



## ANNUAL REPORT 2005

### **The Czech Veterinary Institute and Poland's Main Pharmaceutical Inspectorate join PIC/S; UNICEF accepted as an Observer**

1. In 2005, PIC/S continued its successful expansion by welcoming two new Participating Authorities and one new Observer among its ranks.
2. At its spring meeting in Geneva, the PIC/S Committee invited the Czech Institute for State Control of Veterinary Biologicals and Medicaments (ISCVBM) to become the Scheme's 28<sup>th</sup> Participating Authority as from 1 July 2005. The Czech Institute is the first Agency, exclusively responsible for veterinary products, to join PIC/S. It has been admitted following an evaluation of its GMP system and based on a pre-MRA inspection report by the European Commission, which was shared with PIC/S. The Czech Institute applied for PIC/S membership back in September 2002. It is independent from the Czech State Institute for Drug Control (SÚKL), responsible for medicinal products for human use, which has been a PIC/S Member since 1997.
3. At its autumn meeting in Bucharest, the Committee invited the Main Pharmaceutical Inspectorate (MPI) of Poland to join PIC/S as the Scheme's 29<sup>th</sup> Participating Authority as from 1 January 2006. MPI has been admitted following an evaluation of its GMP system and based on an assessment visit carried out by a PIC/S delegation in 2004.
4. During the same meeting, the Committee also invited the Supply Division of the United Nations International Children's Emergency Fund (UNICEF) to become PIC/S' 4<sup>th</sup> Observer as from 1 January 2006. UNICEF has been granted an Observer status based on the evaluation of written documents. UNICEF is one of the world largest suppliers of vaccines and has agreed to share information on GMP inspections with other PIC/S Participating Authorities on a voluntary basis.

### **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.

### **Operation of the Scheme**

5. The PIC/S Committee met twice in the course of year under the chairmanship of Mr. Hans Smallenbroek (Netherlands / Inspectorate of Health Care): the first time in Geneva (Switzerland) on 8-9 February 2005 and the second time in Bucharest (Romania) on 12-13 September 2005. During these two meetings, the Committee approved the 2004 accounts; discharged the Chairman for the financial year 2004; and adopted a budget for 2006. It also reviewed the operation of the Scheme, the assessment of new Applicants and the reassessment of older Members. It discussed and adopted a number of guidance documents and monitored the activities carried out by the Executive Bureau and the Working on the Training of Inspectors (see below). Finally, it elected a successor to Mr. Smallenbroek, whose mandate ended on 31 December 2005, in the person of Mr. Jacques Moréas (France / AFSSAPS), who will be at the helm of PIC/S for the period 2006-2007.

6. The Committee also successfully adopted a major strategy document entitled "PIC/S Blueprint"<sup>1</sup> which defines PIC/S' mission and sets clear objectives and actions to be achieved during the next decade (i.e. by 2015).

7. The Executive Bureau met three times in Geneva in the course of 2005: on 9 February; 5-6 July; and 14 December. The Bureau underwent significant changes following the departure of three of its Members in early 2005. As a result, a new First Deputy Chairman, a new Second Deputy Chairman and a new Member of the Bureau had to be elected at the Geneva meeting of the PIC/S Committee. A further election took place at the Bucharest meeting of the PIC/S Committee.

8. The PIC/S Working Group on the Training of Inspectors met in Bucharest on 12 September 2005 to discuss training events for PIC/S inspectors (see "Training of Inspectors").

9. As in the past, the PIC/S Secretariat continued to provide secretariat services to the various PIC/S bodies (Committee, Bureau, etc.). In December 2005, the Executive Bureau identified new offices for the Secretariat, thus putting an end to a two-year period during which the Secretariat staff had worked from home.

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<sup>1</sup> The document is available on the PIC/S web site <http://www.picscheme.org>

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

By the end of 2005, PIC/S comprised 28 inspectorates from Australia, Austria, Belgium, Canada, Czech Republic (human & veterinary), 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 (EMA), and the World Health Organization (WHO) enjoy an observer status with PIC/S.

**Membership Applications: The US FDA applies**

10. The US Food and Drug Administration (FDA) applied for PIC/S membership on 16 September 2005. At its meeting in Bucharest, the Committee appointed the United Kingdom's MHRA as the overall co-ordinator of an assessment team involving six other experts from PICS Participating Authorities.

