ANNUAL REPORT 2003

Pharmaceutical Inspection Co-operation Scheme

The Pharmaceutical Inspection Co-operation Scheme (PIC Scheme), which entered into force in November 1995, is an informal and flexible arrangement between the inspectorates of the PIC Contracting States. It is run in parallel with the Pharmaceutical Inspection Convention (see Annex II). It is open to the participation of the inspectorates of other countries.

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.

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.

To ensure greater public security with regard to pharmaceutical products marketed in the PIC/S countries, the Scheme provides that if a participating authority learns of particular circumstances due to which a pharmaceutical product could be of imminent and serious danger, its findings have to be communicated to the other competent authorities under the Scheme.

A year of transition

1. In 2003, the PIC/S Committee met in Bratislava (Slovak Republic) on 2-3 June 2003 and in Geneva (Switzerland) on 11-12 November 2003. Both meetings were chaired by Ms. Lilian Hamilton (Sweden / Medical Products Agency). Mr. Hans Smallenbroek (Netherlands / Inspectorate of Health Care) acted as First Deputy Chairman and Ms. France Dansereau (Canada / Health Products and Food Branch Inspectorate) as Second Deputy Chairperson.

2. Following its decision to cut links with the European Free Trade Association (EFTA), which had provided secretariat services to PIC/S since the early 1970s, the Committee discussed two options for the future of PIC/S and its secretariat. These options were either to find a new host organisation or to become independent.

3. The Committee mandated the Executive Bureau to negotiate an administrative agreement with the World Health Organization (WHO), under which WHO would host the PIC/S Secretariat at its Geneva Headquarters. The Bureau was also requested to prepare alternative plans under which independent offices would be established in Geneva for its Secretariat, should negotiations with WHO not succeed.

4. The Committee also examined the possibility of turning PIC/S into an international organisation. It mandated a Working Group to study the question of whether EU Member States were competent to negotiate and ratify a new international treaty establishing such an organisation. On the basis of a comprehensive report, prepared by the Working Group, the PIC/S Chairperson approached the European Commission to enquire on possible legal impediments.

5. As an intermediate measure, the PIC/S Committee agreed to constitute itself as an "Association" under the Swiss law. It authorised its Secretariat to register PIC/S at the Geneva "Registre du Commerce". The PIC Scheme was revised to meet Swiss legal requirements.

6. As the conclusion of an administrative agreement with WHO did not materialise at the end of the year, PIC/S became de facto a fully independent organisation with autonomous secretariat services as of 1 January 2004.

Latvia invited to join the Scheme

7. The Committee invited Latvia's State Pharmaceutical Inspection (SPI) to join PIC/S as a new Participating Authority as from 1 January 2004.

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 2003, PIC/S comprised 26 inspectorates from Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Liechtenstein, Malaysia, Netherlands, Norway, Portugal, Romania, Singapore, Slovak Republic, Spain, Sweden, Switzerland and the United Kingdom (see also Annex I).

Estonia, Latvia*, the European Agency for the Evaluation of Medicinal Products (EMEA) and the World Health Organization (WHO) enjoy an observer status with PIC/S.

* Full Member as from 1 January 2004

Evaluation of other membership applications

9. In 2003, the Committee reviewed the membership applications made by Estonia, Poland, Chinese Taipei, the Czech Veterinary Institute and Lithuania. UNICEF's request to become an observer was also discussed.

10. On the basis of a progress report presented by Estonia's State Agency of Medicines, the Committee decided that a PIC/S Delegation would return to Estonia for a follow-up visit, if possible in conjunction with the pre-MRA inspection by the Commission.

11. It also agreed that a PIC/S Delegation should be sent to assess Poland's GMP inspection system in general and the Main Pharmaceutical Inspectorate in particular. The visit should be coupled with the pre-MRA inspection by the Commission.

12. The same decision was taken in connection with the membership application of the Czech Institute for State Control of Veterinary Biologicals and Medicaments (ISCVBM). The Czech Institute is the first veterinary agency to apply for PIC/S membership (the Czech State Institute for Drug Control, responsible for medicines for human use, is already a PIC/S Member).

13. The National Laboratories for Foods and Drugs (NLFD) of Chinese Taipei were invited to submit a clear and detailed action plan on the implementation of the PIC/S Delegation's recommendations made back in May 2002.

14. Limited progress was achieved in the evaluation of the membership application made by Lithuania's Department of Pharmacy, due to a number of questions, which remained to be answered by the Department.

15. The Committee examined the application made by UNICEF to become an Observer to PIC/S. As UNICEF qualifies in principle for observer status, the Committee appointed a Rapporteur to evaluate its application.

