PHARMACEUTICAL INSPECTION CONVENTION

PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

A N N U A L R E P O R T 1 9 9 9

Summary of Activities

The PIC/S Committee held its annual meeting in Oxford (United Kingdom) on 7 September 1999. Dr. Bernard Scherz of Switzerland was in the chair. During the meeting, the Committee welcomed the UK Medicines Control Agency, which became the 20th participating authority in the PIC Scheme on 1 April 1999. It also accepted the application for participation in the Scheme made by the Singaporean Inspectorate as from 1 January 2000. Finally, it elected Mr. Robert Tribe of Australia as its new Chairman for the period 2000/2001.

In November 1999, the Austrian Health Department became the 21st participating authority in the PIC Scheme. The increasing number of participating authorities underlines the dynamic expansion of the Scheme since its entry into force in 1995.

Other main activities of the PIC/S were:

* The PIC/S Seminar on Non-Technical Aspects of Inspections (Oxford, September 1999), attended by more than 120 delegates from 34 countries;
* The PIC/S expert circle on hospital pharmacy in Amsterdam (March 1999);
* The PIC/S expert circle on blood and blood products in Pärnu (Estonia) in June 1999;
* PIC/S expert circle on medicinal gases in Györ (Hungary) in October 1999;
* Two visits to Singapore by a delegation of the PIC/S Committee to determine Singapore's suitability for PIC/S membership (April and November 1999);
* Joint visits for the training of inspectors;
* The preparation and updating of guides and recommendations on good manufacturing practice (GMP) on the manufacture of medicinal products.

The PIC/S Joint Committee meets in Oxford

The annual meeting of the PIC/S Joint Committee took place under the chairmanship of Dr. Bernard Scherz (Switzerland) in Oxford on 7 September 1999. The meeting was followed by a PIC/S Seminar on Non-Technical Aspects of Inspections.

The main items discussed during the PIC/S Joint Committee meeting were the relations with other countries and their inspectorates, the training of inspectors, the setting up of workshops in special fields (blood products, medicinal gases and hospital pharmacies), the elaboration of PIC/S Recommendations on GMP or other related matters (e.g. the discussion of GMP issues), and other aspects related to the good functioning of the PIC Scheme.

The Joint Committee elected Mr. Robert Tribe of Australia as its new Chairman for the period 2000/2001. It also elected Ms. Lilian Hamilton of Sweden as the first Deputy Chairperson and Mr. Hans Smallenbroek of the Netherlands as the second Deputy Chairman.

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 PIC 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.

The UK and Austria join the Scheme in the course of 1999 while Singapore's application becomes effective as from 2000

In the course of 1999, two inspectorates, which were already members of the Convention, joined the Scheme: the UK Medicines Control Agency applied for participation in the PIC Scheme in April '99 while the Austrian "Bundesministerium für Arbeit, Gesundheit und Soziales" joined in November of the same year.

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

By the end of 1999, the PIC/S comprised 23 inspectorates from Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Liechtenstein, Netherlands, Norway, Portugal, Romania, Slovak Republic, Spain, Sweden, Switzerland and the United Kingdom (see also Annex I).

In 1999, the PIC/S Joint Committee considered the application for participation in the Scheme by the Singaporean Inspectorate. In April a visit was paid to Singapore by a delegation of the PIC/S in order to assess the inspection system and foster the necessary mutual confidence needed for the good operation of the PIC Scheme. A report was presented to the PIC/S Joint Committee in September and following a follow-up visit in December, the participation of Singapore to the PIC Scheme was accepted. It was agreed that the participation of the Singaporean Inspectorate would become effective as from 1 January 2000.

The Authorities of Germany and Italy, which are signatories to the PIC Convention and PIC/S Participating Authorities, are expected to join the Scheme in the near future. A number of other agencies are in the process of acceding to the Scheme (from Estonia, Latvia and Taiwan) while agencies from Greece, Malaysia, Russia and South Africa have also shown an interest in the Scheme.

