dec 2005) have been successfully implemented and even surpassed in some cases. E.g. membership anticipation.

- **A new PIC/S Blueprint : PIC/S ROAD-MAP FOR 2017-2019** (next 3 years) includes an action plan has been drafted (Status: under finalisation and to be adopted)

  The objectives are to:

  - enhance PIC/S' Sub. Comm. structure and full implementation of PIA;
  - identify PIC/S' next challenges and possible solutions;
  - strengthen the PIC/S Secretariat; and
  - identify new income revenues to support / finance PIC/S' projects.

Where is PIC/S now?

International Harmonisation: 1970: PIC/S Original Goals 1/5

- ✓ Harmonised GMP requirements
- ✓ Mutual recognition of inspections
- ✓ Uniform inspection systems
- ✓ Training of Inspectors
- ✓ Mutual confidence

International Harmonisation 2/5

- 47 years on, Goals remain the same, in the ever changing field of pharmaceuticals.
- PIC/S has had to adapt and change to meet many challenges since its inception in 1970.
- Is PIC/S relevant today?

International Harmonisation 3/5

Drug Regulatory Authorities appear to think so:

- 49 Participating Authorities;
- 5 Applicants;
- 1 Pre-Applicant;
- Preliminary enquiries from a number of Authorities.

International Harmonisation 4/5

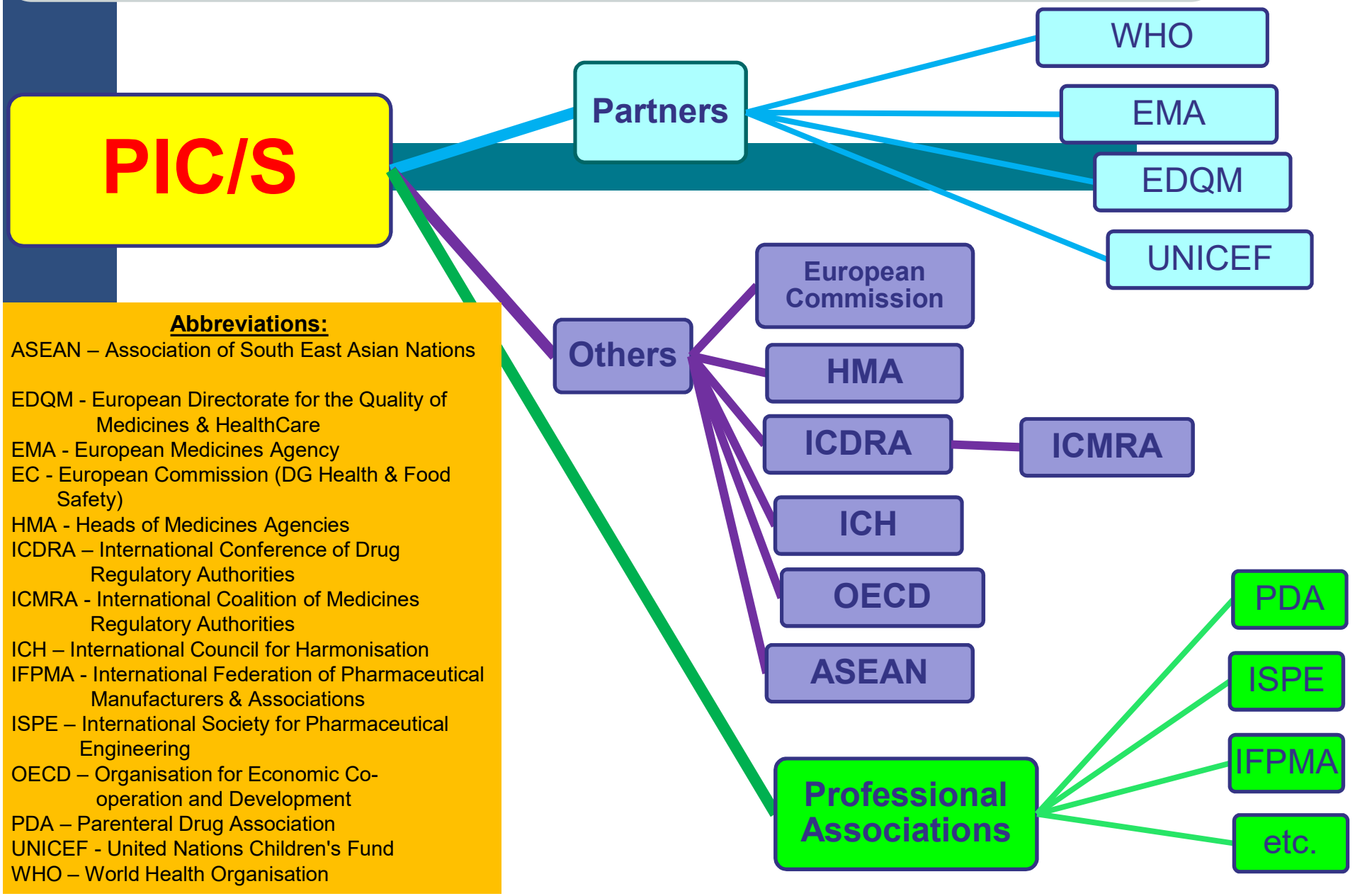
How does PIC/S achieve international harmonisation of inspections and GMP?

