PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PS/W 8/2005
4 Annexes
23 December 2005

PIC/S BLUEPRINT

Blueprint = "blue photographic print representing final stage of engineering or other plans; (fig) detailed plan of work to be done"*

* The Concise Oxford Dictionnary

PIC/S BLUEPRINT

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Acknowledgement: To Mr. Robert Tribe, former PIC/S Chairman, Australia, whose standard presentation on PIC/S has been used in this document to present the various PIC/S activities.

1. Executive Summary

1. The present "Blueprint" aims at reviewing PIC/S' mission and at setting clear objectives and concrete actions to be taken / achieved during the next decade (i.e. by 2015).

2. PIC/S has been a pioneer organisation in the field of pharmaceutical inspections and Good Manufacturing Practice (GMP). It has successfully adapted to a constantly changing environment, notably increased European integration and globalisation. Its membership has grown from 10 to 28 Participating Authorities today[1]. Most of its Members are Authorities of Member States of the European Union (EU).

3. It has become vital for PIC/S to distinguish itself, in a constructive way and in a spirit of complementarity, in its activities from other bodies and organisations, in particular the European Medicines Agency (EMEA) or the EU Heads of Agencies. PIC/S must increasingly focus on its added-value and specificity. In a world, which has become increasingly globalised, PIC/S must turn more global as well and reach out to the world.

4. In order to achieve this and simultaneously improve its position as a "global player" at the international level, PIC/S must become more representative and expand to America, Asia and Africa. It must in particular actively encourage non-EU Members to join PIC/S, notably "key players" such as the US FDA, Brazil, Japan, etc. However, integrating these key players should not result in either a lowering of standards or a reduction in PIC/S activities.

5. As its membership will grow by 10 – 12 new Members by 2015, PIC/S will have to review its organisation and functioning while ensuring that existing and new Members adhere to the existing values and principles. While expanding, the organisation should remain an egalitarian one which is not dominated by one particular bloc or another. In maintaining this equality, it must draw on the best from the different strands of membership and also be cognisant of developments amongst those who remain outside.

6. PIC/S' mission, as defined in 2002, still remains valid today, i.e.: **"To lead the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products."** This is to be achieved by developing and promoting harmonised GMP standards and guidance documents; training competent authorities, in particular inspectors; assessing (and reassessing) inspectorates; and facilitating the co-operation and networking for competent authorities and international organisations.

7. In the field of standards, PIC/S will continue to harmonise and modernise its GMP standards and ensure that the PIC/S GMP Guide remains a high-standard international GMP Guide. Other guidance documents will be developed according to

[1] Status as of 23 December 2005. 29 Participating Authorities as of 1 January 2006

established priorities. The extension of PIC/S' mission to include Good Distribution Practice (GDP) standards will be considered.

8. The various training and harmonisation tools (Seminar, Expert Circles, Joint Visits Programme), which have proved to be effective so far, will be "professionalized" and opened up to include Member-specific training needs. The number of Expert Circles will be increased. Coached inspections for training purposes will be introduced. Training will increasingly focus on improving consistency and uniformity of inspections amongst PIC/S Participating Authorities – an area where Inspectors are sometimes criticised by industry.

9. The assessment of new Members and the reassessment of existing Members will have to be further harmonised so that the same tools can be used in the future.

10. PIC/S will more actively encourage networking by establishing on a regular basis a "PIC/S GMP Forum" which will allow non-Member Authorities, professional and other organisations to meet informally with the PIC/S Committee.

11. The increasing globalisation of public health concerns and the multiplication of actors involved (both in industry and among Regulatory Authorities) makes it necessary to further increase harmonisation efforts in setting regulatory requirements, inspecting and evaluating GMP compliance, licensing manufacturing sites, recalling defective batches, and increasing the exchange of information. PIC/S offers an attractive platform to respond to the challenges of globalisation.

12. The sharing of information on GMP inspections will be further encouraged in order to maximise the use of resources. Regarding overseas inspections, other means than the International Medicinal Inspectorates' Database (IMID) will be used to avoid duplications with the EUDRA GMP Database.

13. Relations with other organisations will be reviewed on the basis of (i) non-discrimination and equal treatment and (ii) non-duplication with Member Authorities. As human and financial resources are getting scarce at the level of national authorities as well as at the level of international organisations, the duplication of tasks must be avoided. The review should also aim at ensuring the support of relevant professional and other organisations to PIC/S' mission.

14. The PIC/S Secretariat will continue to provide professional secretariat services. Available funds will be spent in a conservative and transparent manner to all Participating Authorities in order to keep membership fees stable until 2015.

2. Introduction

15. At its 71st meeting in Geneva on 8-9 February 2005, the Committee decided to adopt a "Road Map" for PIC/S "defining its mission, goals, specificity and usefulness". The main reasons for elaborating such a document were:

(i) to review PIC/S' mission and goals in a changing environment, notably in the context of increased European integration,

(ii) to set a number of objectives and actions, which should be taken in the future (i.e. in the next 10 years) in order to ensure PIC/S' smooth development and the achievement of its mission and goals,

(iii) to raise PIC/S' visibility and explain the benefits of PIC/S membership.

16. The present document is, however, more than a "Road Map", as it also highlights past achievements and provides for a detailed plan of work to be done over the next 10 years (thus the name "Blueprint"). The retrospective is necessary in order to determine where PIC/S is going, notably 10 years after the Scheme was launched. It is essential to look back first and see where PIC/S comes from and where it stands today in order to imagine what PIC/S will look like in around 10 years and what needs to be done in order to achieve PIC/S' mission and goals.

17. The timeframe for the present document is the period 1970 – 2015, which can be segmented as follows:

- past (history): 1970 – 1994
- recent past and present: 1995 – 2005
- future: 2006 – 2015

3. PIC/S in a changing environment

3.1 The past: from PIC to PIC/S

18. On 8 October 1970, Member States party to the European Free Trade Association (EFTA) signed the "Convention for the Mutual Recognition of Inspections in Respect of the Manufacture of Pharmaceutical Products" or "Pharmaceutical Inspection Convention" (PIC). PIC aimed at the removal of non-tariff barriers in the trade of pharmaceuticals in Europe through the mutual recognition of inspection reports and certificates on Good Manufacturing Practice (GMP).

19. The Convention was the first ever Mutual Recognition Agreement (MRA) in the field of pharmaceutical inspections. It was established in a virtual no-man's land at a time where the free trade of pharmaceuticals in Europe was still largely hampered by the non-recognition of national GMP inspection results by European health authorities, whether they were part of the European Economic Community (EEC) or

EFTA. In those times, national health authorities, including those from the EEC, were still exclusively competent for GMP inspections and little or no harmonisation had been made at the European level.

20. The Convention expanded and its membership increased from the initial 10 to 18 by the end of 1992 (for the List of PIC Members, see Annex I). With the exception of Australia, Hungary and Romania, all new Members were from the EEC. During this period, GMP standards were further developed and harmonised between the Convention's Contracting States (see Chap. 5.1). Both the European Commission (EC) and the World Health Organization (WHO) were granted an Observer Status.

21. With the 1992 Treaty of Maastricht, the completion of the European Union' Single Market was accelerated and the EC was conferred extensive powers to negotiate trade and trade-related agreements with third countries. Inevitably, these powers conflicted with the PIC Convention and the ability for PIC to expand was brought to a halt by the EEC Members of PIC. As this particular juncture, PIC was threatened to disappear. To survive, it had to reinvent itself.

3.2 The present: PIC/S

22. On 2 November 1995 PIC Regulatory Authorities decided to establish a new co-operation instrument: the Pharmaceutical Inspection Co-operation Scheme (PIC/S). PIC/S aims at harmonising inspection procedures worldwide by developing common standards in the field of GMP and by providing training opportunities to inspectors and inspectorates. It also aims at facilitating co-operation and networking between competent authorities and international organisations, thus increasing mutual confidence and facilitating the acceptance of inspection results.

23. The main difference between PIC and the Scheme is the non-binding character of PIC/S, which is an informal arrangement between Regulatory Authorities (and not between States) which exchange information on GMP inspections (including certificates) on a purely voluntary basis (see Annex III). Contrary to PIC, the Scheme also applies to veterinary products. In addition, more emphasis has been given to the training of inspectors, the harmonised interpretation of GMP standards through guidance documents and the requirement of a Quality System for pharmaceutical inspectorates.

24. In 1995, the European Medicines Agency (EMEA) was established in London. It rapidly became an Observer to PIC/S and a major partner of co-operation, notably in the field of standards (e.g. joint consultation procedure for changes to the GMP guide), rapid alert (same procedure) and training (the EMEA has always relied on PIC/S to provide continuous training to European inspectors). In February 1996, EU Heads of Member States Competent Authorities (Heads of Agencies) met for the first time in the Netherlands. Co-operation between PIC/S and the EU Heads of Agencies has focused on the EU Joint Audit Programme (see Chap. 5.3).

25. Since 1995, PIC/S has continued the successful expansion started by the PIC Convention and increased the number of members from 18 to 28[2]. First a purely European organisation, PIC/S has increasingly become more global to encompass authorities from countries from North America (Canada), Asia (Malaysia, Singapore) and the Pacific (Australia).

26. In 2002-2003, discussions arose on (i) what to do with the Convention and (ii) whether PIC/S should become independent or whether its Secretariat should be hosted by WHO[3]. In order to become a legally recognised entity in Switzerland, PIC/S constituted itself as an Association under the Swiss law on 3 June 2003. On 1 January 2004, it eventually became an independent organisation. On 1 July 2005, the Czech Institute for veterinary products became PIC/S' first purely veterinary Participating Authority[4].