The 1999 PIC/S seminar focuses on non-technical aspects of inspections

The 1999 seminar, which was organised in Oxford by the UK Medicines Control Agency, dealt with non-technical aspects of inspection. This very practical seminar looked at essential, non-technical skills such as communication and negotiation skills, which are necessary for inspectors to do their job effectively.

The seminar was attended by some hundred and twenty participants from 34 countries (PIC/S countries, as well as from Bulgaria, Estonia, Indonesia, Latvia, Malaysia, New Zealand, Poland, Singapore, Slovenia, Taiwan, Turkey and the USA). The collected papers presented on that occasion will be published in booklet form by the PIC/S Secretariat.

Seminars in 2000 and 2001 will deal with biotech and utilities

The Joint Committee decided that the next PIC/S Seminar would take place in Strasbourg on 25-27 October 2000 and agreed with the proposal of the French Agency for the Safety of Health Products (AFSSAPS) that the seminar's topic be on "The Inspection of the Manufacture of Biotech Products". The Joint Committee also welcomed the proposal by the Czech "State Institute for Drug Control" to host the 2001 Seminar in Prague and agreed with the proposed topic on "Utilities used by the Manufacturer of Pharmaceuticals".

Six new PIC/S Joint Visits groups are set up for the training of inspectors

Six new groups were set up in 1999, bringing the total number of groups participating in the programme to fourteen (four for the 1997-99 period, four for the 1998-2000 period and six for the 1999-2001 period). Inspectors from 17 different nationalities are participating in the programme.

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.

Three Expert circles meet in the course of the year

The Expert circles on blood, medicinal gases and hospital pharmacy met in the course of 1999.

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. Expert circles meet regularly to develop draft guidance, recommendations, etc. in their respective fields of specialisation.

Expert Circle on Blood

The sixth session of PIC/S Expert Circle on Blood was held in Pärnu (Estonia) on 24 and 25 June 1999. The topic was "Plasma trading - Traceability of plasma and intermediate products". It was attended by forty-two participants from twenty-three countries.

The highlight of this session was an appeal by participants that efforts be intensified to prevent the illicit trade of human plasma and plasma products. This could be achieved through the implementation of an internal system of control. Such a system should be designed to collect, maintain and analyse data on export and import of these products, which could provide assistance to governments.

The PIC/S Joint Committee endorsed the appeal at its annual meeting in Oxford.

Expert Circle on Medicinal Gases

The second Expert Circle on Medicinal Gases was held in Györ (Hungary) from 6 to 8 October 1999. 19 inspectors from 15 countries participated in the meeting and discussed about the inspection of medicinal gases; the revision of the GMP Annex on Medicinal Gases; and the regulatory framework on medicinal gases. Two visits of plants manufacturing medicinal gases were organised in and around Budapest.

Participants proposed to form a Steering Committee composed of three members. Its tasks would be to assist in preparing the programme for the next Expert Circle and to update participants on current issues in the field of Medicinal Gases.

Expert Circle on Hospital Pharmacy

The first Expert Circle on Hospital Pharmacy took place in Schiphol (The Netherlands) on 15-16 April 1999. Eleven experts from ten different countries attended the meeting and discussed on how to address issues such as the terminology used in the field of hospital pharmacy, the legislation governing the professional responsibility in hospital pharmacy, the lack of specific technical guidelines in the field of hospital pharmacy, etc. A follow-up to the issues raised will be provided at the occasion of the next expert circle.

PIC/S guidance documents have been or are in the process of being finalised

The revision of the PIC/S Recommendations on Validation Master Plan, Installation and Operational Qualification, Non-Sterile Process Validation, and Cleaning Validation (PR 1/99-1) entered into force on 1 March 1999.

The PIC/S Recommendation on Sterility Testing (PE 001-1) and the PIC/S Recommendation on Validation of Aseptic Processes (PE 002-1) were adopted by the PIC/S Committee on 7 September 1999. They entered into force on 1 January 2000.

The draft PIC/S Recommendations on Isolator Technology is in the process of being finalised, following its circulation to industry for comments.

