ANNUAL REPORT 2004

Pharmaceutical Inspection Co-operation Scheme

The Pharmaceutical Inspection Co-operation Scheme (PIC Scheme) is an informal and flexible arrangement between GMP inspectorates. It entered into force in November 1995. It is run in parallel with the Pharmaceutical Inspection Convention (see Annex II). The common logo for both is PIC/S.

The Scheme retains and improves the Convention's main features, i.e. the networking and confidence building between the national inspection authorities, the development of quality systems, the training of inspectors and other related experts and its work towards global harmonisation of GMP. It is open to the participation of the inspectorates of other countries.

The main decision-making body is the PIC/S Committee in which all Members are represented and which meets at least once a year. The Committee is assisted in its task by an Executive Bureau and a Secretariat.

The PIC/S Executive Bureau was established in 2002 in order to prepare meetings of the Committee, implement the latter's decisions and recommendations, monitor the Scheme's activities and prepare the annual budget. The Bureau is composed of the Chairperson, two Deputies as well as two Members of the Committee.

First year as an independent organisation

1. On 1 January 2004 PIC/S became an independent organisation with an autonomous Secretariat based in Geneva (Switzerland). Prior to that, PIC/S was hosted by the European Free Trade Association (EFTA) for over 30 years. PIC/S' legal status is now that of an Association under the Swiss law. Its official registration at the Geneva "Registre du Commerce" was successfully completed on 11 November 2004.

2. In order to facilitate the transition towards a fully independently run organisation, the Executive Bureau met three times in the course of 2004 under the chairmanship of Mr. Hans Smallenbroek (Netherlands / Inspectorate of Health Care): in London (United Kingdom) on 26-27 January 2004; in El Vendrell (Spain) on 13-14 June 2004; and in Geneva (Switzerland) on 8-10 November 2004. During these meetings, the Bureau focused its attention on staff issues (including the recruitment of a

new Assistant to the Secretary), office matters and finances, notably the drafting of Financial Rules (which were then adopted by the Committee).

3. Contrary to previous years, the PIC/S Committee met only once in 2004. The meeting was held in El Vendrell (Spain) on 14-15 June 2004 under the chairmanship of Mr. Hans Smallenbroek (Netherlands / Inspectorate of Health Care). The Committee devoted much time on organisational and financial matters; the assessment of new Authorities having applied for PIC/S membership; as well as the reassessment of older PIC/S Members.

4. In addition to the annual PIC/S Committee meeting, there were two important meetings of Working Groups (set up by the Committee) in 2004:

- The PIC/S Working Group on the Training of Inspectors met in Geneva on 9 November 2004 (see also "Training of Inspectors").

- The PIC/S Working Group on the International Organisation Status convened in Geneva on 10 November 2004, where it met jointly with the PIC/S Executive Bureau.

5. During this joint meeting, the question of whether to turn PIC/S into an International Organisation was discussed in the presence of two experts in international treaty law: one from Switzerland (the host country) and one from Sweden (the Swedish Ministry for Foreign Affairs is the Depositary of the Pharmaceutical Inspection Convention). On the basis of the legal advice given by these experts, the Working Group came to the conclusion that it would be in PIC/S' best interest to remain an Association under the Swiss law rather than turn into an International Organisation. The matter was referred back to the Committee for decision.

6. Despite the changes, the PIC/S Secretariat continued to provide secretariat services to the various PIC/S bodies (Committee, Bureau and Working Groups) without disruption. In November 2004, a new full-time assistant was recruited in order to assist the Secretary in his task.

Latvia becomes the Scheme's 27th Participating Authority

7. On 1 January 2004 Latvia's State Pharmaceutical Inspection (SPI) became the first Baltic Agency to join PIC/S.

8. SPI was admitted following an evaluation of its GMP system and a visit in December 2000 to assess the local GMP inspection and licensing system. A follow-up visit took place in March 2003 to ensure that SPI had implemented all recommendations, in particular changes to its licensing system and the GMP compliance of industry. SPI applied to join PIC/S back in 1996.

The Participating Authorities of the PIC/S
(Convention and Scheme taken together)

By the end of 2004, PIC/S comprised 27 inspectorates from Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, **Latvia**, Liechtenstein, Malaysia, Netherlands, Norway, Portugal, Romania, Singapore, Slovak Republic, Spain, Sweden, Switzerland and the United Kingdom (see also Annex I).

Estonia, the European Medicines Agency (EMEA) and the World Health Organisation (WHO) enjoy an observer status with PIC/S.