- ✓ PIC/S GMP Guide
- ✓ Guidance documents and Q&As
- ✓ Expert Circles
- ✓ Working Groups
- ✓ Annual Seminars and other tools for training of inspectors :
  - Joint visits programme(JVP),
  - coached inspections programme(CIP),
  - training for new inspectors & train the trainer, training for auditors, API international training programme (all under PIA)

International Harmonisation 5/5

- Joint Reassessment Programme (JRP) harmonised with EMA Joint Audit Programme(JAP)
- Exchange of information on planned foreign inspections
- SOP for informing foreign regulatory authorities for inspections to be conducted in their territory
- Single Point of Contact (SPOC) with 49 Participating Authorities (Committee member)

International co-operation with Partners and other Organisations



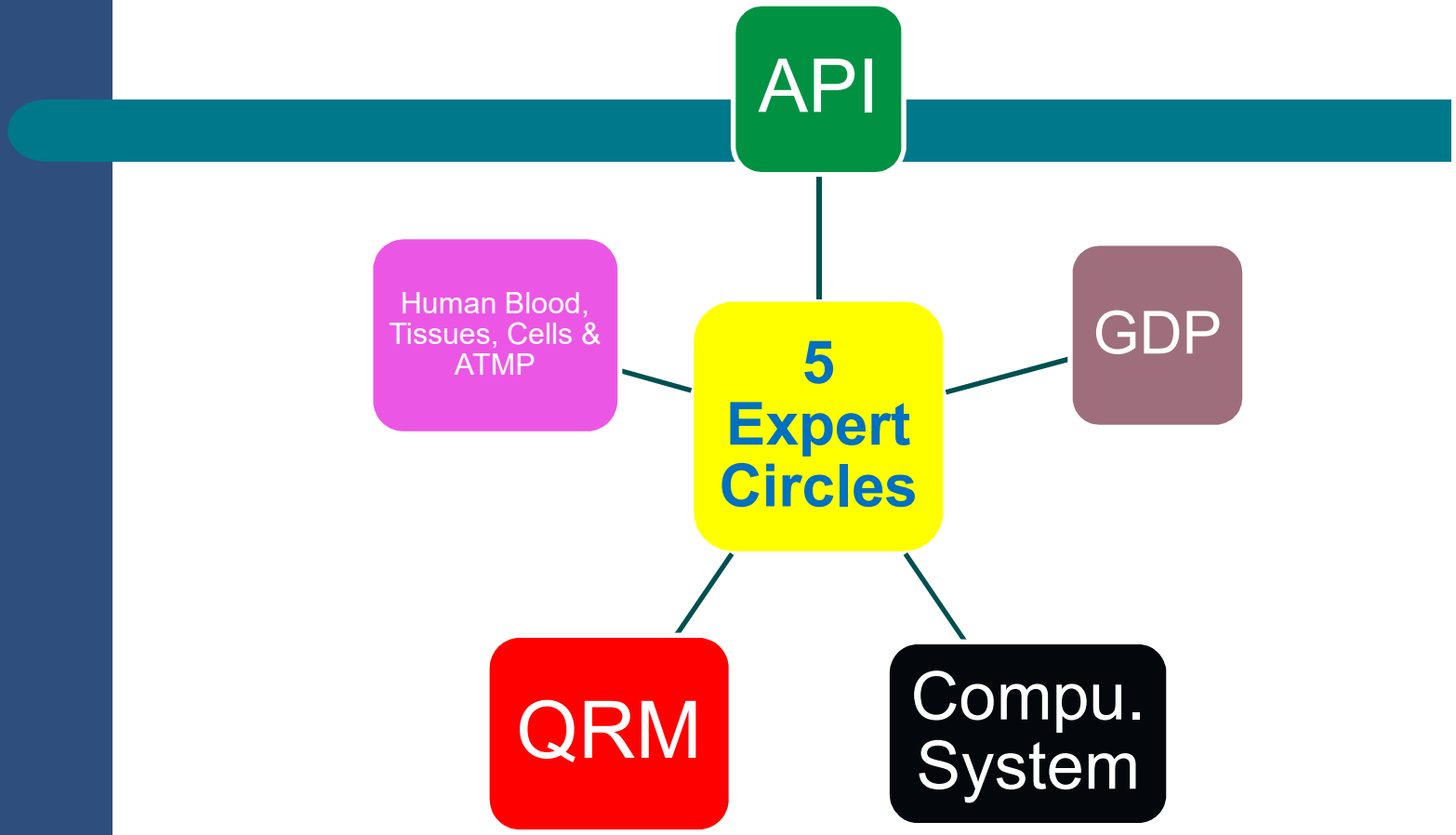
Abbreviations:

ASEAN – Association of South East Asian Nations

EDQM - European Directorate for the Quality of Medicines & HealthCare
EMA - European Medicines Agency
EC - European Commission (DG Health & Food Safety)
HMA - Heads of Medicines Agencies
ICDRA – International Conference of Drug Regulatory Authorities
ICMRA - International Coalition of Medicines Regulatory Authorities
ICH – International Council for Harmonisation
IFPMA - International Federation of Pharmaceutical Manufacturers & Associations
ISPE – International Society for Pharmaceutical Engineering
OECD – Organisation for Economic Co-operation and Development
PDA – Parenteral Drug Association
UNICEF - United Nations Children's Fund
WHO – World Health Organisation

International Harmonisation

PIC/S Expert Circles (EC)

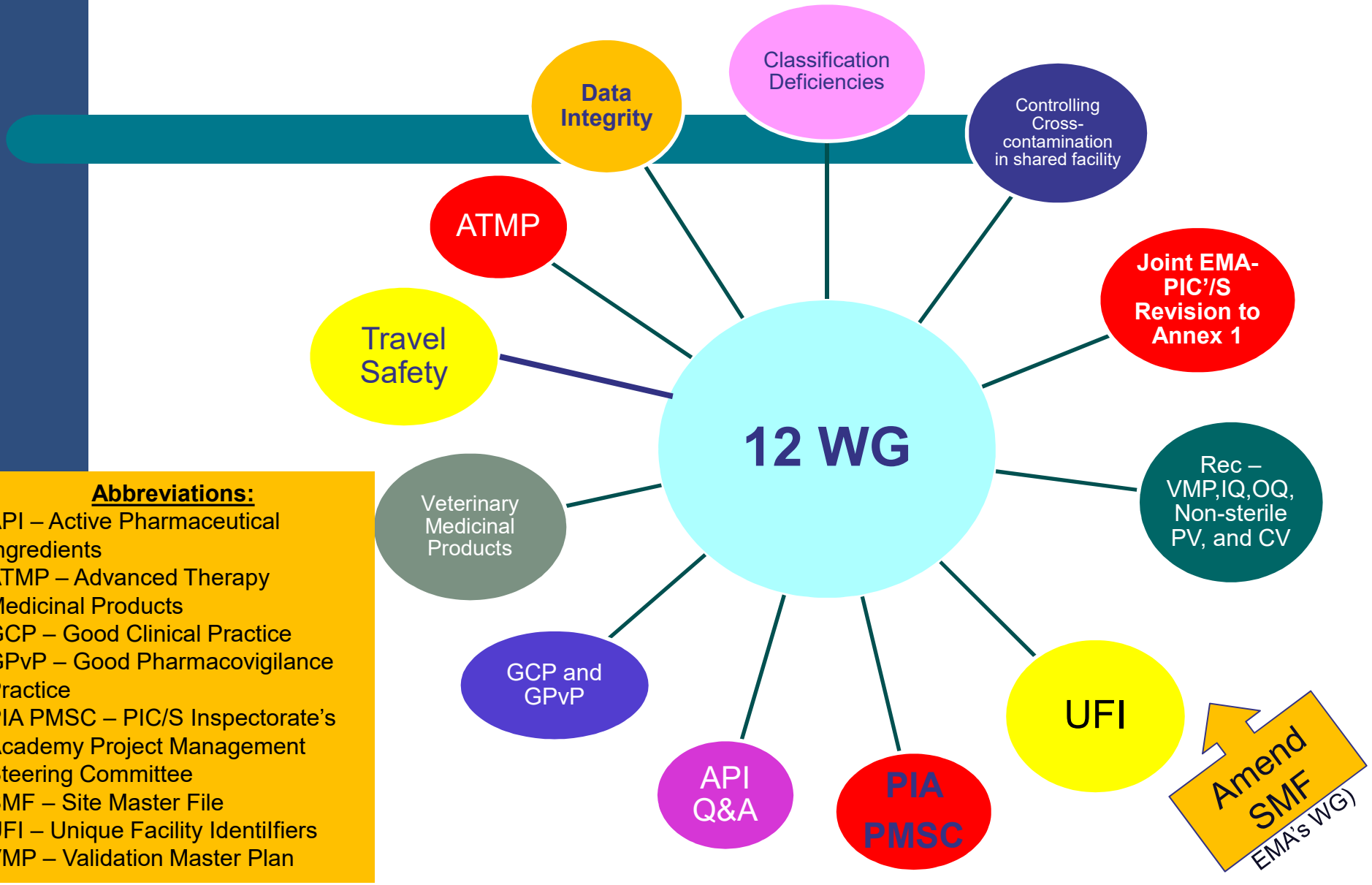


Abbreviations:

API – Active Pharmaceutical Ingredients
ATMP – Advanced Therapy Medicinal Products
QRM – Quality Risk Management
GDP - Good Distribution Practice
Compu. System: Computerised System

International Harmonisation

PIC/S Working Groups (WG)



Abbreviations:

API – Active Pharmaceutical Ingredients
ATMP – Advanced Therapy Medicinal Products
GCP – Good Clinical Practice
GPvP – Good Pharmacovigilance Practice
PIA PMSC – PIC/S Inspectorate's Academy Project Management Steering Committee
SMF – Site Master File
UFI – Unique Facility Identilfiers
VMP – Validation Master Plan

