Pharmaceutical Inspection Co-operation Scheme (PIC/S)

40 years of Co-operation & Mutual Confidence

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Overview

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- Accession procedure
- Guides & recommendations
- Seminars & expert circles
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- Joint re-assessment program
- Liaison with other organisations
- Typical PIC/S inspection of a medicinal product manufacturer
- Moving forwards
- PIC/S contacts

History

Original goals

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

History

PIC = Pharmaceutical Inspection Convention

- Founded by The European Free Trade Association (EFTA) in October 1970
- Is a legal Treaty between countries
- Initially only 10 member countries: Austria, Denmark, Finland, Iceland, Liechtenstein, Norway, Portugal, Sweden, Switzerland and UK.

History

PIC membership as at January 1995

18 Member countries:

Australia, Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Liechtenstein, Norway, Portugal, Romania, Sweden, Switzerland, United Kingdom.

History

Reasons for creating the PIC Scheme

- After 1993, no new members of PIC possible
- Reasons:
- Under EU law, only European Commission authorised to sign agreements with other countries
- Expansion of PIC not possible unless European Commission became a member of PIC
- Amendment of Convention difficult & lengthy
- Inspectorates (& industry) favoured maintaining the principles of PIC
- Consequently, the PIC Scheme was developed & implemented.

Role and functions of PIC/S

PIC	Pharmaceutical Inspection Convention
PIC Scheme	Pharmaceutical Inspection Cooperation Scheme

Both operate in parallel under the logo/abbreviation

Role and functions of PIC/S

Main features of PIC Scheme

- Commenced operating on 2 Nov. 1995
- An informal arrangement between Agencies
- Networking and confidence building
- Exchange of information and experience on GMP
- Development of Quality Systems for Inspectorates
- Training of inspectors
- International harmonisation of GMP
- No obligation to accept inspection reports
- PIC & PIC/S operate in parallel - jointly referred to as **“PIC/S”**