27. During the period under consideration (1995 – 2005) EU Members of PIC/S increased from 8 (out of a total of 18, i.e. 44%) to 19 (out of a total of 28, i.e. 68%).

28. EU Members of PIC/S are in a special position compared to non-EU Members as they are bound by a double allegiance: one to the EU and one to PIC/S. However, their allegiance to the EU is based on legally-binding treaties and thus overrules their allegiance to PIC/S, where decisions are only taken under the form of non-binding recommendations.

29. Double allegiance also means double obligations for EU Members of PIC/S. In some countries such as Germany, the situation is even more complicated because efforts of harmonisation are also necessary at the national / federal level.

30. These obligations have increasingly become a heavy burden for EU Members of PIC/S, as the EU has expanded horizontally (geographically) and vertically (closer integration). Geographically, the EU has grown from the initial 6 founding States in 1958 to 25 by 2004. Normally, not more than 2 or 3 new States have joined the Union at the same time, thus facilitating their integration. However, in May 2004, 10 new countries joined the Union at once[5]. This unprecedented enlargement has put the EU and their Members under strain. In addition, the Commission has embarked on concluding a wide range of Free Trade Agreements and related MRAs in the field of GMP. The resulting obligations have also had an impact on EU Members of PIC/S, which have been entrusted with carrying out pre-MRA visits on behalf of the Commission in the 10 Accession Countries.

31. Simultaneously, the closer integration of EU Member States has forced their Agencies to seek greater harmonisation between themselves (e.g. Directives in the field of GMP, Compilation of Community Procedures, Joint Assessment Programme, etc.) and devolve greater powers to the EMEA (e.g. inspection of centrally-approved products, Community Databases, training, etc.).

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2 Status as of 23 December 2005. 29 Participating Authorities as of 1 January 2006

3 Discussions on the possibility for WHO to host the PIC/S Secretariat on its premises aborted.

4 Many PIC/S Participating Authorities are responsible for medicinal products for both human and veterinary use.

5 Two additional countries will join the EU by 2007

3.3 The future

32. The significant changes undergone in the past few years and PIC/S' international expansion would suggest that emphasis should be put on consolidating PIC/S' recent "acquis".

33. However, PIC/S is facing a number of challenges:

- **With a few exceptions, relations between countries, where the Regulatory Authority is a PIC/S Participating Authority, are nowadays ruled by legally binding obligations, which are defined by the Treaties establishing the EU/EEA[6] and MRAs (see Annex II) – not by PIC/S any longer;**
- **The multiplication of obligations and the various efforts of harmonisation made at different levels have increased the risk of redundancy (e.g. assessment of Regulatory Authorities);**
- **Human and financial resources, previously available for a wide variety of PIC/S purposes, have become scarcer at a time when more and more Regulatory Authorities apply for PIC/S membership.**

34. It has become vital for PIC/S to distinguish itself, in a constructive way and in a spirit of complementarity, in its nature and activities from the EU and focus on its added-value and specificity. Other adjustments will also have to be considered regarding PIC/S' functioning, visibility and transparency.

3.3.1 Membership

35. In 2005, eight Agencies were in the process of acceding to PIC/S[7]: Argentina, Estonia, Israel, Lithuania, Poland[8], South Africa, the Ukraine and the US FDA. UNICEF had applied for Observer Status[9]. Four other GMP inspectorates have also indicated an interest in seeking PIC/S membership: Brazil, Cyprus, Indonesia and Thailand. Considering that it takes between 3 and 6 years to become a full Member, it can be expected that PIC/S will grow by another 10 – 12 Members by 2015.

36. With around 40 Participating Authorities by 2015, PIC/S will be a different organisation. Most new Authorities will not be from Member States of the EU, thus turning PIC/S into a more international forum.

37. However, the membership of PIC/S, consisting of developed or newly-industrialised countries, is unlikely to change over the next decade. To a large extent, PIC/S' membership will remain similar to that of the Organisation for Economic Co-

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6 European Economic Area

7 Both Oman and Russia have also applied but their application is incomplete and has thus not started.

8 Poland's Main Pharmaceutical Inspectorate will join PIC/S on 1 January 2006.

9 UNICEF will become an Observer to PIC/S on 1 January 2006.

operation and Development (OECD). PIC/S and the OECD already share the same members (23 out of 30 OECD countries) with the following exceptions:

- OECD Member only: Japan, Korea, Luxembourg, Mexico, New Zealand, Turkey, United States
- PIC/S Member only: Malaysia, Latvia, Romania, Singapore

38. To a certain extent, PIC/S fulfils a similar role as the OECD but in the field of pharmaceutical inspections. Similar to the OECD, PIC/S will evolve in what could be called a "middle field", which is limited on the one hand by the EU/EEA (and related network of MRAs) and on the other by WHO[10]. Compared to the EU and WHO, PIC/S has some advantages:

- Compared to the EU/EEA (and related MRAs), the main advantage of PIC/S is that under PIC/S, Participating Authorities may, if they wish, exchange information on GMP inspections but do not have to accept the inspection results, as it is the case under an MRA.
- Compared to WHO, PIC/S has more stringent rules regarding membership and expects new Members to have an equivalent GMP inspection and Quality System in place. This implies that the Regulatory Authority applying for PIC/S membership must use the PIC/S or EC[11] GMP Guide (or equivalent) before it can join PIC/S (there is no requirement to apply the WHO GMP Guide or equivalent before a State joins WHO).

39. To become a "global player" in the field of pharmaceutical inspections, PIC/S must actively encourage non-EU / non-MRA Members to join, provided that they have an equivalent GMP regulatory controls and Quality System. Non-EU / non-MRA Members represent an added value for PIC/S in terms of "representativeness". For this, PIC/S must target more pro-actively specific "key players". These "key players" are countries which matter in terms of pharmaceutical industry and GMP inspections. They include countries such as Brazil, China, India, Indonesia, Japan, Korea, Mexico, Russia, Thailand, Turkey, etc.[12]

40. There are different ways to target these "key players" and encourage them to join PIC/S:

- The Secretariat can systematically extend invitations to training events to these "key players";

- Members of the Committee, who meet representatives of these "key players" in other fora (e.g. visits, international meetings – ICH, WHO, ASEAN, PAHO, etc.), can explain the benefits of joining PIC/S;

- The Chairperson (or a person designated by him/her) could pay a courtesy visit to these "key players" in order to initiate contacts and discuss the benefits of PIC/S membership.

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10 For the OECD, it is the World Trade Organization (WTO)

11 For EU Member States this must be the EC GMP Guide

12 The list is not exhaustive. Argentina's National Institute of Medicaments (INAME) and the US FDA have both applied for PIC/S membership.

41. At the same time, PIC/S must avoid creating a situation where too many Authorities would apply simultaneously. This could result in a lack of resources to evaluate all applications and a delayed evaluation process. In terms of capacity, PIC/S has been able to cope in recent years with assessing an average of 5 applications in parallel. Considering that 10 – 12 Authorities may join by 2015, this means that 1 possibly 2 Authorities will become Members every year. This is not considerably more than presently.

Goal:	Improve PIC/S position as a "global player" in the GMP field for Regulatory Authorities.
Means:	(i) Attract non-EU Agencies having an equivalent GMP inspection and quality system; (ii) Integrate at least 10 – 12 new Agencies by 2015.
Actions:	Immediate: Prepare for the assessment of new or expected applications (Argentina, Israel, Thai FDA, Ukraine, US FDA, etc.). Medium to long term: (i) Prepare for the integration of at least 10 – 12 new Members by 2015; (ii) Target key players which have no or limited contact with PIC/S (Brazil, China, India, Indonesia, Japan, Korea, Mexico, Russia, Turkey, etc.).

3.3.2 Relations with Regional Institutions (ASEAN, EU Heads of Agencies, EMEA, Commission, etc.)

42. Co-operation with regional institutions has become increasingly important for PIC/S, as these bodies are actively involved in the field of GMP – whether in terms of harmonisation, standards or training. To ensure their support is important to reduce the risk of unnecessary duplications.

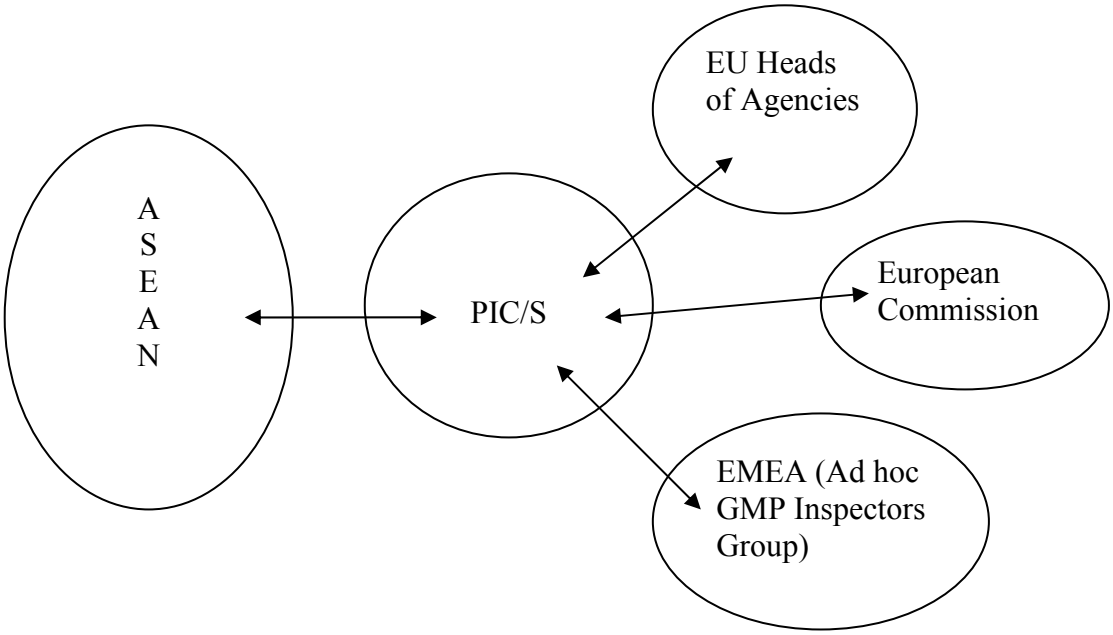
43. Looking at PIC/S' membership, there are currently only two Regional Institutions, which are relevant for GMP matters: the Association of South East Asian Nations (ASEAN) and the EU (Heads of Agencies, EMEA, Commission). Provided that other countries join PIC/S, regional organisations such as Mercosur[13] or NAFTA[14] may also have to be considered if active in the field of GMP.