11. In the course of 2005, the Committee reviewed the following membership applications:

- ◆ It appointed a Rapporteur and a Co-Rapporteur for the assessment of the membership application by Argentina's Instituto Nacional de Medicamentos (INAME);
- ◆ In order to save resources, it decided to await the report on Canada's visit to Estonia's State Agency of Medicines (under the EU-Canada Mutual Recognition Agreement) rather than proceeding with its own follow-up visit;
- ◆ It reviewed the written evaluation on the membership application by Israel's Ministry of Health and decided to await the introduction of a licensing system in Israel before proceeding with an on-site assessment;
- ◆ It reviewed the membership application by Lithuania's Department of Pharmacy, where the Commission's pre-MRA inspection report was still awaited;
- ◆ It appointed a new Rapporteur for the evaluation of the membership application by South Africa's Medicines Control Council and already appointed Members of the Audit Team, which will go to South Africa and assess its GMP inspection system;
- ◆ It discussed the written evaluation on the membership application by Ukraine's Ministry of Health and decided to await the implementation of the PIC/S GMP Guide in the Ukraine before proceeding with further steps.

12. The Committee also took note that the Thai Food and Drug Administration (FDA) had signalled its intention to apply for PIC/S membership. PIC/S membership has been defined as one of the essential criteria for the establishment of a Mutual Recognition Agreement (MRA) by ASEAN in the field of GMP inspections.

### **Joint Reassessment Programme**

13. The Joint Reassessment Programme (JRP) aims at ensuring that older Members of PIC/S still comply with the PIC/S requirements, as demanded from new Applicants. In 2005 the Committee revised all JRP documents and adopted several new ones in order to harmonise its reassessment procedure with that used under the EU's Joint Audit Programme (JAP) thus facilitating the mutual recognition of audit results. It also decided to concentrate on the re-evaluation of older Members which had undergone significant structural changes. Finally, in order to avoid unnecessary duplications, it agreed to accept evaluations made by the European Commission and Canada under their Mutual Recognition Agreement (MRA) as equivalent to a reassessment under the PIC/S Joint Reassessment Programme.

14. In the course of 2005, the reassessments of the Norwegian Medicines Agency (NOMA), Italy's Agenzia Italiana del Farmaco (AIFA) and Romania's National Medicines Agency (NMA) were successfully completed. The reassessment of Romania's NMA was concluded following a follow-up visit to Romania on 4-6 April 2005.

15. Greece's National Organization for Medicines (EOF) continued to update the Committee on follow-up measures taken following its reassessment while the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) was chosen as the next candidate for a JRP reassessment. An audit team comprising Sweden, Malaysia and Portugal was appointed by the Committee.

### **Exchange of Information**

16. GMP-related information on medicinal products, manufactured in PIC/S countries, continued to be exchanged between non-EEA/non-MRA Participating Authorities on a voluntary basis.

17. With regard to medicinal products, manufactured outside the jurisdiction of PIC/S countries, GMP-related information has been exchanged on a case-by-case basis. However, the Committee decided to make the International Medicinal Inspectorates Database (IMID) dormant for the time being until more non-EU players join PIC/S and/or the inspection of API manufacturers are undertaken by more PIC/S member authorities. The IMID was launched by PIC/S in June 2003 with the aim of facilitating the sharing of such information. It will become redundant with the launching in 2006 of the EUDRA GMP database, which will become fully accessible to EU/EEA Regulatory Agencies and partially accessible to non-EU/EEA Participating Authorities of PIC/S.

## **Training of Inspectors**

18. The Working Group on the Training of Inspectors met in Bucharest (Romania) on 12 September 2005 under the chairmanship of the PIC/S First Deputy Chairman, Mr. Jacques Morénas (France / AFSSAPS). The Working Group reviewed the operation of the Joint Visits Programme; past and future Expert Circles meetings; the evaluation of the 2004 Seminar on the Inspection of Active Pharmaceutical Ingredients; the preparations for the 2006 Seminar on “Risk Management and related ICH Issues” and for the 2007 Seminar on “The Inspection of the Manufacture of Solid Dosage Forms”.

19. It approved the setting up of a new Expert Circle on Active Pharmaceutical Ingredients (APIs) and adopted the revision of the Aide-Memoire on the Organising of Seminars (PI 003-2) and a new Guideline for PIC/S Expert Circles (PI 022-1).

## Joint Visits Programme

20. At the end of 2005, there were thirty-five joint visit groups under the Joint Visits Programme representing around 120 inspectors from 25 different nationalities.

21. At its meeting in Bucharest, the Working Group also discussed the possibility of introducing “coached visits” for inspectors in addition to the already existing “joint visits”. The concept was approved in principle by the PIC/S Committee.