Role and functions of PIC/S

PIC/S Goal

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

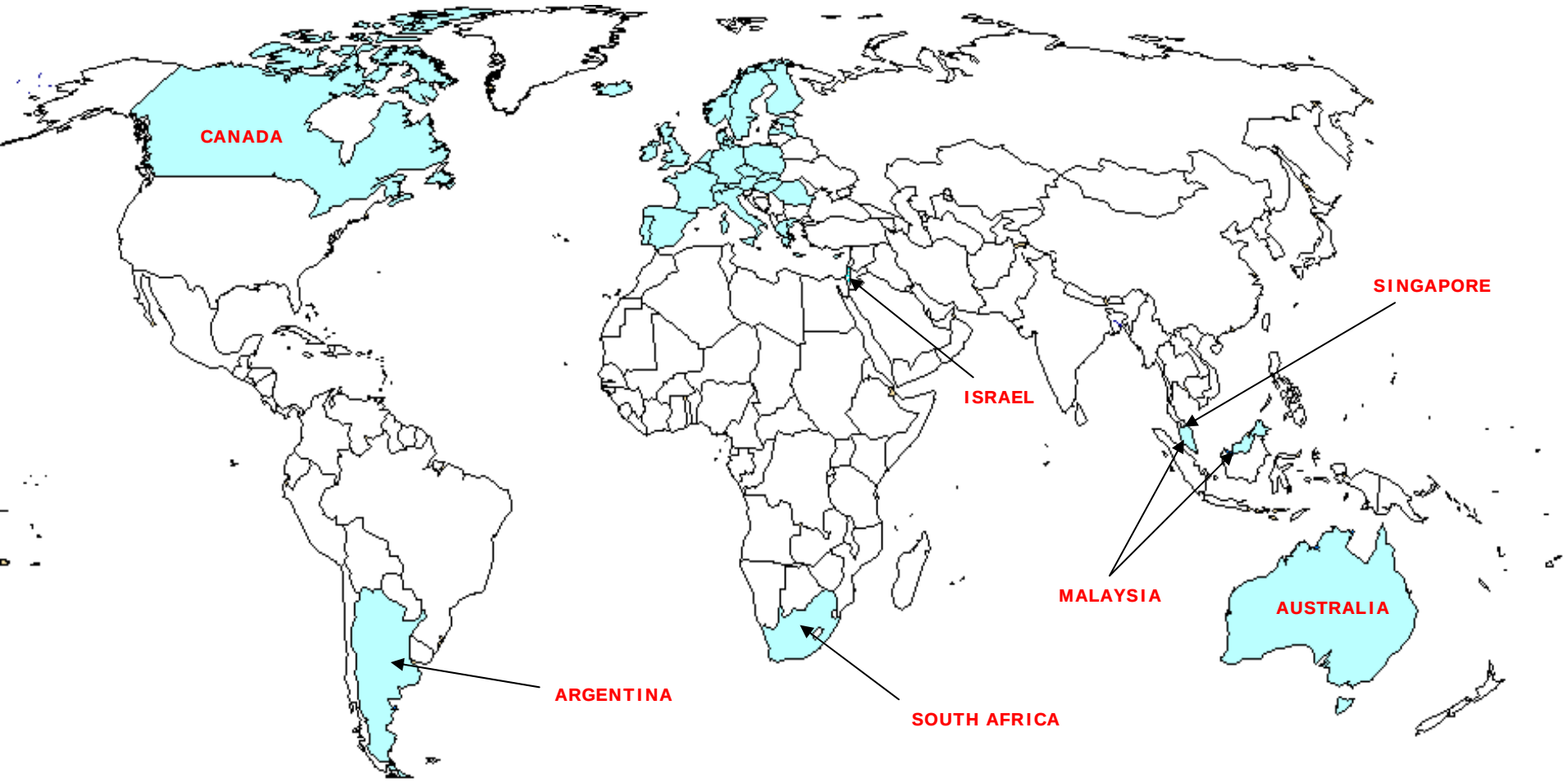
Role and functions of PIC/S

Achievement of PIC/S Goal

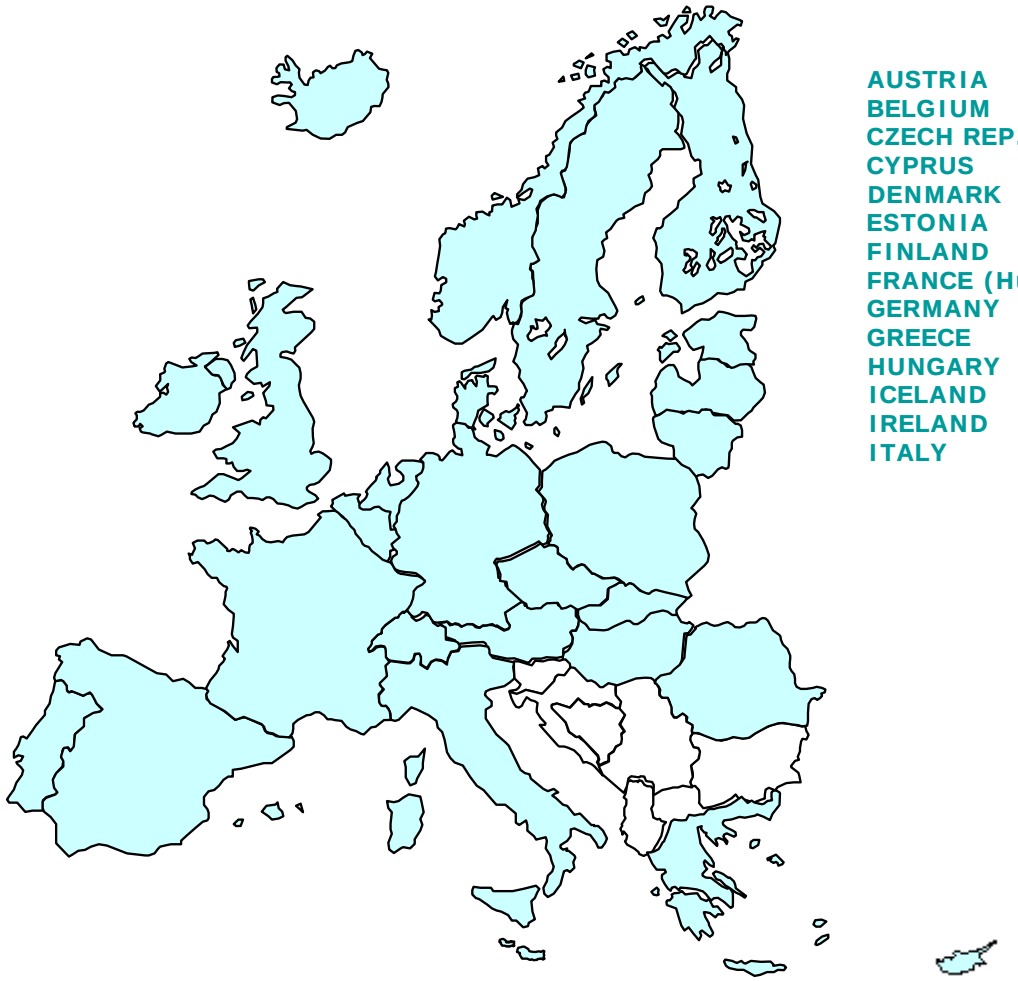
PIC/S Goal to be achieved by:

- ✓ 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.