44. Regarding ASEAN, PIC/S membership was recently defined as one of the essential criteria for the establishment of a MRA by ASEAN in the field of GMP inspections. GMP training, funded by the EC under EU-ASEAN co-operation, has also been provided to ASEAN GMP inspectors.

[13] Mercado Común del Sur (Argentina, Brazil, Paraguay, Uruguay)
[14] North American Free Trade Agreement (Canada, Mexico, USA)

45. Regarding the EU, PIC/S has always tried to act pragmatically and avoid unnecessary duplications. It has encouraged the exchange of already available information with the Commission such as on assessment reports of new Members (e.g. Poland, Czech Veterinary Agency). For the time being, this exchange of information relies on the good will of the various actors involved at the EU level (see box below).

46. To ensure the complementarity of its activities with those of ASEAN, the Commission, the EU Heads of Agencies and the EMEA (notably the Ad Hoc Group of GMP inspection services), PIC/S should aim at consolidating its relations with those bodies involved in GMP matters.



47. This consolidation should result in a closer co-operation and increased complementarity, notably in the field of the exchange of information; the mutual recognition of inspectorates' assessment results (PIC/S Joint Reassessment Programme, EU Joint Audit Programme); the development of standards (GMP Guides and guidance documents); and GMP training.

Partner of Co-operation	**Field of Co-operation**
ASEAN	Training
	Standards
EU Heads of Agencies	EU Joint Audit Programme
	Sharing of resources
European Commission	Standards (consultation procedure)
	Training
EMEA (Ad hoc GMP Inspectors Group)	Standards (consultation procedure)
	Training

48. This would have a number of advantages for all parties involved:

- ❖ Framework: For EU or ASEAN Members of PIC/S, ensuring PIC/S' complementarity to the goals fostered by the EU and ASEAN, respectively, would eliminate the risk of duplication and constitute a better framework under which GMP inspectorates are working.

- ❖ GMP training: EU or ASEAN specific training needs could be better taken care of when elaborating the programmes of PIC/S Seminars and Expert Circles. Parallel or additional sessions on EU- or ASEAN-specific requirements could be built into PIC/S training programmes, thus making PIC/S training sessions more appealing to EU and ASEAN GMP inspectors.

- ❖ Exchange of information: Duplications in the field of assessment (including pre-MRA inspections) or reassessment of Inspectorates could be avoided assessment results, notably under the EU Heads of Agencies' Joint Audit Programme (JAP) and the PIC/S Joint Reassessment Programme (JRP), could be exchanged.

- ❖ Enlargement / MRA: While acknowledging the Commission's tremendous efforts to facilitate the integration of new EU Member States through EU sponsored training programmes (Pan European Regulatory Forum, Twining Programmes, etc.), experience has shown that it is easier for a country whose GMP authority is participating in PIC/S to integrate into the EU than for a non-PIC/S Participating Authority. The same can be said about ASEAN and its objective to establish an MRA within ASEAN in the field of GMP inspections.

49. There are various ways of achieving both consolidation and complementarity (in addition to those already in place) such as:

- Direct contacts and occasional visits by the PIC/S Chairperson to the EC in Brussels or the ASEAN Secretariat in Jakarta;

- Exchange of letters (with ASEAN, with the Commission, with the EU Heads of Agencies, with the EMEA);

- Update of already existing co-operation instruments (e.g. consultation procedure with the EMEA);

- Ensuring that PIC/S is mentioned in important documents of its EU or ASEAN partners (e.g. ASEAN or Heads of Agencies' documents, EMEA Road Map).

Goal:	Ensure complementary of PIC/S activities with those of ASEAN, the EU Heads of Agencies, the Commission and the EMEA in order to improve co-operation and avoid unnecessary duplications.	
Means:	Contacts, meetings, exchange of letters, etc.	
Actions:	By 2006:	PIC/S Chairperson to visit the Commission; to write to Heads of Agencies and ASEAN; etc.
	By 2007:	Possible visit of the Chairperson to the ASEAN Secretariat (in the margins of the 2007 Seminar); Update Joint Consultation Procedure with the EMEA.
	By 2010:	Review co-operation with ASEAN, the EU Heads of Agencies, the Commission and the EMEA.

3.3.3 PIC/S concepts and principles

50. With non-EU Members being increasingly attracted by PIC/S, will their integration be smooth? Looking at past experience (Canada, Singapore, and Malaysia) there is no reason to fear that the integration of future non-European Members will cause any problems. PIC/S' success has been possible due to the common sharing of unwritten concepts or principles, which may, however, not be that obvious to non-PIC/S Members. These concepts or principles are:

- **A technical experts' organisation**: PIC/S has always taken great pride in featuring itself as a purely technical organisation in the field of regulatory GMP. Not becoming politically involved or discriminating against e.g. religion or race has always been PIC/S' firm believe. Moreover, PIC/S is a major "think-tank" in the GMP field, the place where new ideas related to GMP are debated by highly competent experts.

- **Based on consensus and mutual trust**: Consensus in PIC/S has been based on the understanding that all Members have equal rights and obligations and that no Member is more "equal" (larger, richer…) than others. Despite the difficulty of having to negotiate compromises acceptable to all Members, PIC/S has always found a way forward without isolating a Member, which finds itself alone against the vast majority. Mutual trust is a key value in PIC/S and largely relies on the concept of

  a) voluntary co-operation (there is no legal obligation under PIC/S) and

  b) each Member being assessed for equivalence before being admitted.

  As all PIC/S Members are supposed to be equivalent, Members find it easier to exchange information on GMP on a voluntary basis.

- **Driven by Members**: PIC/S is an organisation which is mainly driven by Participating Regulatory Authorities and where the Secretariat has remained

small, flexible and productive. As a result, PIC/S is a flexible and dynamic organisation, which is neither bureaucratic nor expensive. This also implies that Participating Authorities are expected to contribute to either PIC/S events (e.g. by hosting training events) or to PIC/S functioning (e.g. by allowing Members to carry out official duties for PIC/S such as chairing PIC/S meetings or representing PIC/S during conferences).

- **Cemented by strong professional and personal links**: PIC/S' strength relies on its informal character, networking and the strong personal links between individual Members or Inspectors which have created a forum for brain storming, discussing new ideas and sharing information. It is not a coincidence that the first draft of the ICH Q7A Guide was initiated by PIC/S.

51. All these unwritten concepts and principles have been fundamental in PIC/S' success, clearly distinguishing itself from other organisations, which are more formal. Some of these concepts, notably the GMP "think-tank", could be further elaborated and refined. In addition, some kind of review mechanism to monitor the co-operation between PIC/S Participating Authorities could also be considered.

Goal:	Remain an internationally known technical experts' organisation in the field of regulatory GMP based on consensus and mutual trust, driven by Members and cemented by strong personal and professional links.	
Means:	(i) Stick to values and principles which have made the success of PIC/S; (ii) Further elaborate on the concept of GMP "think-tank"; (iii) Consider a review mechanism to monitor the co-operation between PIC/S Participating Authorities.	
Actions:	By 2008:	Finalise concept of GMP "think-tank" and put in place review mechanism.
	By 2014:	Review values and principles.

3.3.4 Functioning / Organisation

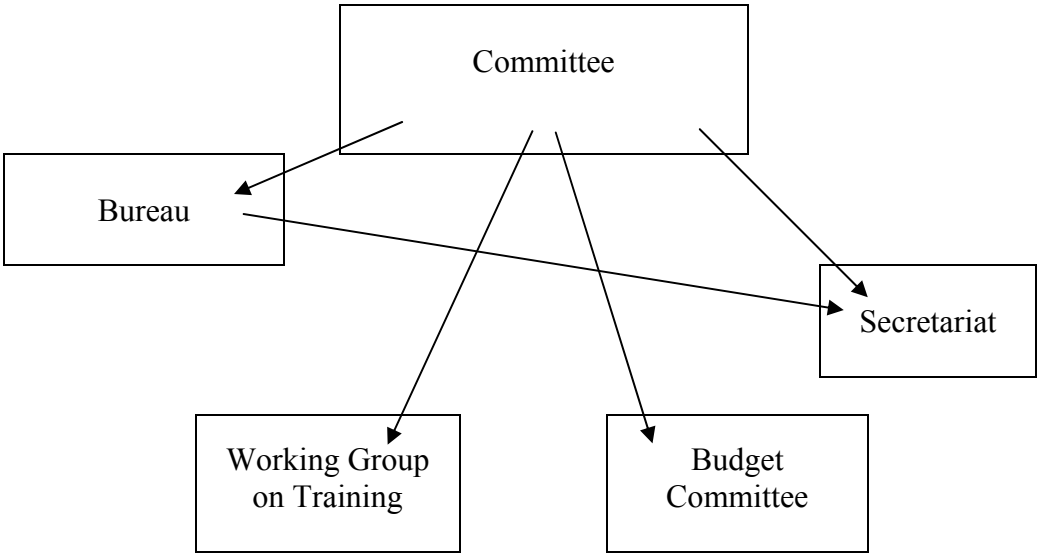
52. The current status of PIC/S is that of an Association under the Swiss law. Will PIC/S still have the same status by 2015? Recent discussions have taken place on whether to turn PIC/S into an international organisation but the conclusion was that there were more disadvantages than advantages. Therefore, the PIC/S Committee decided in early 2005 against turning into an international organisation in order not to undermine the Scheme's main assets, notably its flexibility and dynamism. As a result, PIC/S will remain an Association under the Swiss law for the years to come. Experience will demonstrate whether the status of a Swiss Association is a sufficiently strong and efficient basis for PIC/S.