Argentina, Israel, South Africa and the Ukraine apply for membership

9. In the course of 2004, four Agencies applied for PIC/S membership:

- Argentina's Instituto Nacional de Medicamentos (INAME) is Latin America's first Regulatory Authority to apply for PIC/S membership;
- Israel's Ministry of Health sent a PIC/S membership application on 27 May 2004. It is the first complete application from the Middle East, which PIC/S has received so far.
- South Africa's Medicines Control Council is Africa's first Regulatory Authority to request PIC/S membership. As a matter of fact, it is the second time that South Africa has sought to join PIC/S. It applied back in 1998 but following the political changes in the country, its application was put on hold.
- Ukraine's Ministry of Health applied for PIC/S membership on 4 June 2003 (partial application) and completed its application on 30 October 2004.

10. For all these new membership applications, the Committee appointed Rapporteurs to evaluate whether these Agencies have a GMP system equivalent to that of PIC/S countries.

US FDA decides to seek PIC/S membership

11. In a press release dated 29 September 2004 the US Food and Drug Administration (FDA) signalled its decision to seek PIC/S membership as part of its 21st Century Initiative on the Regulation of Pharmaceutical Manufacturing (no application has been submitted yet).

Evaluation of membership applications

12. The following membership applications were reviewed in the course of the year: Estonia, Poland, Chinese Taipei, the Czech Veterinary Institute, Lithuania and UNICEF (the latter wishing to become an observer).

13. The review was done against the background of the European Commission's decision to carry out pre-MRA[1] inspections to the ten new EU Member States, which acceded to the Union on 1 May 2004. The Commission agreed to share its reports with PIC/S, provided that the assessed country had given its consent.

14. As a result, PIC/S agreed to await the Commission's pre-MRA inspection reports before further assessing Estonia's State Agency of Medicines; Lithuania's Department of Pharmacy; and the Czech Institute for State Control of Veterinary Biologicals and Medicaments (ÚSKVBL).

15. A PIC/S Delegation visited Poland on 20-24 September 2004 in order to asses whether the GMP inspection system in general and the Main Pharmaceutical Inspectorate in particular complied with PIC/S requirements.

16. A report on the application made by UNICEF was discussed and the Committee agreed to invite UNICEF to a first hearing at its next meeting.

17. Following a final hearing in El Vendrell (June 2004), the Bureau of Food and Drug Analysis (BFDA) of Chinese Taipei was re-invited to re-apply once all PIC/S recommendations, made during the visit to Taipei in May 2002, had been implemented. The BFDA applied for PIC/S membership back in May 1998.

18. The incomplete membership application made by Bulgaria back in May 2001 was returned to the Bulgarian Drug Agency (BDA).

19. Revised Guidelines for Accession were adopted at the Committee meeting in El Vendrell. The revised Guidelines now include a timeframe of maximum six years, during which the Applicant must complete the application process.

Joint Reassessment Programme

20. During 2004, both the Norwegian Medicines Agency (NOMA) and Italy's Agenzia Italiana del Farmaco (AIFA) were re-evaluated under the Joint Reassessment Programme (JRP). The latter aims to ensure that older Members comply with the PIC/S requirements, as demanded from new Applicants.

21. Greece's National Organization for Medicines (EOF) updated the Committee in El Vendrell on measures taken following its reassessment in 2003 while Romania's National Medicines Agency (NMA) reported on the implementation of PIC/S

---

1 Mutual Recognition Agreement

recommendations made following its reassessment (also in 2003). A follow-up visit to Romania is scheduled to take place in spring 2005.

22. In order to harmonise the various existing evaluation and re-evaluation procedures (PIC/S evaluation of new Applicants, PIC/S JRP, EEA Joint Audit Programme, Canada MRA evaluation procedure), the Committee agreed in principle to use the new MRA evaluation procedure, elaborated by Canada's Health Products and Food Branch Inspectorate (HPFBI), as a basis in order to evaluate Applicants and re-evaluate Participating Authorities. The relevant procedures must now be amended accordingly.

Exchange of Information

23. While GMP-related information on medicinal products, manufactured in PIC/S countries, is usually exchanged between Participating Authorities outside the framework of PIC/S on the basis of legally-binding agreements such as the treaties establishing the European Union (for EU Members) or MRAs (e.g. between EU and Switzerland, Australia and Canada, etc.), some PIC/S Members have continued to rely on either the PIC Convention (e.g. Australia and Switzerland) or the Scheme (e.g. Singapore and Canada) to exchange such information.

24. With regard to medicinal products, manufactured outside the jurisdiction of PIC/S Regulatory Authorities, GMP-related information has been exchanged on a case-by-case basis. The International Medicinal Inspectorates Database (IMID), launched by PIC/S in June 2003, aims at facilitating the sharing of such information. At the end of 2004, there were 15 PIC/S Authorities participating in the IMID.