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 1/12

WG on Harmonisation of Classification of Deficiencies

- A guidance drafted to harmonise risk classification of GMP deficiencies
- "Calibration" among PIC/S PAs to facilitate consistency

Status:

- Integrating (i) input from the PIC/S Seminar 2016 and (ii) comments received from the PIC/S QRM Expert Circle and the WG on DI.
- 2nd Internal consultation will follow… (Q2 or Q3 / 2017)

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 2-1/12

WG on Advanced Therapy Medicinal Products (ATMPs)

- To draft an Aide-Memoire to support the inspection of ATMPs.
- Status: on hold while awaiting the outcome of discussions on ATMPs in the EU.

Geneva (Feb 2017) Committee Meeting:

Unanimous concern at the EC's proposed stand-alone ATMP GMP Guidelines

- Lower GMP standards for ATMP at the risk of patients safety
- Lead to an international non-harmonised approach to the implementation of GMP for ATMP. (Loss of harmonisation, lack of integration, risk of confusion, double-standards, impact ATMP availability and regulatory burden and etc.)
- EC's proposal will also trigger a revision of EU GMP Guide Annex 2 (Biologics) and the repeal and replacement of Annex 13 (IMP), these actions will also result in the PIC/S GMP Guide and the EU GMP Guide no longer being equivalent.

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 2-2/12

WG on Advanced Therapy Medicinal Products (ATMPs)

Since the launch of the EU stakeholder consultation back in 2015, PIC/S has repeatedly tried to engage with the EC to draw attention on the potential detrimental effects of this initiative.

The EC ignored all PIC/S's voicing / requests for co-operation, including a proposal by PIC/S to form a joint working party with the EMA IWG

The PIC/S Committee reviewed various options and concluded that all PIC/S can do is to draw the EC's attention on its responsibilities. A letter to this effect dated 24 Feb 2017 has been addressed to the Director General for Health and Food Security of the EC. The letter is also published on the PIC/S website for reasons of transparency.

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PIC/S Secretariat
14, Rue du Roveray
CH-1207 GENEVA
Tel: +41 22 738 92 15/16
E-mail: [illegible]
Web site: [illegible]

PS/L 11/2017
24 February 2017

By registered mail & e-mail
(xavier.prats-monne@ec.europa.eu)

Mr
Xavier Prats Monné
Director General
Health and Food Security (DG SANTE)
European Commission
B-1049 Brussels
Belgium

Dear Mr Prats Monné,

Subject: Guidelines on Good Manufacturing Practice for Advanced Therapy Medicinal Products

With reference to our previous exchange of communication, in particular our letter dated 7 October 2016 and your reply dated 21 November 2016, we would like to revert to the European Commission's proposal to lower GMP requirements for Advanced Therapy Medicinal Products (ATMPs), as contained in the above-mentioned, stand-alone GMP Guidelines.

The PIC/S Committee, which comprises representatives of PIC/S' 49 Participating Authorities as well as representatives from Partner Organisations such as EMA, EDQM and WHO, has discussed the matter at its last meeting in Geneva on 9-10 February. As you know, PIC/S is a purely technical experts' organisation active in the field of GMP since 1971. PIC/S' expertise in the field of GMP is undisputed.

The PIC/S Committee is unanimously concerned about the impact on public health and for the safety of patients that the ATMP GMP Guideline will cause. By lowering the GMP requirements for ATMPs, the European Commission is not only exposing patients to an increased risk to their health; it is also engaging its individual and collective responsibility for any health incident (and related court action) that lower ATMP standards may occasion. We would like you to duly ponder this aspect.

The PIC/S Committee is also concerned that due to the European Commission's initiative in the field of ATMP, the PIC/S GMP Guide and the EU GMP Guide will no longer be equivalent. Since 1989, both Guides have been developed in parallel and systematically kept aligned on the basis of a harmonised consultation procedure, which PIC/S and the EMA have duly and respectfully implemented. Your decision to amend Annex 2 and repeal Annex 13 of the EU GMP Guide is a serious setback in terms of co-operation between the EU and PIC/S. It is very unfortunate that under your leadership the process of GMP harmonisation between the EU and PIC/S GMP Guides has resulted in a divergence that may be difficult to reconcile in the future. We deeply regret the lack of consultation in this matter.

With regard to allegations that some PIC/S Participating Authorities have enacted lower GMP requirements for ATMP, as mentioned in your letter, we believe that there may have been a misunderstanding on the European Commission's part. Some Participating Authorities may have introduced non-binding guidelines regarding ATMPs. However, these guidelines do not overrule GMP requirements, as enshrined in the national GMP Guide. Moreover, where ever there is a slight difference in terms of requirements for ATMPs, PIC/S Participating Authorities have expressed their will to align and harmonise their requirements with those of PIC/S. The international harmonisation of GMP standards is a never-ending process, which PIC/S aims to facilitate. PIC/S Participating Authorities are disappointed in the decision made by the European Commission to enact its standalone Guidelines on ATMPs, which will add barriers in the field of GMP and make harmonisation efforts more difficult.