### **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.

### 2005 PIC/S seminar in Bucharest

22. The topic of the 2005 PIC/S Seminar was “Primary packaging material, labelling and the prevention of mix-ups”. The Seminar was held Bucharest (Romania) from 14 to 16 September 2005. It was organised by the Romanian National Medicinal Agency (NMA).

23. The Seminar was attended by 90 participants from 38 countries. This number includes inspectors from a number of non-Member agencies coming from Argentina, Cyprus, the European Medicines Agency (EMA\*), the European Directorate for the Quality of Medicines (EDQM), Estonia\*, Israel, Japan, Lithuania, New Zealand, Poland, Thailand, South Africa, Ukraine, UNICEF and US FDA.

24. It was the first time that a PIC/S Seminar was attended by representatives from Argentina’s National Institute of Medicaments (INAME), Japan’s Institute for Standardisation and Control of Pharmaceuticals (Ministry of Health) and Pharmaceutical and Medical Devices Agency (PMDA), Thailand’s Food and Drug Administration (Ministry of Public Health) as well as Malta’s Medicines Authority.

25. The Seminar focused on:

- (i) the training of inspectors regarding the quality, safety and security of packages used for medical products;
- (ii) the critical aspects to be identified and clarified regarding GMP inspection for the final stage of manufacturing processes (primary and secondary packaging and labelling);
- (iii) the uniform interpretation of the GMP Guide regarding packaging of medicinal products

26. The Seminar resulted in the setting up of a Working Group whose task will consist in drafting an Aide-Memoire on the inspection of packaging materials.

### Expert Circles & Working Groups

#### *Expert Circle on Human Blood and Tissue*

27. The 12<sup>th</sup> meeting of the Expert Circle on Human Blood and Tissue was held in Ottawa (Canada) on 10-14 October 2005. It was organised by Canada’s Health Products and Food Branch Inspectorate. It was attended by 56 participants from 27 countries (of which 6 non-Members). The meeting mainly focused on the inspection of cell therapy, tissue products, and related matters. It also covered general inspection topics, which apply to both blood and tissue establishments e.g. laboratory tests, computerised systems, inspection techniques. The Circle also reviewed guidance documents drafted by its four Working Groups (e.g. “Draft recommendation on qualification and training of inspectors in the field of human blood, cells and tissues”).

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\* Observer to PIC/S Committee

The Expert Circle also addressed a number of recommendations for consideration to the PIC/S Committee.

#### *Expert Circle on Hospital Pharmacy*

28. The 8<sup>th</sup> meeting of the Expert Circle on Hospital Pharmacy was held in Riga (Latvia) on 4-5 April 2005. It was organised by Latvia's State Pharmaceutical Inspectorate and attended by 18 participants from 15 countries. The meeting focused on the drafting of the guide on "Good Manufacturing Practices for Medicinal Products in Pharmacies".

#### *Expert Circle on Computerised Systems*

29. The 4<sup>th</sup> meeting of the Expert Circle on Computerised Systems, organised by IGZ, took place in Utrecht (Netherlands) from 31 October to 2 November 2005. It was attended by 49 inspectors from 26 countries (including Argentina, Brazil, Cyprus, Israel, Japan, South Africa and USA). The meeting was split up into two parts: a basic course on "how to inspect Computerised Systems during GxP-inspections" followed by regular Expert Circle meeting focused on computer validation.

#### *Expert Circle on Medicinal Gases*

The 5<sup>th</sup> meeting of the Expert Circle on Medicinal Gases took place in Prague (Czech Republic) on 20-22 September 2005. It was organised by the Czech State Institute for Drug Control (SÚKL) and attended by thirty-one inspectors from 23 countries. The meeting focused on the training of inspectors for the inspection of medicinal gases; on discussion on GMP issues in connection with qualification and validation of medicinal gases; and on the finalization of the draft Aide Memoire on Medicinal gases.

#### *Expert Circle on Active Pharmaceutical Ingredients*

30. The first meeting of the Expert Circle on Active Pharmaceutical Ingredients (APIs) was held in Paris (France) on 10-12 October 2005. It was organised by the French Health Products Safety Agency (AFSSAPS). 47 persons attended the meeting from 28 different agencies (including from non-Members e.g. Argentina, China, Japan, USA, Chinese Taipei). The meeting resulted in the setting up of Working Groups which will elaborate guidance documents related to the inspection of APIs.