The draft Guidance on Parametric Release was circulated to industry for comments in December 1999.

The PIC/S is also in the process of drafting / revising the following documents:

- PIC/S Guidance on Best Practises for Computerised Systems (draft)
- PIC/S Recommendation on Quality System (revised)
- GMP Annex on Medicinal Gases (revised)
- GMP Guide for Blood Centres (draft)

A list of PIC/S publications is attached at Annex III.

LIST OF PIC/S PARTICIPATING AUTHORITIES
(in 1999)

AUSTRALIA	GMP Audit and Licensing Section Therapeutic Goods Administration Department of Health and Age Care GPO Box 100 Woden Act 2606, Australia
AUSTRIA	Federal Ministry of Labour, Health and Social Affairs Stubenring 1 A-1010 Vienna
BELGIUM	Ministère de la Santé Publique et de l'Environnement Cité administrative de l'Etat Quartier Vésale, 311 B-1010 Brussels
CANADA	Therapeutic Products Programme Health Canada 11, Holland Ave., 2nd Floor Holland Cross, Locator 3002C Ottawa, Ontario K1A 1B6
CZECH REPUBLIC	State Institute for Drug Control Srobárova 48 100 41 Prague 10
DENMARK	Danish Medicines Agency 378 Frederikssundsvej DK-2700 Brønshøj
FINLAND	National Agency for Medicines Mannerheimintie 166 P.O. Box 55 FIN-00301 Helsinki
FRANCE	French Agency for the Safety Of Health Products (AFSSAPS) 143-145 Boulevard Anatole France F-93200 Saint Denis

GERMANY	Federal Ministry for Health Am Probsthof 78a D-53108 Bonn
HUNGARY	National Institute of Pharmacy P.O. Box 450 H-1372 Budapest 5
ICELAND	State Drug Inspectorate Eidistorg 15 P.O. Box 240 IS-172 Seltjarnarnes
IRELAND	Irish Medicines Board Block A Earlsfort Centre Earlsfort Terrace IRL-Dublin 2
ITALY	Ministero della Sanità Viale della Civiltà Romana 7 I-00144 Rome
LIECHTENSTEIN	Kontrollstelle für Arzneimittel Im Rietacker 4 FL-9494 Schaan
NETHERLANDS	Inspectorate of Health Care P.O. Box 16119 NL-2500 BC Den Haag
NORWAY	Norwegian Board of Health Pharmaceutical Department P.O. Box 8128 Dep. N-0032 Oslo 1
PORTUGAL	Instituto Nacional da Farmácia e do Medicamento (INFARMED) Avenida do Brasil, no 53 Pavilhaõ 21-A P-1700 Lisbon
ROMANIA	National Medicines Agency Strada Maior Aviator Stefan Sanatescu 48 Sectorul I RO-Bucharest

SLOVAK REPUBLIC	State Institute for Drug Control Kvetná 11 SK-825 08 Bratislava 2
SPAIN	Unidad de Inspección y Control Farmaceútico Subdirección General de Control Farmaceútico Paseo del Prado 18-20 28071-MADRID
SWEDEN	Medical Products Agency Box 26 S-751 03 Uppsala
SWITZERLAND	
For sera and vaccines	Division of Biologicals Federal Office of Public Health CH-3003 Berne
For all other medicinal products	Intercantonal Office for the Control of Medicines Erlachstrasse 8 CH-3000 Berne 9
UNITED KINGDOM	Medicines Control Agency Market Towers 1 Nine Elms Lane GB-London SW8 5NQ

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 1999 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.