We have tried our best to draw your attention to the risks that lower ATMP standards may have on the patients' health. Patient health risks aside, PIC/S would like to remind the European Commission of liabilities to which it may be exposed.

For the sake of transparency and the rights of patients, this letter will be published on the PIC/S website.

Yours sincerely,

Paul Hargreaves
PIC/S Chairman
United Kingdom / MHRA

Boon Meow Hoe
PIC/S Deputy Chairman
Singapore / HSA

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 3/12

WG on Data Integrity (DI)

Status:

- Completed draft guidance document on “PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments”.
- Will review the PIC/S-internal comments to the draft (6 months trial ended 28 Feb 2017)
- WII also review guidance documents issued by other organisations on DI in order to make the PIC/S guidance as complete as possible.
- Will then develop an Aide Memoire and Q&A.

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 4/12

WG on Controlling Cross-Contamination in Shared Facilities (CCCISF)

Status:

- An Aide Memoire has been drafted. Focusing on harmonising terminology used in relation with the control of cross-contamination in shared facilities and relevant inspection questions in connection to risk management.
- Under internal consultation within PIC/S (deadline: 21 Apr 2017)
- Committee Meeting (Geneva Feb 2017) agrees to turn the WG on CCCISF into an Expert Circle.

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 5/12

WG on Veterinary Medicinal Products

- Aims to better take into account the needs and specificities of Veterinary Agencies within PIC/S

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 6/12

WG on Good Clinical Practice (GCP) and Good Pharmacovigilance Practice (GPvP)

- 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
- Very active WG using the PIC/S Joint Visits Programme (JVP).
- Status: Contemplating to convert WG to an Expert Circle

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 7/12

EMA – PIC/S Joint Drafting Group on the revision of Annex 1 (sterile manufacturing) of the PIC/S-EU GMP Guide

Status:

- A joint public consultation will be launched with the EMA after approval of the final draft by the PIC/S Committee and the EMA.
- The Committee Meeting (Geneva, Feb 2017) also agreed to involve WHO in the joint publication of this document, as well as in several other future PIC/S guidance documents (E.g. DI, Deficiency classification and etc.).

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 8/12

PIC/S Project Management Steering Committee (PMSC) in charge of the PIC/S Inspectorates' Academy (PIA)

- Development of web-based platform.
- Aim: 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 current 1,800 PIC/S inspectors.

- Status: Stage 1: Completed
  Stage 2: Current stage
  Stage 3: Will commence after end of Stage 2

- Will be illustrated more in later slides on PIA

International Harmonisation: PIC/S PIC/S Working Groups (WG) 9/12

WG 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.

- Status: Created at Manchester Meeting (July 2017)

International Harmonisation: PIC/S PIC/S Working Groups (WG) 10/12

WG on the API Q&A developed by PIC/S

- **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.**

- Status: Created WG at Manchester Meeting (July 2016)

International Harmonisation: PIC/S PIC/S Working Groups (WG) 11/12

- Established a new Working Group on inspector travel safety with the objective of developing guidance for inspectors on managing travel risks;
  - Status: A new WG -- newly created at Geneva Feb 2017 Meeting

International Harmonisation: PIC/S
PIC/S Working Groups (WG) 12/12

WG on Unique Facility Identifiers (UFI)

Last Committee meeting (Geneva , Feb 2017) established a new WG on Unique Facility Identifiers (UFI), to respond to the need for an internationally recognized UFI to be selected for use by international regulators;

- Status: A new WG

International Harmonisation: PIC/S EMA's Working Groups (WG) 13/12

- Participation of PIC/S in:
  - EMA Drafting Group to amend **Site Master File** re: mitigation of drug shortages
  - Status: WIP

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 1/5

Expert Circle on Active Pharmaceutical Ingredients (API)

Leads PIC/S API International Training Programme:

- ICH Q7 Training for inspectors and industry, co-organised with PDA;
- Advanced API Training for inspectors only (e.g. counterfeits, data integrity, etc.)
- API Q&A, including PIC/S contribution to ICH Q&A document on Q7 published in June 2015

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 1/5 continue…

Expert Circle on Active Pharmaceutical Ingredients (API)

- PIC/S - PDA ICH Q7 trainings:
  - 2012 in China and Portugal;
  - 2014 in USA, South Africa and Belgium;
  - 2015 in South Korea, Brazil, India and China, with the support of the European Commission;
  - 2016 in Puerto Rico

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 1/5 Continue…

Expert Circle on Active Pharmaceutical Ingredients (API)

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

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 2/5

Expert Circle on Quality Risk Management

- Advanced training for inspectors:
  - 2014 hosted by PMDA Japan
  - 2015 hosted by FDA USA
  - 2016 hosted by the EMA in London (United Kingdom), 26 – 28 September 2016

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 3/5

Expert Circle on Human Blood, Tissues, Cells and ATMPs

- 21st EC Meeting in Rome (Italy), 26–30 Oct 2015 hosted by AIFA/Italy. 120 inspectors from 36 countries attended.
- 22nd EC Meeting - hosted by Hong Kong SAR / PPBHK in Hong Kong SAR, 24-28 Oct 2016
- 23rd EC Meeting - To be hosted by Korea (Republic of) / MFDS on 26-28 June 2017 in Seoul (Republic of Korea)

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 4/5

Expert Circle on Computerised Systems

- After a very busy and active few years this EC has now been turned into a Working Group focusing on:
  - Revision of the PIC/S Guidance Document on Good practices for Computerised Systems in regulated GxP environments.