37 PIC/S Members



PIC/S Members (Europe)



AUSTRIA
BELGIUM
CZECH REP. (Human & Vet)
CYPRUS
DENMARK
ESTONIA
FINLAND
FRANCE (Human & Vet)
GERMANY
GREECE
HUNGARY
ICELAND
IRELAND
ITALY
LATVIA
LIECHTENSTEIN
LITHUANIA
MALTA
NETHERLANDS
NORWAY
POLAND
PORTUGAL
ROMANIA
SLOVAK REPUBLIC
SPAIN
SWEDEN
SWITZERLAND
UNITED KINGDOM

Role and functions of PIC/S

PIC versus PIC/S

PIC

- Convention
- Between countries
- A formal treaty
- Has legal status
- Focus on inspection
- Mutual recognition of inspections

PIC/S

- Scheme
- Between agencies
- An informal arrangement
- Has no legal status
- Focus on training & Developing guidelines
- Exchange of information

Role and functions of PIC/S

Benefits of PIC/S Membership

- ✓ Accession forced improvements – i.e. discipline
- ✓ Cost saving – import control mechanism
- ✓ Facilitated exports of medicines
- ✓ Training (seminars, Joint Inspections, etc.)
- ✓ Involvement with developing international GMPs
- ✓ Facilitated MRA with EC
- ✓ Networking & personal contacts

Role and functions of PIC/S

How PIC/S operates

- PIC/S Committee
- Secretariat
- Executive Bureau : Chairman, two Deputy Chairmen, past Chairman, two Members of PIC/S Committee, two alternate Members
- Small Budget
- Good relationship and collaboration
- Training opportunities
- Exchange of information, rapid alerts
- Development of GMP guidelines

Accession procedure

Useful Documents

- Pharmaceutical Inspection Cooperation Scheme (PIC/S 1/95)
- Guidelines for Accession to PIC/S (PIC/S 1/98)
- Application form and Questionnaire on National Inspection Systems (PS 2/99)
- Recommendations on quality system requirements for pharmaceutical inspectorates (PI 002)

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.

Accession procedure

Accession to PIC		Accession to PIC/S
Austria	May 1971	Nov 1999
Denmark	May 1971	Nov 1995
Finland	May 1971	Jan 1996
Iceland	May 1971	Nov 1995
Liechtenstein	May 1971	Nov 1995
Norway	May 1971	Nov 1995
Portugal	May 1971	Jan 1999
Sweden	May 1971	Feb 1996
Switzerland	May 1971	Feb 1996
UK	May 1971	Jun 1999
Hungary	Aug 1976	Dec 1995
Ireland	Dec 1977	Feb 1996
Romania	May 1982	Nov 1995
Germany	Sep 1983	Dec 2000
Italy	Aug 1990	Feb 2000
Belgium	Sep 1991	Feb 1997
France	Dec 1992	Feb 1997
Australia	Jan 1993	Nov 1995

Accession procedure

Accession to PIC		Accession to PIC/S
Netherlands	-	Nov 1995
Czech Republic	-	Jan 1997
Slovak Republic	-	Jan 1997
Spain	-	Jan 1998
Canada	-	Jan 1999
Singapore	-	Jan 2000
Greece	-	Jan 2002
Malaysia	-	Jan 2002
Latvia	-	Jan 2003
Czech Rep (Vet)	-	Jul 2005
Poland	-	Jan 2006
Estonia	-	Jan 2007
South Africa	-	Jul 2007
Argentina	-	Jan 2008
Malta	-	Jan 2008
Cyprus	-	Jul 2008
France (Vet)	-	Jan 2009
Israel	-	Jan 2009
Lithuania	-	Jul 2009

Accession procedure

Applicants being assessed for membership from:

- Brazil
- China / Taiwan
- Indonesia
- Iran
- New Zealand
- Philippines
- Slovenia
- Thailand
- Ukraine
- United Kingdom / Vet
- USA

Accession procedure

Agencies showing interest in joining PIC/S. From:

- China / Hong Kong
- Japan
- Russia
- Saudi Arabia
- South Korea
- Turkey

Guides and recommendations

PIC/S GMP Guide

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

Guides and recommendations

Plus annexes, covering notably:

- 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

Guides and recommendations

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 EMEA (& vice versa)

Guides and recommendations

PIC/S works on validation

- 1994 PIC Seminar in Ireland on Validation identified need to develop guidance document
- PIC/S Recommendations prepared covering:
  - Validation Master Plan
  - Installation & Operational Qualification (IQ & OQ)
  - Non-sterile Process Validation
  - Cleaning Validation
- PIC/S entry into force on 1st March 1999
- Adopted by the EU as Annex 15 to EU GMP Guide

Guides and recommendations

- ✓ PIC/S GMP Guide (similar to EU GMP Guide).
- ✓ PIC/S GMP Guide for Blood Establishments.
- ✓ PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments.
- ✓ Validation (master plan, IQ/OQ, process, cleaning).
- ✓ Validation of Aseptic Processes.
- ✓ Inspection of Isolator Technology.
- ✓ Quality Systems for Inspectorates.
- ✓ Sterility Testing.
- ✓ Validation of Computerised Systems.