53. In line with the recommendation made by its Depositary, the PIC Convention should be terminated once Australia and Switzerland have concluded a MRA and the latter has entered into force. These two countries are the last of the PIC member

countries to use the legally binding nature of the PIC Convention to exchange GMP certificates. Thus, the need for PIC to continue to operate no longer exists once the MRA between Australia and Switzerland is concluded. Because of this, the PIC Convention should be terminated by 2015. This would also help reducing frequent confusions and mix-ups between PIC and PIC/S such as (erroneously) believing that the Scheme provides for the mutual recognition of inspections.

54. Regarding its organisational structure, PIC/S created an Executive Bureau back in 2003. The Executive Bureau assists the Chairperson in exercising his/her functions, which have increased over time. It is also responsible for preparing PIC/S Committee meetings and administrating the organisation in-between two Committee meetings. In order to facilitate its functioning, the Bureau will need to adopt its own Rules of Procedure. The latter must ensure that the Executive Bureau seeks approval from the Committee prior to making any commitments. In addition, Executive Bureau meetings will be open to Observers from Participating Authorities in order guarantee full transparency of its deliberations and decisions.

55. Contrary to other organisations, there is no clear-cut separation between the Committee (Assembly) and the Bureau (Executive). The Secretariat has also a reduced role (i.e. preparing meetings) and mainly assists Members in their duties. This structure is unlikely to change in the future, as it is functioning very well. The fact that Members of the Bureau also sit on the Committee allows a better co-operation between the two bodies and diminishes the risk of conflicts.



56. Regarding the frequency of meetings, the Committee has met on average every 6 months (i.e. twice a year). The Bureau is meeting slightly more often (normally 3 times a year) in order to prepare for meetings of the Committee and to steer the organisation in-between two Committee meetings. The frequency of meetings is likely to remain unchanged in the future.

57. Consensus has been a long tradition in PIC/S and should remain the overarching principle and basis on how decisions are reached in PIC/S.

Goal:	Remain a well-functioning and internationally recognised organisation.	
Means:	Remain an Association under the Swiss law.	
Actions:	By 2006:	The Executive Bureau to adopt its Rules of Procedure.
	By 2015:	Terminate PIC Convention.

3.3.5 Visibility

58. Although PIC/S will become more visible while growing in Members, there might nevertheless be a need to further increase PIC/S' visibility. While solid training is definitely an excellent way to increase PIC/S' reputation and visibility, other means could be considered.

59. So far, the PIC/S web site has been the main instrument of dissemination of information on PIC/S. It is well known by industry and frequently visited. The site is rather clear and comprehensive for the average user, although there is room for improvements, e.g. related PIC/S guidance documents such as Quality system documents could be grouped together. More information could be released on the web site. This could be done through short press releases or by making documents, such as the present Blueprint, available on the web site. This would also make PIC/S more transparent to the outside world.

60. In addition to the web site, presentations made at industry conferences have been another privilege channel of communication to disseminate information on PIC/S. Invitations to such conferences have substantially increased over the past few years: around 10 to 12 presentations (based on a standard module) are given by Members of the Executive Bureau every year.

61. A possible way of increasing the awareness of key players could be a more active public relations policy. The first step of such a policy would be to elaborate an information brochure on PIC/S, which could be distributed during conferences, sent to industry associations and downloaded from the web site. The brochure could underline PIC/S achievements and membership benefits (see Chapter 4). A glossy print version of the present "Blueprint" could also be distributed to key interlocutors.

62. The idea of creating a "PIC/S GMP Forum", where Members and non-Members of PIC/S as well industry could meet informally, is raised under Chapter 5.4 "Networking".

Goal:	Increase PIC/S' visibility.	
Means:	Adopt a higher profile! Elaborate an information brochure on PIC/S; Release more information on the web site (e.g. the Blueprint); Make use of the standard presentation on PIC/S (PowerPoint slides).	
Actions:	By 2006:	PIC/S to agree on an information brochure.

4. Benefits of PIC/S membership

63. Although this list is not exhaustive, these can be considered as being the main benefits for Regulatory Authorities resulting from PIC/S membership:

- **Training opportunities**: PIC/S provides a forum for the training of GMP inspectors thus allowing the latter to benefit from increased training opportunities by attending PIC/S Seminars and Expert Circles and by participating in the PIC/S Joint Visits Programme. In this respect, PIC/S is unique as there is no other international training forum run jointly by Regulatory Authorities (individually, Regulatory Authorities or organisations such as WHO or the EMEA provide basic training courses, mainly to new inspectors).

- **International GMP harmonisation:** By taking part in the meetings of the PIC/S Committee, PIC/S Participating Authorities are involved in the development and harmonisation of international GMP guides and guidelines. The PIC/S Committee also actively promotes the uniform interpretation of GMP and Quality Systems for GMP Inspectorates.

- **Networking:** By attending PIC/S activities, participants benefit from personal contacts with other agencies, whether they are part of PIC/S or not. This networking often simplifies contacts and the exchange of GMP related information. In addition, PIC/S is **one of the few international GMP fora** for networking and confidence building amongst regulatory inspectors where experts (GMP inspectors, specialist GMP inspectors and chief inspectors) can meet, discuss issues of mutual concern and share experiences and information. In other fora, participation is either at the level of Heads of Agencies (e.g. WHO) or at the level of experts in a particular field (ICH[15]).

- **High standards:** PIC/S ensures that all Members comply with PIC/S standards at all times (assessment of new applicants and reassessment of existing member inspectorates). Preparing for the accession to the Scheme (or reassessment) forces improvements in the GMP inspection system and procedures. This result in increased efficiency of the GMP inspectorate.

[15] International Conference on Harmonisation

This is particularly true for Quality System requirements, where PIC/S standards are high, and for GMP training, which is essential in PIC/S.

- **Sharing of information:** PIC/S allows for a more effective use of inspection resources through the voluntary sharing of GMP inspections reports. Membership is also a cost-saving measure for the inspection authorities confronted with an increase of inspections, notably in the field of active pharmaceutical ingredients (APIs).

- **Rapid Alert System:** Through PIC/S membership, Regulatory Authorities automatically benefit from being part of the PIC/S Rapid Alert and Recall System arising from quality defects of batches of medicinal products, which have been distributed on the market. The PIC/S alert and recall system is part of a wider system, which includes the alert and recall system of EU/EEA/MRA partners.

- **Facilitating the conclusion of other Agreements:** Membership in the PIC/S may also facilitate the conclusion of other agreements, e.g. Mutual Recognition Agreements, between Members at various levels (e.g. Australia-Canada MRA, EU-Switzerland MRA, etc.). During the recently concluded initial negotiation on ASEAN MRA on GMP Inspection, PIC/S membership accession was accepted as one of the essential criteria for MRA.

64. There are also indirect benefits to industry when their relevant regulatory authority becomes a member of PIC/S. These benefits may include the following:

- Reduced duplication of inspections
- Cost savings
- Export facilitation
- Enhanced market access

65. Although PIC/S is not a trade agreement, membership in PIC/S may facilitate the export of pharmaceuticals. Some non-PIC/S Authorities in e.g. Colombia and South Africa accept GMP certificates from PIC/S Participating Authorities. Reputable organisations such as the "Global Fund to Fight AIDS, Tuberculosis and Malaria" consider PIC/S Participating Authorities as "stringent Regulatory Authorities" meaning that a medicinal product may be pre-qualified by the Global Fund if it has been authorised by a PIC/S Participating Authority. This means that non-PIC/S authorities and organisations have a greater confidence in medicines manufactured in countries where the Regulatory Authority is a PIC/S Participating Authority. Consequently, the pharmaceutical industry located in these countries indirectly benefits from PIC/S membership.

Goal:	Highlight the benefits of PIC/S membership.
Means:	Put the list of benefits on the PIC/S web site and in PIC/S documentation (see also "visibility").
Actions:	By 2006: Update the PIC/S web site to include membership benefits.

5. PIC/S Mission and Goals

66. While in the past, the main goal of the PIC Convention was to mutually recognise GMP inspections in order to facilitate the trade of pharmaceuticals, the goals of PIC/S since it was launched back in 1995 are the harmonisation of GMP standards, GMP training and networking. In 2000, the reassessment of PIC/S Participating Authorities was added.

67. At its 65th meeting in Geneva on 22-23 April 2002, the PIC/S Committee succeeded in adopting a clear mission with precise goals for PIC/S, which is:

> "To lead the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products"
>
> This is to be achieved by:
> - Developing and promoting harmonised GMP standards and guidance documents;
> - Training competent authorities, in particular inspectors;
> - Assessing (and reassessing) inspectorates;
> - Facilitating the co-operation and networking for competent authorities and international organisations.

68. By and large, the overall mission and the way the goals should be achieved (see also subsequent chapters) are still valid today. They do not need to be changed or amended in the near future but should be revisited by 2015 at the latest.