International Harmonisation: PIC/S
PIC/S Expert Circles (EC) 5/5

Expert Circle on Good Distribution Practice (GDP)

- The 4th meeting was hosted by South Africa / MCC on 12-14 April 2016 in Pretoria.
- 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.
- Completed draft Aide Memoire for GDP Inspections and draft Q&A on GDP.

PIC/S INSPECTORATES ACADEMY

PIA = PIC/S Inspectorates' Academy

Inspection Excellence Through Harmonised Training

What is PIA & What is PIA going to be ?

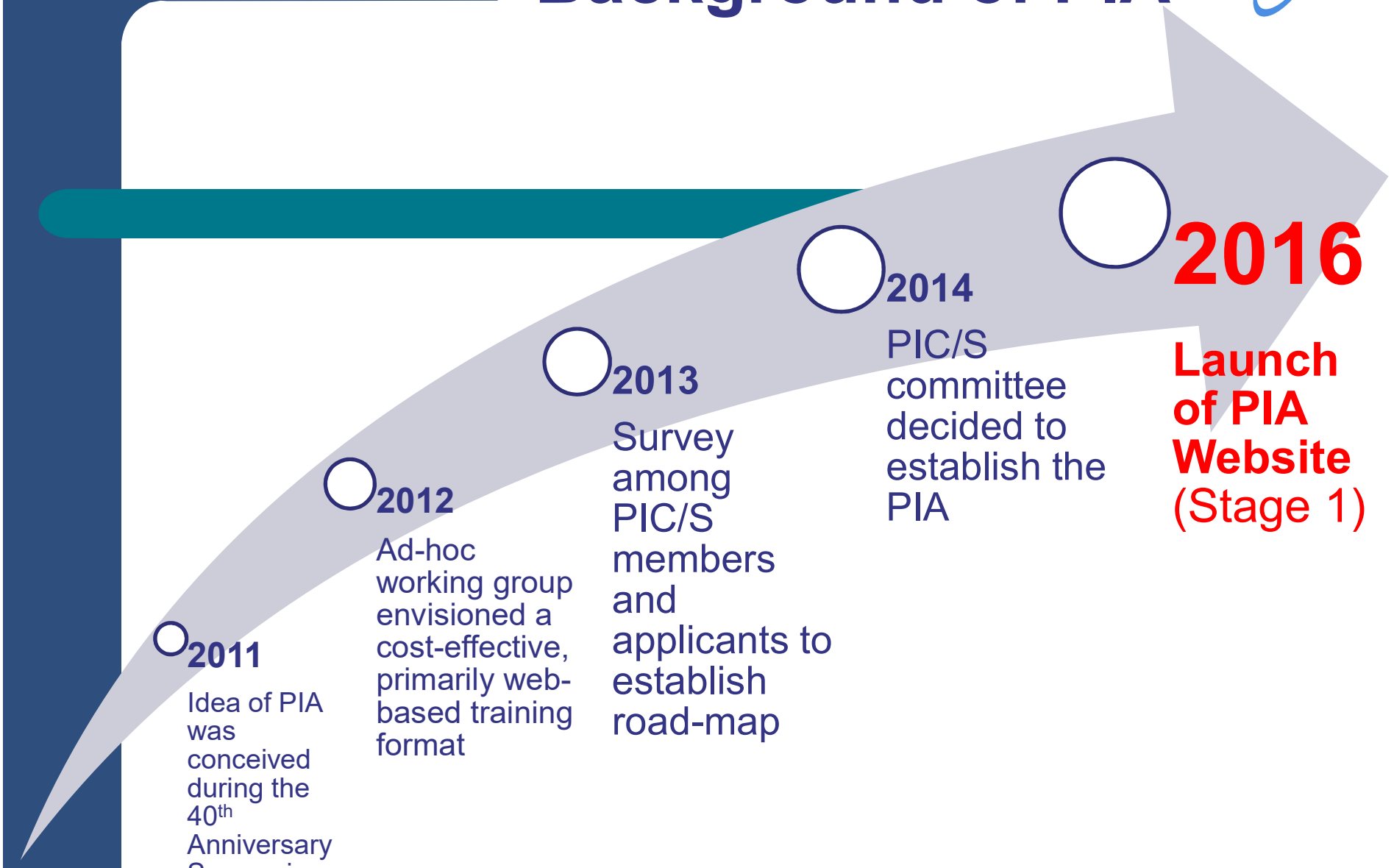
Web-based educational centre &
Accredited qualification system

Single Point of access to all
PIC/S training activities

Platform for discussion &
Sharing among inspectors

Inspection Excellence Through Harmonised Training

Background of PIA



Stages of Development

Stage 1

- Establishment of the PIA and development of website
- Launch of PIA Website

Stage 2

- Identification of training needs
- Development of modules (e-learning) with possible co-operation with external stakeholders
- Seeking funding
- Establish recognition and certification process

Stage 3

- Formal incorporation of PIA
- Development of PIA training curriculum
- International recognition

Official launch of PIA Webpage

The new (enhanced) PIC/S web site and PIA (the sub-site), rolled out on 18th July 2016.