New Membership Applications (Oman, Russia, Ukraine)

16. Three applications were received in the course of 2003: one from Oman's Ministry of Health, one from the Ministry of Health of the Russian Federation and one from the Ukrainian Ministry of Health. The representatives of Oman, Russia and the Ukraine were also met in the margin of the PIC/S 2003 Seminar. From the three applications, only the one from the Ukraine was duly completed with all the supporting documents by the end of the year.

Joint Reassessment Programme (JRP)

17. The pilot phase of the PIC/S Joint Reassessment Programme (JRP) was concluded positively following the experience made during the reassessment of Romania, Sweden and Australia. The procedure was amended to allow auditors to make use of other evaluation reports. It was agreed that the results of the EU Heads of

Agencies' Joint Audit Programme (JAP) should be accepted on a mutual basis in order to avoid unnecessary duplications between the two programmes (see also "Co-operation with other organisations").

18. The Committee reviewed reports on the reassessment of Greece's National Organization for Medicines (EOF) and Romania's National Medicines Agency (NMA). It selected the next authorities to be reassessed: Italy's Dipartimento per la Valutazione dei Medicinali e la Farmacovigilanza (DVMF); the Norwegian Medicines Agency (NOMA); the Slovak State Institute for Drug Control (SIDC), in conjunction with the Commission's pre-MRA visit; and Germany (subject to the mutual acceptance of result between JAP and JRP).

International Medicinal Inspectorates Database

19. The International Medicinal Inspectorates Database (IMID) was officially launched at the PIC/S Committee spring meeting in Bratislava, where its statute was adopted. The IMID started its operations on 1 July 2003. At the end of 2003, there were 13 Authorities participating in the IMID: TGA/Australia, DGM/Belgium, HPFBI/Canada, SÚKL/Czech Republic, AFSSAPS/France, NIP/Hungary, IMCA/Iceland, DVMF/Italy, SPI/Latvia, IGZ/Netherlands, NMA/Romania, HSA/Singapore, and MPA/Sweden.

> The International Medicinal Inspectorates Database (IMID) aims at establishing – on a voluntary basis – a database containing information on GMP inspections carried out (or to be carried out) by IMID participating Regulatory Authorities. The IMID exclusively targets medicinal products (finished products, active pharmaceutical ingredients (APIs) and investigational medicinal products), which have been manufactured in non-PIC/S countries. The main aim of the IMID is to alleviate the workload of PIC/S Members with regard to third-country inspections. This is to be achieved by sharing information on the GMP compliance status of manufacturing sites. The IMID will result in a reduction in the number of inspections, in particular of duplicative inspections. For more information on the IMID, see http://www.picscheme.org/IMID/imid.htm

Co-operation with other organisations

20. A number of proposals were discussed in order to optimise PIC/S' co-operation with the **EMEA** and avoid a duplication of efforts. The Committee agreed – with the exception of HPFBI/Canada – to co-operate with the **European Commission** with a view to accept the results of audits carried out under Mutual Recognition Agreements (MRAs) or pre-MRA visits such as those to be carried out by the Commission in the 10 Accession Countries in 2004 (see also Joint Reassessment Programme).

21. A representative of the **European Directorate for the Quality of Medicines (EDQM)** was invited to the autumn meeting of the PIC/S Committee to give a presentation on EDQM's recently launched programme on certificates of suitability for Active Pharmaceutical Ingredients (APIs).

22. A Memorandum of Understanding regarding secretariat services was signed with the **Convention on the Control and Marking of Articles of Precious Metals** (www.hallmarkingconvention.org).

23. The Committee also supported a proposal aiming at obtaining an observer status for PIC/S in the **International Conference on the Harmonisation (ICH)**.

First meeting of the Executive Bureau

24. 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 and her two Deputies as well as two other Members, elected by the Committee.

25. The Bureau met for its first, constitutional meeting in Geneva (Switzerland) on 6-7 February 2003. It met again later in the year in Geneva (9-10 September 2003). During these two meetings, the Bureau focused its attention on the future of the organisation as well as on the financial situation.

Annual Meeting of the Working Group on the Training of Inspectors

26. The Working Group on the Training of Inspectors met in Geneva on 11 November 2003 under the chairmanship of Mr. Hans Smallenbroek (Netherlands / IGZ). The Working Group reviewed the preparations of the 2004 and 2005 PIC/S Seminars (in Spain and Romania, respectively) as well as the operation of the various Expert Circles.

27. The Working Group also established seven new joint visits groups and modified the composition of three existing groups. Twenty-nine joint visit groups were operational at the end of 2003 representing 98 inspectors from 27 different nationalities.