69. However, one of the recurrent questions, which PIC/S has to address in the coming years, is whether PIC/S should limit itself to GMP or whether it should also become involved in more categories of GMP as well as to non-GMP fields such as Good Clinical Practices (GCP), Good Distribution Practices (GDP), Good Laboratory Practices (GLP), pharmacovigilance, etc. In addition, relations between (i) inspectors and assessors and (ii) inspectors and enforcement officers could also be reviewed.

70. For the time being, the Scheme applies to the industrial manufacturing of "medicinal products", i.e. finished products and active pharmaceutical ingredients.

Sub-categories of medicinal products include e.g. radiopharmaceuticals, human blood and tissue, medicinal gases, etc.

71. PIC/S is also competent for the GMP of medicines prepared in hospital pharmacies but not for the dispensing of such medicines in the wards. Although the distinction makes sense, it may be considered arbitrary and failing to address the issue as a whole. For example, the risk and consequences for a hospital patient are the same whether in one case the wrong medicine has been administered to him in the ward or whether in another case his medicine has not been produced according to GMP in a hospital pharmacy. Consequently, also monitoring the distribution aspect of medicines prepared in hospital pharmacy would seem to make sense, although there is no consensus among PIC/S Participating Authorities on this particular issue[16].

72. PIC/S is, however, not competent for GCP, GLP and GDP as well as for enforcement.

Extending PIC/S to GCP and GLP?

73. PIC/S only considers the GMP aspect of e.g. GCP as being relevant to its mandate but not GCP as a whole. Similarly, GcLP (Good Control of Laboratory Practice) is considered as an integral part of GMP. To a large extent, the difference is justified: while GMP's main "customer" is the manufacturer, GCP and GLP address themselves to mainly hospitals, laboratories and CROs (Clinical Research Organisations), respectively, which are very different entities compared to manufacturers.

74. The consequences of opening up PIC/S to these fields would be far-reaching, as common standards would have to be elaborated at PIC/S' level. Some of these standards already exist at EU (GCP) or OECD (GLP) level. Although this may be a big challenge for PIC/S, it would monopolise a lot of resources at a time when the latter are rather scarce. In addition, training may already be in place in some of these fields (e.g. GLP training at OECD level). For these reasons, PIC/S should refrain from opening up to GCP and GLP.

Extending PIC/S to GDP?

75. The situation is again different regarding GDP, as GMP and GDP both address themselves to manufacturers and their inspection methodologies are very similar. The role of GDP in detecting counterfeits is also very significant. Therefore, it would make sense if PIC/S training programmes (e.g. the Joint Visits Programme) would be opened up to GDP inspectors in priority. Whether common GDP standards should be elaborated by PIC/S should be considered by 2007. If so, a Working Group could be established to draft GDP standards for PIC/S.

76. Effective systems of GDP are essential for product traceability and for minimising the potential for counterfeit and diverted medicinal products to enter the legitimate supply chain. The same is valid for active substances. As a result of

[16] It is suggested that the matter be addressed by a Special Interest Group (SIG), see 5.2.2.

market opening, globalisation and the development of parallel imports, as well as the growing threat of medicines counterfeiting, it necessary to strengthen control over pharmaceutical distribution, notably wholesale distributors. Very little is currently done in other fora to co-ordinate and harmonise GDP inspections. An initiative by PIC/S could thus fill a gap in the control system of medicines.

Reaching out to Assessors and Enforcement Officers?

77. Relations between inspectors and assessors could also be reviewed, possibly during a future PIC/S seminar in order to optimise the relations between assessors and inspectors and consider how the inspector could contribute to the assessment process and ongoing compliance with the marketing authorisation.

78. Although enforcement activities are handled by those with the appropriate expertise and there are a number of appropriate fora in which these activities are discussed, it would nevertheless behove inspectors to be aware of the possibilities for illegal activities within their area of activity. Accordingly, occasional updates on such activities would be useful to inspectors.

Goal:	Strive at achieving PIC/S mission and goals; Opening up PIC/S to GDP.	
Means:	For achieving PIC/S mission and goals, see subsequent sub-chapters; Open up PIC/S training programmes to GDP inspectors.	
Actions:	Immediate:	The Joint Visits Programme to be opened up to GDP inspectors.
	By 2007:	The Committee to consider whether to elaborate common standards in GDP and if to set up a Working Group.
	By 2015:	Review PIC/S mission and goals; Review relations inspectors – assessors; Update inspectors on illegal activities.

5.1 GMP standards

Past

79. Since its creation, PIC and then PIC/S have been active in the development and promotion of high and harmonised GMP standards and guidance documents. Keeping GMP standards high has always been considered a duty. The reason is obvious: to mutually accept inspection results (PIC) or have a GMP system equivalent to other Members (PIC/S), you need to rely on common standards. Other reasons for adopting common standards were:

- to ensure the maintaining of high standards of quality assurance in the development, manufacture and control of medicinal products;

- to promote uniformity in licensing decisions;
- to promote consistency and uniformity of inspections;
- to facilitate the removal of barriers to trade in medicinal products.

80. The main instrument for harmonisation has been the PIC/S GMP Guide. Originally, the latter derived from the WHO GMP Guide and was further developed in order to comply with stringent manufacturing and health requirements in PIC/S countries, to cover new areas (e.g. biologicals, radiopharmaceuticals, etc.) and to adapt to scientific and industrial technology (e.g. biotech, parametric release etc.). The aim of such improvements was to ensure that high quality medicines were produced in line with the PIC Convention and then the Scheme. For a long time, both guides remained equivalent but this is no longer the case, as the PIC/S GMP Guide has become more stringent than the WHO GMP Guide regarding e.g. sterile products.

81. In the late 1980s / early 1990s the PIC/S GMP Guide was adopted by the EU and further developed in close co-operation with PIC/S. Since that time, the EU and the PIC/S GMP Guides have been developed in parallel and whenever a change has been made to one, the other has been amended so that both Guides are practically identical.

82. In addition to the GMP Guide, PIC/S has also be a pioneer in developing a number of guidelines and guidance documents such as the Site Master File (and related explanatory notes, PE 008), the Recommendation on Quality System Requirements for Pharmaceutical Inspectorates (PI 002) and the first Guideline for the Manufacture of Active Pharmaceutical Ingredients (PH 2/87).

83. PIC/S was also instrumental in elaborating a first draft for the ICH Q7A Guide on APIs. It convened a government/industry conference in 1996 in Canberra (Australia) to discuss the need for an internationally harmonised GMP on APIs. Consensus to proceed was unanimous and PIC/S utilised the resources of many Member Authorities to prepare an initial draft GMP Guide. After further work by PIC/S, the draft was transferred to ICH in order to allow industry to become involved in further refinement of the document, and its finalisation in November 2000. PIC/S adopted the ICH GMP Guide as a stand alone PIC/S GMP Guide on APIs (PE 007).

Present

84. In order to minimise duplication of effort in the development of GMP guidance documents and GMP Guides, PIC/S has worked closely and cooperatively with the EMEA and EU through its Ad Hoc Group of GMP Inspectors. In 2000, PIC/S and the EMEA agreed on a joint procedure for the consultation of industry and each other when revising guidance documents (PS/W 6/2000). Under this co-operative arrangement, documents developed by PIC/S can be adopted by the EU through its Pharmaceutical Committee; likewise documents developed by EU can be adopted by PIC/S. This procedure has been successfully implemented.

85. While the EMEA and its Ad Hoc Group of GMP Inspectors have been very active in proposing amendments to the GMP Guide (notably Annex 1), PIC/S has been more active in elaborating new guidance documents such as on parametric

release, aseptic processes, blood establishments, etc. Often, these new guidance documents have led to a revision of the relevant chapter of the GMP Guide or the elaboration of a new Annex (e.g. Annex 17 on Parametric Release).

86. In addition to the GMP Guide, PIC/S has been extremely prolific in elaborating guidance documents, as shown by the following non-exhaustive list:

- GMP Guide for Blood Establishments;
- Guide to Inspections of Source Plasma Establishments and Plasma Warehouses (and related Site Master Files);
- Explanatory Note for Industry on the Preparation of a Site Master File;
- Guidance on Parametric Release;
- Recommendations on Validation Master Plan, Installation and Operational Qualification, Non-sterile Process Validation, Cleaning Validation;
- Recommendation on the Validation of Aseptic Processes;
- Recommendation on Sterility Testing;
- Recommendation on Isolators used for Aseptic Processing and Sterility Testing;
- Aide-Memoire on the Inspection of Utilities.

87. A number of these documents have resulted from annual PIC/S Seminars (see 5.2 Training). For example, the 1994 PIC/S Seminar on Validation resulted in the preparation and issue of a PIC/S guidance document on Validation in Pharmaceutical Manufacture covering validation master plan, installation and operational qualification (IQ, OQ), process validation and cleaning validation.

Future

88. Thanks to the input from the EMEA and PIC/S Seminars, the PIC/S GMP Guide will be further adapted and updated to comply with health and manufacturing requirements and technological progress. Seen from this angle, the PIC/S GMP Guide will remain an international GMP guide with high standards, which specifically addresses the needs of countries where consumer protection and the protection of health are highly regarded.

89. The question of whether the EU and PIC/S GMP Guides will remain equivalent depends basically on two factors:

- ♦ whether both parties are interested in keeping their GMP guides equivalent regarding requirements; and
- ♦ whether more EC legislation will be integrated in the EU GMP Guide, making it an EU specific guide rather than a universal guide.