Training of Inspectors

25. The Working Group on the Training of Inspectors met in Geneva (Switzerland) on 9 November 2004 under the chairmanship of Ms. France Dansereau (Canada / HPFBI). The Working Group reviewed the operation of the Joint Visits Programme, the evaluation of the 2004 Seminar, preparations for the forthcoming PIC/S Seminars (in particular the 2005 Seminar in Romania) and Expert Circles meetings. It also improved the operation of PIC/S Seminars with regard to their organisation and finalised a new Aide-Memoire on the organisation Expert Circle meetings (to be adopted by the Committee).

Joint Visits Programme

26. In 2004, six new joint visits groups were established and the composition of four existing groups modified. Twenty-eight joint visit groups were operational at the end of 2004 representing over 100 inspectors from 25 different nationalities.

27. At its meeting in Geneva on 9 November 2004, the Working Group also discussed the evaluation made on eight Joint Visits Groups which had completed their 3-year visit cycle (including the main differences observed during joint visits).

PIC/S Joint Visit Groups

Another means of training inspectors of the PIC/S countries has been devised in the form of joint visits to manufacturers by inspectors of different countries. Groups of three inspectors are set up on the basis of applications sent to the PIC/S Secretariat. Each inspector is assigned within his/her group to act in turn as host for one year and guest for the other two years.

Visits are carried out in English or in a language commonly agreed by inspectors. Joint reports are drafted after each visit and sent to the Committee for evaluation.

The organisation of the joint visits has proved an excellent means for the further training of inspectors through mutual exchange of experience and a useful contribution to the maintenance of mutual confidence between competent authorities. Participants have also the possibility to discuss and compare their inspection methods and their interpretation of GMP rules.

2004 PIC/S seminar in El Vendrell (Spain)

28. The 2004 PIC/S Seminar was devoted to the Inspection of Active Pharmaceutical Ingredients (APIs). The Seminar was held in El Vendrell (Catalonia, Spain) from 16 to 18 June 2004. It was organised by the "Agencia Española de Medicamentos y Productos Sanitarios" (AEM) in co-operation with the "Generalitat de Catalunya, Departement de Salud".

29. The PIC/S Seminar was attended by 94 participants from 40 countries. This number includes inspectors from a number of non PIC/S countries/entities and agencies such as Brazil, China, Cyprus, European Directorate for the Quality of Medicines (EDQM), European Medicines Agency (EMEA*), Estonia*, Israel, Lithuania, New Zealand, Poland, Serbia-Montenegro, South Africa, Chinese Taipei, Ukraine and US FDA. It was the first time that a PIC/S Seminar was attended by representatives from China's State Food and Drug Administration, Israel's Ministry of Health and the European Directorate for the Quality of Medicines (EDQM).

30. The Seminar focused on major differences between APIs and Medicinal Products in terms of regulations, manufacturing process, inspections, etc. It concretely resulted in the setting up of a PIC/S Expert Circle on the Inspection of APIs, whose first task will be to finalise draft guidance documents elaborated during the Seminar, in particular an Aide Memoire on the inspection of APIs and the classification of deficiencies and findings.

* Observer to PIC/S Committee

Expert Circles & Working Groups

Expert Circle on Human Blood and Tissue

31. The 11th meeting of the Expert Circle on Human Blood and Tissue, "Back to the roots – Outlook for the future", took place in Langen (Germany) on 26-30 September 2004. It was its 10th anniversary meeting following the very first meeting held in Langen back in 1994. The anniversary meeting was organised by Germany (BMGS, ZLG & Paul-Ehrlich-Institut). 70 participants from 28 countries and organisations attended the meeting.

Expert Circle on Hospital Pharmacy

32. The 7th meeting of the Expert Circle on Hospital Pharmacy was held in Cologne (Germany) on 29-30 March 2004. It was organised by the "Gesundheitsamt" of the City of Cologne and attended by 15 participants from 13 countries. The meeting focused on the drafting of the guide on "Good Manufacturing Practices for Medicinal Products in Pharmacies".

Expert Circle on Computerised Systems

33. The 3rd meeting of the Expert Circle on Computerised Systems, organised by Swissmedic, took place in Berne (Switzerland) on 21-22 June 2004. It was attended by 24 inspectors from 17 countries.

Expert Circle on Active Pharmaceutical Ingredients

34. At its meeting in Geneva on 9 November 2004, the PIC/S Working Group on the Training of Inspectors recommended to establish a new Expert Circle on Active Pharmaceutical Ingredients.

Working Group on Biotechnology

35. In 2004, the Working Group on Biotechnology, mainly driven by the Danish Medicines Agency, finalised a first draft for an Aide-Memoire on the Inspection of Biotech products (to be released for comments to Members of the PIC/S Committee).

Why Expert Circles?