#### *Working Group on Biotechnology*

31. In 2005, following the successful finalisation of the Aide-Memoire on the Inspection of Biotech products, the Working Group on Biotechnology, which had been mainly driven by the Danish Medicines Agency, was dissolved.

### **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**

32. The following PIC/S documents were adopted at the Bucharest meeting of the Working Group on Training and entered into force on 1 May 2005:

- (Revised) Aide-Memoire on the Organising of Seminars (PI 003-2);
- Guideline for PIC/S Expert Circles (PI 022-1).

33. The following PIC/S documents were adopted at the Bucharest Committee meeting with entry into force on 1 January 2006:

- Aide Memoire on the Inspection of Pharmaceutical Quality Control Laboratories (PI 023-1);
- Aide Memoire on GMP Particularities in the Manufacture of Medicinal Products to be used in Clinical Trials on Human Subjects (PI 021-1);
- Aide Memoire on the Inspection of Biotechnology Manufacturers (PI 024-1).

34. The Committee also endorsed in principle a concept paper by the EMEA on the revision of some annexes to the EU GMP Guide in the context of GMP for active substances. It also reviewed the first draft of a GMP Guide for the Preparation of Medicinal Products in Pharmacies (PE 010-1 (Draft 1)).

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

### **Relations with other organisations**

36. In the course of 2005, PIC/S was invited to the following conferences and meetings:

#### Argentine Association of Industrial Pharmacy and Biochemistry

Argentine Congress of Industrial Pharmacy and Biochemistry, Buenos Aires (Argentina), 5-9 September 2005



Council of Europe

Seminar on Counterfeit Medicines, Strasbourg (France), 21-23 September 2005

Global Fund to Fight AIDS, Tuberculosis and Malaria

Meeting with the Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva (Switzerland), 1 December 2005

Institute of Validation Technology (Fort Lauderdale, Florida)

Conference on “Aseptic Processing and Sterile Processes”, Dublin (Ireland), 29 September 2005

ISPE

- ◆ ISPE Conference, Prague (Czech Republic), 19-23 September 2005
- ◆ Meeting with Mr. Mike Bennoson from ISPE, Geneva (Switzerland), 15 December 2005

University of Rhode Island, College of Pharmacy

Conference on “FDA and Current Challenges of GMPs”, University of Rhode Island College of Pharmacy, New Jersey (USA), 25-27 July 2005

WHO

WHO Expert Committee on Specifications for Pharmaceutical Preparations, Geneva (Switzerland), 25 October 2005

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**LIST OF PIC/S  
PARTICIPATING AUTHORITIES & OBSERVERS**  
(as of 31 December 2005)

**I - PARTICIPATING AUTHORITIES**

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

	<b>PARTICIPATING AUTHORITY</b>	<b>ACRONYM</b>
Australia	Therapeutic Goods Administration	TGA
Austria	Bundesministerium für Gesundheit und Frauen ( <i>Federal Ministry for Health and Women</i> )	BMGF
Belgium	Direction Générale Médicaments	DGM
Canada	Health Products and Food Branch Inspectorate	HPFBI
Czech Republic <sup>1</sup>	Státní Ústav pro Kontrolu Léčiv ( <i>State Institute for Drug Control</i> )	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv ( <i>Czech Institute for State Control of Veterinary Medicaments and Biologicals</i> )	ÚSKVBL
Denmark	Danish Medicines Agency	DMA
Finland	National Agency for Medicines	NAM
France	Agence Française de Sécurité Sanitaire des Produits de Santé ( <i>French Health Products Safety Agency</i> )	AFSSAPS
Germany <sup>2</sup>	Bundesministerium für Gesundheit ( <i>Federal Ministry for Health</i> )	BMG
	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten ( <i>Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices</i> )	ZLG
Greece	Εθνικός Οργανισμός Φαρμάκων ( <i>National Organization for Medicines</i> )	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 Agency of Medicines	SAM
Liechtenstein	Kontrollstelle für Arzneimittel	KA
Malaysia	National Pharmaceutical Control Bureau	NPCB

<sup>1</sup> SÚKL and ÚSKVBL count as two distinct Participating Authorities.

<sup>2</sup> BMG and ZLG count as one Participating Authority.

Netherlands	Inspectie voor de Gezondheidszorg ( <i>Inspectorate of Health Care</i> )	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 y Productos Sanitarios	AEMPS
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)

	<b>OBSERVERS</b>	<b>ACRONYM</b>
	European Medicines Agency	EMA
Estonia	State Agency of Medicines	SAM
	World Health Organization	WHO

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**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.

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