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LIST OF PIC/S PUBLICATIONS

NEW PRICES AS OF 1 JANUARY 2000
(postage included)

o	**Guide to Good Manufacturing Practice for Medicinal Products**	**(PH 1/97)**
	Guidelines:	
o	- for the Manufacture of Sterile Medicinal Products	(PH 2/97)
o	- for the Manufacture of Veterinary Medicinal Products other than Immunological Veterinary Medicinal Products and for the Manufacture of Immunological Veterinary Medicinal Products	(PH 6/92)
o	- for the Manufacture of Investigational Pharmaceutical Products	(PH 3/97)
o	- for the Manufacture of Products derived from Human Blood or Blood Plasma	(PH 7/93)
o	- for the Manufacture of Active Pharmaceutical Ingredients	(PH 2/87)
	Explanatory Notes:	
o	- for Industry on the Preparation of a site master file to be part of the information requested under Article 2 of the Pharmaceutical Inspection Convention	(PH 4/93)
	Recommendations:	
o	- on Quality System Requirements for GMP Inspectorates	(PH 7/94)
o	- on a Quality System for Official Medicines Control Laboratories	(PH 2/95)
o	- on Validation Master Plan, Installation and Operational Qualification, Non-Sterile Process Validation and Cleaning Validation	(PR 1/99-1)
NEW➡➡ o	- on Sterility Testing	(PE 001-1)
NEW➡➡ o	- on the Validation of Aseptic Processes	(PE 002-1)
	Aide-Memoire:	
o	For the Inspection of Blood Donation and Plasmaspheresis	(PH 5/97)

Prices	The Guide to Good Manufacturing Practice for Medicinal Products (PH 1/97) is invoiced at	S.Frs. 40.- per copy
	All seminar booklets are invoiced at	S.Frs. 40.- per copy
	The Guidelines, Supplementary Guidelines, Explanatory Notes, Recommendations and Aide-Memoire are invoiced at	S.Frs. 25.- per copy

Booklets on Seminars organized under the auspices of the Pharmaceutical Inspection Convention (in English only**)**

- o - Manufacture and quality control under contract (Berne, July 1974)
- o - The manufacturer's quality control department. Structural and functional aspects (Copenhagen, June 1975)
- o - Stability of pharmaceutical products (Salzburg, June 1976)
- o - Modern methodology for the isolation, identification and quantification of drugs and related substances (Uppsala, June 1977)
- o - Inspection in tablet manufacture (Copenhagen, June 1980)
- o - Good manufacturing practice in the manufacture of active ingredients (Liestal/Basle, June 1980)
- o - Application of GMP rules in the control laboratory (Budapest, June 1981)
- o - Safety aspects of the packaging of pharmaceutical products (Lisbon, June 1983)
- o - Requirements of good manufacturing practice and quality control in the production of biological products (Frankfurt a/Main, May 1984)
- o - Premises for pharmaceutical manufacture (Oslo, June 1985)
- o - Plastics and their pharmaceutical applications (Sigtuna, June 1986)
- o - The business of pharmaceutical inspection (Cambridge, September 1987)
- o - Water for pharmaceutical purposes (Jongny, September 1988)
- o - Contamination risks in the manufacture of parenterals (Baden, September 1989)
- o - Blood and blood products (Hillerød, September 1990)
- o - Audit - Pharmaceutical Inspection (Felsötárkány, June 1991)
- o - New aspects of products derived from biotechnology (Montecatini, May 1992)
- o - The Role of Inspection and Testing in relation to the Marketing authorization (Louvain, September 1993)
- o - Qualification and validation in Pharmaceutical Manufacture (Dublin, July 1994)
- o - Inspecting the Manufacture of Sterile Products - Current and Future Trends (Hveragerði, June 1995)
- o - Inspection of computer systems (Sydney, September 1996)
- o - Manufacture and inspection of Active Pharmaceutical Ingredients (Naantali, June 1997)
- o - Quality System for Pharmaceutical Inspectorates (Zeist, June 1998)
- o - PIC/s Expert Circle on Medicinal Gases (Sigtuna, November 1997) (PH 1/98)

These publications can be obtained from the

Secretariat to the Pharmaceutical Inspection Convention
c/o EFTA Secretariat
9-11, rue de Varembé
CH - 1211 GENEVA 20
e-mail: daniel.brunner@secrgva.efta.be
Tel.: +41 22 / 749.12.65
Fax: +41 22 / 740.14.37