90. Recently, the EU started to adopt EU-specific Annexes to its GMP Guide such as Annex 16 on Certification of a Qualified Person and Batch Release while introducing in other Annexes (e.g. Annex 13 on Investigational Medicinal Products) a number of specific references to EC legislation. While this is understandable from a purely EU point of view, the question arises on whether the EU and PIC/S GMP

guides can remain equivalent in terms of requirements. EU Members of PIC/S, which are in the majority in PIC/S, will have to double their efforts to ensure that the two GMP Guides remain equivalent. The EMEA Ad Hoc Group of GMP inspection services may wish to discuss the future of the EU GMP Guide in relation with the PIC/S GMP Guide.

91. On its side, PIC/S will strive to keep its GMP Guide equivalent in terms of GMP requirements with the EU GMP Guide and respectively equivalent to other GMP guides. This is notably the case of the Canadian GMP Guide but could also be true for other GMP guides, which will be deemed equivalent to the PIC/S GMP Guide.

92. As for guidance documents, the PIC/S Committee will start a reflection on the priorities in developing future guidance documents. Until now, a number of guidance documents have been the direct result of PIC/S seminars or the discussions in Expert Circle meetings such as the GMP Guide on Hospital Pharmacy, which is in the process of finalisation. However, in order to be coherent and determine where guidelines are needed and where they may just be useful, priorities will have to be established. For example, particular attention could be given to the activities that are ongoing in relation with the ICH process in general and Q8, Q9 and Q10 in particular. The guidelines which will emerge from these groups are likely to have a significant impact on the work of the GMP inspector in the years ahead. The following is a non-exhaustive list of guidance documents, which could be drafted by PIC/S in the years to come:

- Guidance documents to facilitate the application of the ICH Q7A on APIs;
- Guidelines to assist inspectors in the area of risk assessment and management (ICH);
- SOPs related to an Inspectorate quality system (e.g. "GMP inspection procedure" for operations such as manufacturing, testing operations and facilities);
- Guideline to harmonise the classification of pharmaceutical dosage forms among the PIC/S Participating Authorities;
- Guideline to harmonise the classification of deficiencies with a view to include annexes to list the specific examples of deficiencies corresponding to critical, major and other categories.
- Guideline to harmonise the approach in handling non-compliance medicinal products manufacturers

93. The harmonisation of the interpretation of GMP has also become an important issue. PIC/S has started a project to harmonise the interpretation made of a number of GMP issues, which it intends to made available to the public on-line. However, there is a growing need among PIC/S Participating Authorities to consider improving the existing platform for discussion and resolution of any ad-hoc GMP related issues. Such an exchange of professional views would be useful to harmonise / calibrate expectations from Drug Regulatory Authorities when it comes to the interpretations of each requirement stipulated in the PIC/S GMP Guide. The Committee will look into practical ways of establishing a platform for the purpose of harmonising GMP issues.

Goal:	Make the PIC/S GMP Guide a high-standard international GMP Guide Keep GMP standards identical or equivalent between PIC/S and the EU and equivalent between PIC/S and Canada	
Means:	Continued harmonisation of PIC/S and EU & Canada GMP Guides Determine priorities among guidance documents Continue the harmonisation of interpretation of the GMP Guide	
Actions:	By 2006:	PIC/S, in co-operation with its Expert Circles, to propose which guidance documents should be given priority.
	By 2008:	Finalise Questions and Answers project (putting on the web site the interpretation of GMP issues)
	By 2015:	Evaluate if PIC/S, EU and other GMP Guides have remained equivalent;

5.2 Training

94. The training of GMP inspectors has been one of PIC/S' main features since the beginning. The various modules have been put in place progressively: at the beginning, there was only one annual Seminar, which was organised by one of the PIC (then PIC/S) Members. Then, a Joint Visits Programme was added to train inspectors and harmonise both GMP standards and inspection procedures. In the 1990s, Expert Circles in specialised areas such as blood, medicinal gases, etc. were established.

5.2.1. Annual Seminar

95. Every year, a PIC/S Participating Authority has arranged an annual Training Seminar for GMP inspectors, with each seminar dealing with a different topic each year. Seminar topics for the past ten years (1996 – 2005) have been as follows:

Year	Seminar Topic	Country
2005	Primary packaging material, labelling and the prevention of mix-ups	Romania
2004	Inspection of APIs	Spain
2003	Inspection of QC laboratories	Slovak Republic
2002	Interface between GCP and GMP	Canada
2001	Utilities Used by the Manufacturer of Pharmaceuticals	Czech Republic
2000	Inspection of Products Derived from Biotechnology	France
1999	Non Technical Aspects of Inspection	UK
1998	Quality Systems for Inspectorates	Netherlands
1997	Inspection of Active Pharmaceutical Ingredients	Finland
1996	Inspection of Computer Systems	Australia

Note: For the topic of seminars after 2005, see http://www.picscheme.org

96. The particular features of PIC/S Seminars are:

- The 2.5 day seminar is attended on average by around 80-100 participants from over 30 countries.
- All participants must pay for their own costs (registration fee & accommodation).
- Seminars are not profit-oriented: they are organised by Regulatory Authorities for Regulatory Authorities. Industry cannot attend as such PIC/S Seminars except as invited speakers, where it can give its point of view (in line with the Aide Memoire on the Organisation of PIC/S Seminars).
- Most presentations are given by active inspectors while only a few are given by speakers from other fora (university, organisations, industry, etc.).
- An Aide-Memoire on the Organisation of Seminars establishes the main principles which a PIC/S Seminar must respect.
- The presentations made at the seminar are published by the Secretariat and made available for purchase by interested parties.

97. While the attendance of PIC/S seminars is good, professional organisations such as ISPE[17] or PDA[18] have come up with training seminars for industry, which are also attracting inspectors. In order to remain competitive and professional, efforts will be made in the future regarding the level of presentations / speakers.

98. This can be achieved by asking the ad hoc Scientific Committee (in which Members of the Organising Authority and the PIC/S Working Group on Training are represented) to co-ordinate, prior to a seminar, the presentations in terms of quality and in order to avoid overlaps. Evaluation instruments should help maintaining and even improving the quality of seminars. Other options could also be considered:

- ♦ Ask the ad hoc Scientific Committee for each PIC/S Seminar to provide guidance notes to the speakers;
- ♦ Hire a professional to oversee the content and format of presentations;
- ♦ Rely more on speakers / workshop leaders with proven educational skills.

99. PIC/S Seminars could also consider the particular needs of ASEAN or EU inspectors participating in seminars. If there is a need expressed by Participating Authorities, additional sessions (e.g. 0.5 day) and/or parallel sessions (e.g. workshops) on region-specific regulations may be organised jointly with e.g. ASEAN, the Commission and/or the EMEA.

100. Consideration should also be given to what additional methods can be applied to further standardise training for inspectors and to make it more readily accessible to a greater number of inspectors. In this context, the use of Information Technology or the elaboration of training modules may be worthy of consideration.

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17 International Society for Pharmaceutical Engineering

18 Parenteral Drug Association

101. The possibility for professional organisations such as PDA and ISPE to run short training courses on specific technical subjects prior to or after PIC/S Seminars (or on-line) could also be explored, thus (i) making it possible to share industry's GMP know-how and experience with regulatory GMP inspectors and (ii) substantially reducing travel and accommodation costs.

102. Regarding accommodation, efforts must be made to find alternative hotels for seminar participants at a reasonable price.

Goal:	Provide high-quality training seminars.	
Means:	Improve presentations given at seminars; Include where necessary a region-specific training module (ASEAN, EU); Possible "Joint Venture" training courses with professional organisations; Possible elaboration of training modules.	
Actions:	By 2007:	The PIC/S Committee to consider how to improve presentations given at Seminar (various options).
	By 2008:	Include a regional training module in PIC/S Seminars (if needed).

5.2.2 Expert Circles

103. PIC/S Expert Circles have been set up by the PIC/S 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 documents (or draft new Annexes to the GMP Guide) and offer training in their respective fields of specialisation.

104. A good example of a PIC/S Expert Circle is the Expert Circle on Human Blood and Tissue, which has been very active and prolific in terms of guidance documents. It has notably elaborated the GMP Guide for Blood Establishments and the Guide to Inspections of Source Plasma Establishments and Plasma Warehouses (and related Site Master Files).

105. Akin to Seminars, meetings of Expert Circles are organised on a regularly basis by PIC/S Participating Authorities. Each Circle has a Steering Committee which is responsible for steering the Circle and organise future meetings. Attendance and the length of the meetings vary between Expert Circles.

106. Currently, there are Expert Circles in the following areas (in brackets: year when established):

- Human Blood & Tissue (1994)
- Medicinal Gases (1997)
- Hospital Pharmacy (1999)

- Computerised Systems (2002)
- Active Pharmaceutical Ingredients (2005)

107. The Working Group on Training should periodically review the Terms of Reference for Expert Circles and evaluate whether the Circles are still needed, in particular for training purpose. In some cases, where a topic is Expert Circles could have a defined outcome and formal close-out, i.e. not be open-ended. If a topic is important to a significant minority of Authorities but there is no consensus in the PIC/S Committee on creating a PIC/S Expert Circle, a Special Interest Group (SIG) could be created instead and its Terms of Reference will be defined by the Working Group on Training. The dispensing in the wards of medicines, prepared in hospital pharmacies, could be the first such SIG.

108. Irrespective of the review of existing Expert Circles and the creation of SIG, future Expert Circles could be created in:

- Human Tissues (to be possibly separated from Human Blood);
- Biotechnology;
- Sterile Products;
- Veterinary Products;
- Non-GMP fields (e.g. GDP);
- Quality Risk Management.

109. In addition, Expert Circles could in the future introduce additional and/or parallel training sessions on region-specific regulations which could be organised jointly with either ASEAN or the Commission or the EMEA. Following the recent entry into force of EU directives, there is already a need for such specialised training for Experts in the field of Human Blood and Tissue.