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.

2003 PIC/S seminar in Bratislava

28. The Seminar on "The Inspection of Quality Control Laboratories" took place in Bratislava (Slovak Republic) on 4-6 June 2003. It was organised by the Slovak State Institute for Drug Control (SIDC).

29. The PIC/S Seminar was attended by 95 participants from 36 countries. This number also includes invited inspectors and speakers from a number of non PIC/S countries or agencies such as Cyprus, EMEA, Estonia, FDA, Latvia, Lithuania, Macedonia, New Zealand, Oman, Poland, Russia, Serbia, South Africa, Ukraine, UNICEF, and WHO.

30. The Seminar focused on experts discussions on current regulatory issues related to GMP in pharmaceutical quality control laboratories; the harmonisation of inspection standards and practices; and the drafting of guidance documents, in particular an Aide Memoire on the inspection of pharmaceutical quality control laboratories.

Four Expert Circles / Working Groups meetings in 2003

Expert Circle on Human Blood and Tissue

31. The 10th meeting of the Expert Circle on Human Blood and Tissue, organised by the Hungarian National Institute of Pharmacy (NIP), took place in Visegrad (Hungary) from 8 to 11 September 2003. It was attended by 42 participants from 21 countries and was devoted to questions related to the quality and safety of material of human origin.

Expert Circle on Medicinal Gases

32. The 4th meeting of the Expert Circle on Medicinal Gases was organised by Finland's National Agency for Medicines. 37 participants from 16 countries attended the meeting held in Hämeenlinna (Finland) on 9-11 June 2003.

Expert Circle on Computerised Systems

33. The 2nd meeting of the Expert Circle on Computerised Systems, organised by Australia's Therapeutic Goods Administration (TGA), took place in Canberra on 17-18 February 2003. It was attended by 36 inspectors from 15 countries.

Working Group on Biotechnology

34. The second meeting of the Working Group on Biotechnology, organised by the Danish Medicines Agency, was held in Brønshøj (Denmark) on 29 August 2003. It was devoted to the drafting of an Aide-Memoire on the Inspection of biotech products.

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 and computerised systems. Expert Circles meet regularly to develop draft guidance, recommendations, etc. and offer training in their respective fields of specialisation.

PIC/S guidance documents

35. The following PIC/S internal documents entered into force in the course of 2003 (with the exception of the revised Annex 13):

- Guide to Inspections of Source Plasma Establishments and Plasma Warehouses (PI 008-1); Site Master File for Source Plasma Establishments (PI 019-1); and Site Master File for Plasma Warehouses (PI 020-1);
- PIC/S Guidance on Best Practices for Computerised Systems in Regulated "GxP" Environments (PI 011-1);
- Annex 1 to the PIC/S GMP Guide (revision in parallel with the EU);
- Annex 13 to the PIC/S GMP Guide (revision in parallel with the EU).

36. The list of PIC/S publications is available on the PIC/S web site http://www.picscheme.org

Elections

37. The Committee elected Mr. Hans Smallenbroek from the Netherlands' Inspectorate of Health Care as Chairman for 2004-2005. Ms. France Dansereau of Canada's Health Products and Food Branch Inspectorate (HPFBI) was elected First Deputy Chairperson while Mr. Jacques Morénas of the French Health Products Safety Agency (AFSSAPS) was elected Second Deputy Chairman for the same period. As due to the election of Mr. Morénas as Second Deputy Chairman, one of two positions (*) for Member of the Executive Bureau became vacant, the Committee elected Dr. Vassiliki Revithi of Greece National Organization of Medicines (EOF) as new Member of the PIC/S Executive Bureau.

(*) The other position is held by Dr. Martin Valchár (Czech Republic / SÚKL)

New co-ordinates of the PIC/S Secretariat

(as of 1 January 2004)

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LIST OF PIC/S
PARTICIPATING AUTHORITIES & OBSERVERS
(in 2003)

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 Léciv *(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/ Federal Ministry for Health	BMG
	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	*(National Organization for Medicines)*	EOF
Hungary	National Institute of Pharmacy	NIP
Iceland	The Icelandic Medicines Control Agency	IMCA
Ireland	Irish Medicines Board	IMB
Italy	Dipartimento per la Valutazione dei Medicinali e la Farmacovigilanza	DVMF
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 Control Agency	MCA

II - OBSERVERS

(in the alphabetical order of their acronyms)

	OBSERVERS	**ACRONYM**
	European Agency for the Evaluation of Medicinal Products	EMEA
Estonia	State Agency of Medicines	SAM
Latvia	State Pharmaceutical Inspection	SPI
	World Health Organization	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.