PIC/S Expert Circles have been set up by the PIC/S Joint Committee to facilitate the discussions and the exchange of information among inspectors specialised in a specific area of GMP such as blood, medicinal gases, hospital pharmacy, computerised systems, etc. Expert Circles meet regularly to develop draft guidance, recommendations, etc. and offer training in their respective fields of specialisation.

Harmonisation of guidance documents

36. The following PIC/S documents entered into force in the course of 2004:

- (Revised) Guidelines on Accession (PIC/S 1/98 (Rev. 2));
- (Revised) PIC/S recommendation on Quality System Requirements for Pharmaceutical Inspectorates (PI 002-2);
- (Revised) Annex 13 to the PIC/S GMP Guide (in parallel with the EU).

37. The list of PIC/S publications is available on the PIC/S web site, which was upgraded in the course of the year: http://www.picscheme.org

---

New co-ordinates of the PIC/S Secretariat

(since 1 January 2004)

PIC/S Secretariat
P.O. Box 5695
CH - 1211 Geneva 11
Switzerland

Tel: +41 22 738 92 16
Fax: +41 22 738 92 17
e-mail: daniel.brunner@picscheme.org
web site: http://www.picscheme.org

LIST OF PIC/S
PARTICIPATING AUTHORITIES & OBSERVERS
(in 2004)

I - PARTICIPATING AUTHORITIES

(in the alphabetical order of the country in which they are located)

	PARTICIPATING AUTHORITY	**ACRONYM**
Australia	Therapeutic Goods Administration	TGA
Austria	Bundesministerium für Gesundheit und Frauen *(Federal Ministry for Health and Women)*	BMGF
Belgium	Direction Générale de la Protection de la Santé Publique: Médicaments	DGM
Canada	Health Products and Food Branch Inspectorate	HPFBI
Czech Republic	Státní Ústav pro Kontrolu Léčiv *(State Institute for Drug Control)*	SÚKL
Denmark	Danish Medicines Agency	DMA
Finland	National Agency for Medicines	NAM
France	Agence Française de Sécurité Sanitaire des Produits de Santé *(French Health Products Safety Agency)*	AFSSAPS
Germany	Bundesministerium für Gesundheit und soziale Sicherung *(Federal Ministry for Health and Social Security)*	BMGS
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten *(Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices)*	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων *(National Organization for Medicines)*	EOF
Hungary	National Institute of Pharmacy	NIP
Iceland	The Icelandic Medicines Control Agency	IMCA
Ireland	Irish Medicines Board	IMB
Italy	Agenzia Italiana del Fármaco	AIFA
Latvia	State Pharmaceutical Inspection	SPI
Liechtenstein	Kontrollstelle für Arzneimittel	KA
Malaysia	National Pharmaceutical Control Bureau	NPCB
Netherlands	Inspectie voor de Gezondheidszorg *(Inspectorate of Health Care)*	IGZ
Norway	Norwegian Medicines Agency	NOMA
Portugal	Instituto Nacional da Farmácia e do Medicamento	INFARMED
Romania	National Medicines Agency	NMA

Singapore	Health Sciences Authority	HSA
Slovak Republic	State Institute for Drug Control	SIDC
Spain	Agencia Española del Medicamento	AEM
Sweden	Medical Products Agency	MPA
Switzerland	Swiss Agency for Therapeutic Products	Swissmedic
United Kingdom	Medicines and Healthcare Products Regulatory Agency	MHRA

II - OBSERVERS

(in the alphabetical order of their acronyms)

	OBSERVERS	**ACRONYM**
	European Medicines Agency	EMEA
Estonia	State Agency of Medicines	SAM
	World Health Organisation	WHO

From the Pharmaceutical Inspection Convention to the Pharmaceutical Inspection Co-operation Scheme

The Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmaceutical Products (Pharmaceutical Inspection Convention) entered into force in 1971.

The Convention applies to inspection of the manufacture of medicinal and related products intended for human use, which are subject to control under health legislation. It provides that the Contracting States will exchange, on the basis of inspections, such information as is necessary for the health authorities in an importing Contracting State to be able to recognise inspections carried out in the Contracting State of the manufacturer.

In 2000 the Convention was operating between eighteen countries, namely, Australia, Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Liechtenstein, Norway, Portugal, Romania, Sweden, Switzerland and the United Kingdom

Due to some incompatibility for the Member States of the European Union (and for the States parties to the European Economic Area) between their obligations under the Convention and under the EU, the conclusion of another type of agreement than the Convention was agreed upon. This is an arrangement between the inspectorates of the present Contracting States to the Convention but also open to the participation of the inspectorates of other countries. The new arrangement called "Pharmaceutical Inspection Co-operation Scheme" (or PIC Scheme) " was put into force in November 1995.

The Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme are run concurrently by one joint Committee and one Secretariat. The common logo for both is PIC/S.