110. As for seminars, presentations given during Expert Circle meetings could be reviewed by the Steering Committee. Expert Circle meetings should normally not last longer than seminars (2.5 days). To the extent possible, a clear distinction should be made in the Expert Circle programmes between (i) the drafting of guidance documents; (ii) experts discussions; and (iii) training.

Goal:	Provide high-quality Expert Circle meetings with the aim of further harmonising standards and providing training; Increase the number of Expert Circles.	
Means:	Improve the quality of presentations; Include region-specific training sessions (if needed); Establish Special Interest Groups; review Terms of References of existing Expert Circles and establish more Expert Circles (according to needs);	
Actions:	By 2007:	Steering Committees to consider how to improve presentations given at Circle meetings. ./..

	By 2008:	Include a regional training module in Expert Circles (if needed).
	By 2015:	Review Terms of References of Expert Circles; establish Special Interest Groups; and increase the number of Expert Circles and SIG from 5 to 8.

5.2.3 Joint Visits Programme

111. Another avenue for the training for inspectors has been the PIC/S Joint Visits Programme. Under this program three inspectors from three different countries are teamed up to observe typical GMP inspections in each country with a view to comparing inspection procedures and techniques and to uniform GMP interpretation. Joint reports are drafted after each visit. Any differences are reported to a PIC/S Working Group on Training for appropriate action. Joint visit groups are also encouraged to recommend specific training needs for inspectors, including topics for future PIC/S Seminars.

112. In 2005, 28 joint visit groups were operational representing over 100 inspectors from 25 different nationalities.

113. 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.

114. However, a number of improvements should be aimed at:

- All PIC/S Participating Authorities must encourage participation in this programme (a few Participating Authorities are either not or underrepresented).
- Reports made after a joint visit should be made available to the Secretariat within 30 days.
- "Coached inspections" (one experienced inspector and one very junior inspector) should be introduced.

Goal:	Ensure that the Joint Visits Programme remains both an effective training tool and an efficient means to harmonise GMP standards.	
Means:	Encourage participation by all Participating Authorities; Monitor the implementation of the Programme's Guidelines; Introduce coached visits for training purposes.	
Actions:	By 2008:	(i) Encourage all PIC/S Participating Authorities to have at least one inspector involved in the programme; (ii) Coached inspections are introduced by the Working Group on Training (Guidelines to be elaborated).

5.3 Assessment / Reassessment

115. Before a Regulatory Authority is accepted for PIC/S membership, a detailed assessment is undertaken to determine whether the authority has the arrangements and competence necessary to apply an inspection system equivalent to that of current PIC/S members. This assessment involves an examination of the authority's GMP inspection and licensing system (or equivalent), quality system, legislative requirements, inspector training, etc, and is followed by a visit by a PIC/S delegation to observe inspectors carrying out routine GMP inspections.

116. It usually takes between 3 and 6 years before membership is achieved. During this period, various changes and improvements recommended by the PIC/S Committee may have to be implemented; if necessary, follow-up assessment visits are undertaken by a PIC/S delegation to verify the suitability of corrective actions. The Guidelines for Accession were recently revised and are now also applicable to organisations applying for observer status.

117. Nevertheless, in order to facilitate non-Member Inspectorates to apply for PIC/S membership, the Committee will consider whether to develop a Guideline to describe the expectations in relation to the national legislation (legal system), requirements as specified in the Pharmaceutical Inspection Co-operation Scheme (PIC/S 1/95) and Recommendation on Quality System Requirements For Pharmaceutical Inspectorates (PI 002).

118. Authorities from the following countries were assessed in the past 5 years: Canada, Czech Republic (Veterinary Agency), Chinese Taipei[19], Greece, Latvia, Malaysia, Poland, Singapore (UNICEF can also be added to the list). A number of Authorities are today still in the process of being assessed: Argentina, Estonia, Israel, Lithuania, South Africa, Ukraine, and US FDA.

119. For many years, only Applicants to the Convention or the Scheme were subject to assessment. Founding Members were, however, never assessed. In order ensure that both new applicants and older members fulfil the same requirements, a Joint Reassessment Programme (JRP) was launched in 2000 under which existing PIC/S members are now also reassessed for equivalence on a regular basis.

120. In 2003, the pilot phase of the JRP was concluded positively and the procedure was amended to allow auditors to make use of other assessment reports. The procedure will also be amended to accept the results of other assessments such as those under the EU Heads of Agencies' Joint Audit Programme (JAP)[20], the (pre-) MRA inspections by the Commission. The assessment results under the JAP should be accepted on a mutual basis in order to avoid unnecessary duplications. Of course, the principle of mutual acceptance will only apply between programmes using equivalent sets of tools (e.g. PIC/S JRP and EU JAP) and not between PIC/S Members, which may be bound by MRAs (e.g. Canada – Australia).

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19 Chinese Taipei has been invited to reapply once it has implemented all PIC/S recommendations

20 The JAP is the EU version of the JRP and directly derives from the latter.

121. The authorities of the following countries have been reassessed so far: Australia, Italy, Norway, Romania and Sweden. Greece is still in the process of undergoing a reassessment. In 2005, the Committee accepted the idea that older Members, having undergone significant structural changes, should be reassessed in priority. As a result, the United Kingdom' MHRA (formerly MCA) will be reassessed in 2005-2006. Other Agencies will follow. In addition, the results of the following assessments will be recognised by PIC/S:

- Austria and France: assessed under JAP;
- Czech Republic, Slovak Republic, Hungary: pre-MRA visit by the Commission and MRA assessment by Canada;
- Iceland, Liechtenstein, Switzerland: MRA assessment by Canada.

122. A tentative plan covering the reassessment of the remaining PIC/S Members, notably those which joined before 1995 and those which have undergone significant structural changes, will be elaborated by the Executive Bureau (12 Authorities subject to reassessment). The question of whether the frequency of audits should be increased will be reviewed against the background of available human and financial resources.

123. To be coherent, the assessment and reassessment tools within PIC/S should be the same. Preferably, in order to facilitate the mutual acceptance of assessment results, the PIC/S tools should be equivalent to those used under the JAP. A proposal by the First Deputy Chairman to adapt the Canadian questionnaire (used for the assessment of MRA partners) to JRP and JAP needs is underway.

124. By 2007, there should be only one tool for the assessment and reassessment of PIC/S Members.

125. Preferably, auditors used under the assessment / reassessment should be trained according to the JAP training module.

Goal:	Reassess PIC/S Members, which acceded before 1995, by 2015; Harmonise assessment and reassessment tools; Clarify expectations from new Members.	
Means:	Elaborate tentative plan of reassessment (12 Authorities); Merge assessment and reassessment tools; Elaborate guideline on PIC/S requirements.	
Actions:	By 2007:	Harmonise tools, train auditors, develop training module and draft reassessment plan.
	By 2009	Elaborate guideline on PIC/S requirements.
	By 2015:	Reassess Members which joined before 1995.

5.4 Networking

126. One of PIC/S' main function and mission has been to provide a forum for networking and confidence building amongst inspectors and Regulatory Authorities. So far, most of the networking has been channelled through training activities (mainly Seminars and Expert Circles) and the attendance by the PIC/S Chairperson (or his/her Deputy) of international conferences on GMP organised by industry associations and other organisations. In the future, PIC/S will more actively encourage networking.

127. Although the annual seminar provides for an ideal platform for networking, it should primarily be a training event to be attended by GMP inspectors who need to undergo training. For this very reason, networking and training should be kept apart.

128. The issue could be addressed by creating on a regular basis a one-day event shortly before a PIC/S Committee meeting (i.e. independently from a seminar). This event, to be known as the "PIC/S GMP Forum", will be a GMP forum which can be attended by Heads of Agencies or Inspectorates of PIC/S and non-PIC/S countries on a voluntary basis (no obligation to participate). International industry associations and organisations will also be invited to attend and either give their input to various GMP topics or share useful data and information on GMP issues. The forum's main function will be networking and co-operation in the field of GMP between Members, non-Members of PIC/S and industry. It may also provide a good opportunity to "consult" on GMP needs for further harmonisation. Its parameters should be clearly defined so that the relationship is an entirely professional one with no possibility of others seeing it as another "club".

Goal:	Increase PIC/S' attractiveness for networking; Better interact with industry.	
Means:	Create a "PIC/S GMP Forum" in connection with PIC/S Committee meetings.	
Actions:	By 2010:	Launch first "PIC/S GMP Forum" (40 year-jubilee of PIC/S!)

5.5 Exchange of Information between Participating Authorities

129. The exchange of GMP related information has been at the very heart of PIC/S. The PIC Convention provided for the mutual recognition of inspections based on the exchange of GMP certificates. The Scheme relies on the exchange of information on GMP inspections (including certificates) but on a purely voluntary basis, making the Scheme very attractive to those Authorities which want to remain in full control of the acceptance (or non-acceptance) of inspection results. The company's prior approval is always required.

130. The exchange of information applies to "medicinal products" which are defined as follows in the Scheme:

> "(a) any pharmaceutical, medicine or similar product intended for human or veterinary use which is subject to control by health legislation in the manufacturing Country or in the importing Country, and
>
> (b) any active pharmaceutical ingredient which the manufacturer uses in the manufacture of a product referred to in sub-paragraph (a) above."

131. There are, however, important limitations to the exchange of information under PIC/S:

- The first is that it does not apply to the exchange of information between the Participating Authorities of countries party to the European Economic Area (EEA). For these Authorities, the EU legislation is applicable – not PIC/S rules.
- The second is that the due to the national legislation the German Regulatory Authority is obliged to carry out a GMP inspection in non-EU/EEA/MRA countries e.g. in Singapore or Malaysia. A similar restriction also applies in the United Kingdom.
- The third limitation is that the exchange of information is mainly limited to locally manufactured products (i.e. medicinal products manufactured under the jurisdiction of PIC/S Participating Authorities). The exchange of information on products manufactured outside the jurisdiction of PIC/S Participating Authorities has only been recently addressed by PIC/S (see box below).