Guides and recommendations

PIC/S Involvement in the ICH GMP Guide on APIs

- PIC/S Conference in Canberra 1996:
  - consensus obtained to prepare international GMP.
- PIC/S draft document prepared during ‘97 & ‘98.
- ICH Q7 took over the work of PIC/S mid-1998 to enable industry to become involved:
  - ICH involves 3 regions (USA, Europe & Japan).
- ICH GMP Guide finalised in November 2000 after extensive public consultation.
- Most countries have adopted ICH document as a GMP requirement for APIs by 1st April 2001 (EU).
- ICH document became Part II of PIC/S GMP Guide in 2007

Seminars and expert circles

- 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

Seminars and expert circles

- Tablet Manufacture	Denmark, 1980
- Manufacture of Active Ingredients	Switzerland, 1980
- 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

Seminars and expert circles

- 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
- Inspection & Testing in Relation to the Marketing Authorisation	Belgium, 1993
- Qualification & Validation	Ireland, 1994
- Manufacture of Sterile Products	Iceland, 1995
- Computer Systems	Australia, 1996
- GMP Standards for APIs	Australia, 1996

Seminars and expert circles

- 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
- Sterile Aseptic Manufacturing	Sweden, 2009

Seminars and expert circles

Future PIC/S Seminars

- Herbal / Traditional Medicines — Malaysia, 2010
- Good Inspection Practices — South Africa, 2011

Seminars and expert circles

Expert Circles / Working Groups

- ✓ APIs
- ✓ Computerised Systems
- ✓ Human Blood and Tissues
- ✓ Quality Risk Management
- ✓ Good Distribution Practices

Aim: Develop draft guidance documents
Training in specialised field

Other training tools

PIC/S Joint Visits

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

Quality system requirements for pharmaceuticals inspectorates

Main topics

- Quality Improvement and Corrective / Preventive Action
- Complaints
- Issue and Withdrawal of Licences and GMP certificates
- Handling Suspected Quality Defects and Rapid Alert System
- Liaison with OMCL
- Sub-Contracting and Assessing

Quality system requirements for pharmaceuticals inspectorates

Main topics

- Quality Manual
- Administrative Structure
- Organisation and Management
- Documentation and Change Control
- Records
- Inspection Procedures
- Inspection Resources
- Internal Audit

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

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

Liaison with other organisations

- The European Department for the Quality of Medicines (EDQM): Associated Partnership negotiated in 2007,
- The European Medicines Agency (EMA): Associated Partnership negotiated in 2007
- UNICEF: Associated Partnership negotiated in 2008,
- WHO: Co-operation Arrangement negotiated in May 2009
- ICH,
- European Commission (DG Health & Consumers)

Typical PIC/S inspection of a medicinal product manufacturer

Before the inspection:

- 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.

Typical PIC/S inspection of a medicinal product manufacturer

After the inspection:

- 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.

Typical PIC/S inspection of a medicinal product manufacturer

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”

Moving forwards

- PIC/S Blueprint adopted by PIC/S Committee in December 2005

  Aim:

  - To review PIC/S' mission & goals in a changing environment.
  - To set a number of objectives and actions for the next 10 years.
  - To raise PIC/S' visibility and explain the benefits of PIC/S membership.
  - To make PIC/S more of a global organisation rather than European focused.

(PIC/S Blueprint is available at www.picscheme.org)

Moving forwards

Recent developments

- Participation in European Commission's initiative for enhanced international co-operation in the field of APIs;
- Application of New Zealand / Medsafe, Taiwan / FDA, UK / Vet and Brazil / ANVISA;
- MoU signed with Russia / Roszdravnadzor;
- Follow-up visit to US FDA (August 2010);
- Adoption of Technical Interpretation on Annex 1;
- Accession of Lithuania / SMCA as 37th Participating Authority

Moving forwards

Recent developments

- Preparation of the 40th anniversary of PIC-PIC/S in May 2011,
- Facing new challenges as increasing the number of participants versus available resources,
- Better work-sharing of tasks (e.g. training of inspectors) with other organisations as WHO,
- Acting proactively with certain key agencies

PIC/S Contacts

Composition of the Executive Bureau

- Mr. Tor Gråberg (Chairman),
- Ms. Helena Baião (1st Deputy Chairperson),
- Dr. Joey Gouws (2nd Deputy Chairperson),
- Mr. Paul Hargreaves,
- Dr. Vassiliki Revithi,
- Mr. Boon Meow Hoe,
- Mr. Jirí Holy,
- Mr. Jacques Morénas (past Chairman)

PIC/S Contacts

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Thank you for your attention