STAGE 1 COMPLETED

The official launch marks end of Stage 1

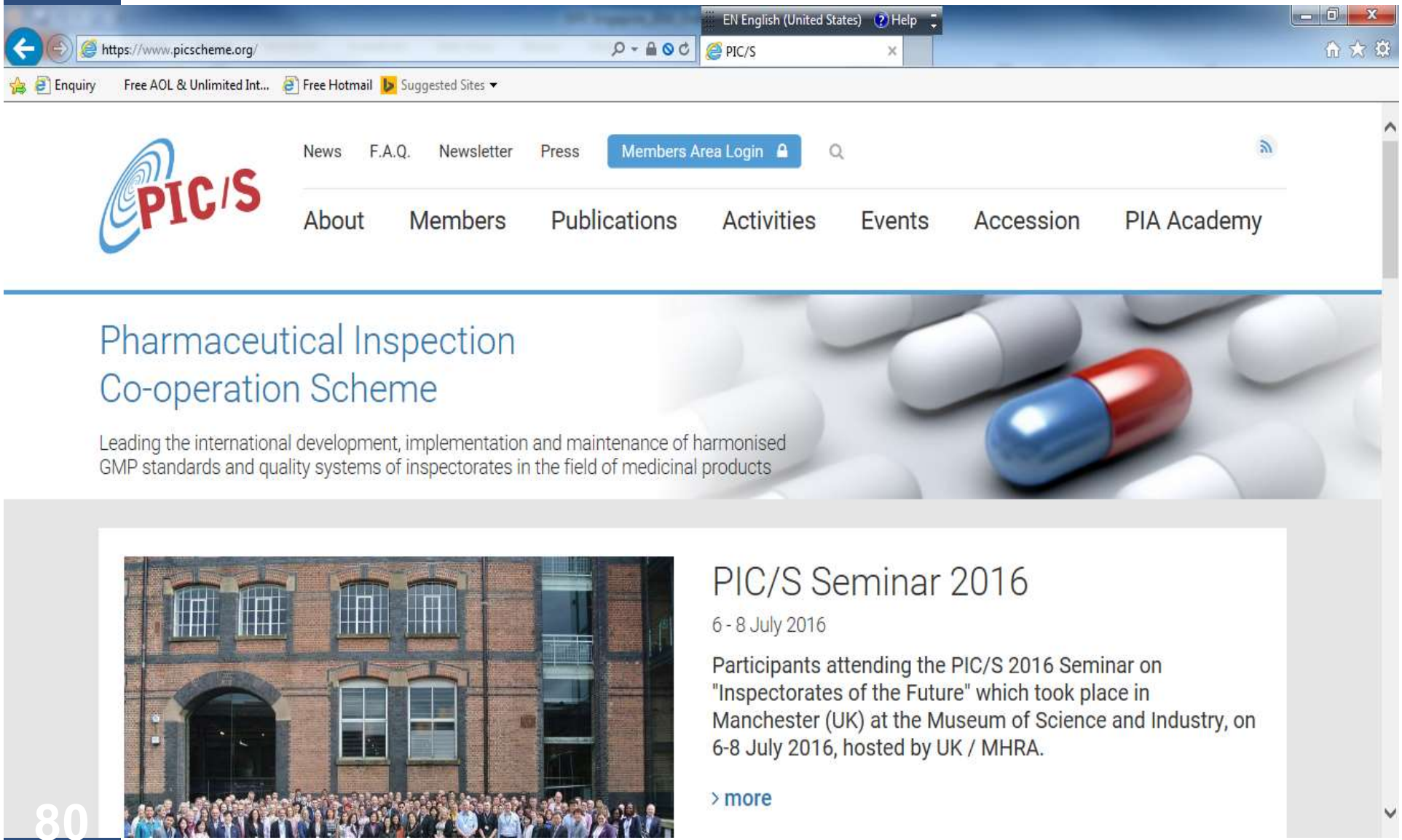
It also marks commencement of Stage 2

PIC/S INSPECTORATES' ACADEMY (PIA)

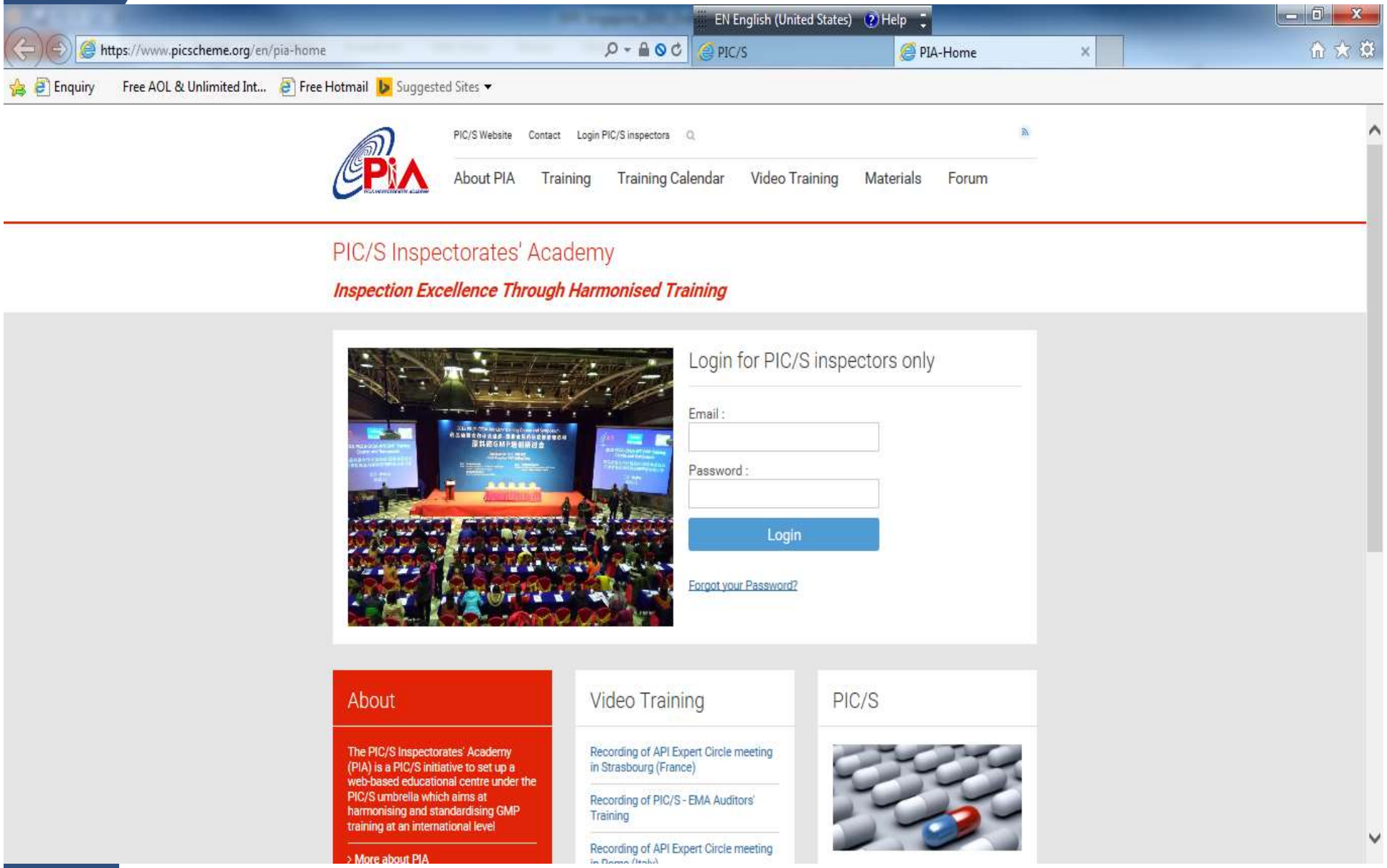
Status: As at last PIC/S Committee meeting (Geneva Feb 2017):

- The PIC/S EB reviewed and discussed priorities in the implementation of the PIA .
- The EB 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) as well as consultants.
- Funding remains a key consideration.

NEW (Enhanced) PIC/S Webpage
www.picscheme.org



NEW PIA Webportal



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Update on PIC/S GMP Guide

(If time permits to cover this section)

Revised PIC/S GMP Guide – Last Revision & Adoption - If time permits

Annex 15 – Qualification and Validation (PE 009-12)	With effective from: 1 Oct 2015

Revised PIC/S GMP Guide - Main changes - If time permits

Chapter 1- Pharmaceutical Quality System (f.k.a. Quality Management)

Chapter 2 - Personnel

Chapter 6 - Quality Control

Chapter 7 - Outsourced Activities

(f.k.a. Contract Manufacture and Analysis)

With effective from:

1 Jan 2017

Revised PIC/S GMP Guide:
Under consultation If time permits

Chapter 3- Premises and Equipment

Chapter 5 - Production

Chapter 8 – Complaint and Product Recall

Notes: The same applies to the following EMA guidance documents, which have been transposed for PIC/S purpose and reached Step 1 adoption process:

- Guidelines on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (PI 041-1 (Draft 1)).
- Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (PI 042-1 (Draft 1));
- Guidelines on the principles of Good Distribution Practices for actives substances for medicinal products for human use (PI 043-1 (Draft 1)).

Status: Under Stage 1 adoption process

Deadline: Extended to **31 Jan 2017**

The philosophy of PIC/S:

TRUST

+ COOPERATION

+ COLLABORATION

+ COMMUNICATION

HARMONISATION