132. The sharing of information between PIC/S Members has become increasingly important at a time when resources – whether in terms of staff or finance – are scarce. With the notable exception of Participating Authorities from Germany and UK, PIC/S Members can share the results of GMP inspections and thus do not have to send their inspectors on expensive (overseas) trips to control GMP standards of fellow Member Authorities. This is particularly appreciated by smaller inspectorates, which would not have the means to send their inspectors abroad to inspect all imported medicines.

133. While there is a need to improve the sharing of such information, this can only be purely voluntarily and based on the spirit of mutual co-operation prevailing in PIC/S.

134. To facilitate the exchange of GMP information, the PIC/S Committee may also consider elaborating a uniform format for GMP Certificate (to be based on the EU GMP Certificate).

135. Last but not least: the sharing of information between PIC/S Participating Authorities also applies to quality defects of batches of medicinal products, which have been distributed on the market. Through the PIC/S Rapid Alert and Recall System, such critical information is circulated among PIC/S Members, which are in a better position to oversee the withdrawal of the defective batches from their markets.

The International Medicinal Inspectorates Database (IMID)

In 2003, PIC/S launched the International Medicinal Inspectorates Database (IMID), which includes on voluntary basis information on GMP inspections carried out (or to be carried out) by the PIC/S Members outside of their respective domestic jurisdiction (foreign inspections).

The aim of the IMID is to share information on the GMP compliance status of third-country manufacturing sites for finished medicinal products, APIs and investigational medicinal products. It is supposed to be cost efficient by allowing inspection reports to be shared among all Participating Authorities and result in a reduction in the number of inspections, in particular of duplicative inspections.

Since the launching of the IMID, 15 out of 28[21] PIC/S Participating Authorities have joined the IMID. Out of the 15, eight Authorities are from the EU. While the Authorities of the UK and Germany have clearly indicated that they would not participate, other authorities have not made up their mind, mainly due to the obligation (as stipulated in the IMID Statute) *"to refrain from re-inspecting GMP-compliant manufacturers, which have been inspected (…) in the last three (3) years and whose inspection report is available on the database."*

Another reason why EU Authorities have been lukewarm to the concept of the IMID is the fact that in the EU, Member States are now obliged to share information on third-country inspections, which shall also be made available on the EUDRA GMP database. The partial access of MRA partners to the database and the inclusion of third-country inspections carried out by these partners in the database is being considered. The same applies to non-EU/EEA/MRA Participating Authorities of PIC/S, which may also be granted partial access to the database.

The response to IMID from industry has not been overwhelming. This may be due to a lack of information or to the fact that some key players within PIC/S (notably Germany and the UK) and outside PIC/S (e.g. US FDA) are not part of the IMID.

Clearly, the concept of the IMID must be reviewed in the light of the EMEA database (EUDRAGMP) containing information on third-country inspections. Outside the systems established for EEA Members and MRA partners, it is important that any system for the exchange of reports is of high quality, while remaining non-binding. For the time being, the concept will be "frozen" until: (i) more non-EU players join PIC/S; (ii) the inspection of API manufacturers is undertaken by more PIC/S member authorities. In the meantime, the IMID concept will not be actively pursued by its Members and no new contract will be concluded with manufacturers interested in the concept.

[21] Status as of 23 December 2005. 29 Participating Authorities as of 1 January 2006

Goal:	Subject to national and supranational law, share information on GMP inspections.
Means:	Exchange GMP information either directly or through the EUDRA GMP database.
Actions:	Immediate: IMID is made dormant. By 2009: review the situation and if necessary re-activate the IMID following a revision of its Statute.

6. Relations with other organisations

136. PIC/S has relations with a number of organisations and industry associations. Relations with ASEAN, the EU Heads of Agencies, the EMEA and the EC have been reviewed under Chapter 3.3.2. While relations with the EU are of a privileged nature, due to the fact that many PIC/S Members are also EU Member States, PIC/S must aim at remaining impartial and avoid giving more importance to one organisation over another. **All organisations must be treated equally.** This is particularly true for UN organisations such as WHO and UNICEF, where a difference in treatment can no longer be justified (see chapter 6.1).

137. In addition, co-operation between PIC/S and other organisations should be based on the principle of complementarity. Where PIC/S Participating Authorities are already actively co-operating, PIC/S as an organisation should not duplicate Members' efforts.

138. With PIC/S' membership expanding to e.g. America, relations with other (regional or health) organisations such as PAHO[22] could be explored.

Goal:	Treat all organisations, which entertain contacts with PIC/S, equally Co-operation between PIC/S (as an organisation) and other organisations should not duplicate efforts made by PIC/S Participating Authorities
Means:	Non-discrimination (notably in terms of status, rights and privileges) Non-duplication of co-operation Establish relations with other regional (health) organisations (if desired)
Actions:	See specific sub-chapters below

[22] Pan American Health Organization

6.1 Relations with WHO

139. Although relations to WHO date back to the very beginning of PIC, when the first PIC GMP Guide was elaborated on the basis of the WHO GMP Guide, PIC/S granted WHO an observer status in 1994 only. WHO in turn has invited PIC/S to various experts meetings but has never granted an observer status to PIC/S.

140. Relations between PIC/S (as an organisation) and WHO have been very limited, the main reason being that PIC/S Members are also WHO Members and thus actively and directly participate in WHO activities:

- PIC/S Participating Authorities and Members of the PIC/S Committee, in their personal capacity, have been actively involved in various WHO Expert Committees such as the WHO Expert Advisory Panel on the International Pharmacopeia and Pharmaceutical Preparations.

- PIC/S Participating Authorities have also actively assisted WHO in carrying out GMP inspections under the Pilot Procurement, Quality and Sourcing Project on HIV/AIDS Drugs in order to identify GMP compliant producers of HIV/AIDS drugs (nowadays also extended to malaria and TB drugs).

- Co-operation between WHO and individual PIC/S Members has also been fruitful in the field of counterfeit drugs.

- PIC/S Participating Authorities also provide directly comments to WHO on GMP guidance documents.

- PIC/S Participating Authorities co-operate very closely with WHO and some of them have an agreement with WHO (e.g. AFSSAPS signed a co-operation agreement on 12 July 2005).

141. In order to avoid unnecessary duplications, PIC/S (as an organisation) has thus refrained from competing with Participating Authorities in terms of co-operation with WHO. At an institutional level, PIC/S and WHO exchange information and occasionally co-operate in the field of GMP training (the Expert Circle on Human Blood and Tissue has provided some training to WHO Members, notably from Latin America).

142. Considering the limited co-operation between the two institutions and the risk of duplication, the question arises on the benefits for PIC/S (as an organisation) to grant WHO an Observer Status since (i) co-operation is essentially done between individual PIC/S Members and WHO; and (ii) co-operation between PIC/S and WHO is purely formal and informative.

143. The question is even more pertinent as UNICEF, which will become an Observer to PIC/S on 1 January 2006, has gone through the standard PIC/S assessment process and will pay for an annual fee, which is half of that of Members, while WHO has been exonerated from paying the same fee. UNICEF is in addition

one of the world largest suppliers of vaccines and has also agreed to share information on GMP inspections with other PIC/S Participating Authorities on a voluntary basis. Provided that the scope of the inspection is the same, UNICEF will in the future rely on PIC/S inspection reports. There is no similar exchange or sharing of information with WHO.

144. To be consistent, if WHO is interested in co-operating with PIC/S at the institutional level, it should be invited to apply for observer status, as UNICEF did. Alternatively, both organisations could negotiate and conclude a Memorandum of Understanding (MoU) specifying potential areas for co-operation as well as mutual rights and obligations. Potential areas of co-operation could be standards and guidance documents; GMP training; and the mutual acceptance of assessment results.

Goal:	Review relations with WHO in the light of non-duplication and the principle of non-discrimination between organisations	
Means:	Either invite WHO to apply for Observer (akin UNICEF) or negotiate a MoU	
Actions:	By 2006:	Committee to decide which way to go
	By 2013:	Conclude assessment of new application / Sign MoU

6.2 Relations with Industry and other Organisations

Industry and professional organisations

145. Since the manufacturer is at the heart of the GMP process, it is essential for PIC/S to maintain good relations with industry and professional organisations, notably those more active in the field of regulation, guidance documents and training. The support of industry associations and professional organisations to the goals of PIC/S is a prerequisite for the latter's successful expansion. As a matter of fact, industry is generally favourable to PIC/S' expansion: the harmonisation of GMP facilitates trade and also means fewer inspections for manufacturers. The latter are increasingly worried by the multiplication and duplication of inspections, which means not only more fees but also more staff immobilised and possibly a lower-than-usual production output during these inspections.

146. PIC/S mainly entertains privileged relations with two professional associations: the International Society for Pharmaceutical Engineering (ISPE) and the Parenteral Drug Association (PDA). These two organisations provide valuable feedback and comment on draft PIC/S guidance documents. While PDA has occasionally invited PIC/S to some of its local Chapters (Ireland, Israel, etc.), ISPE has been very active in providing speakers to PIC/S seminars and in inviting PIC/S to regional conferences (mainly in Asia, Europe and the Pacific). In addition, ISPE has opened up its training courses to Regulatory Authorities, in particular to those of PIC/S, by providing a specific number of complimentary registrations.

147. Relations with other industry and professional associations, which are more occasional, could be further developed notably with:

- The International Federation of Pharmaceutical Manufacturers Associations (IFPMA)
- Fédération Internationale Pharmaceutique (FIP)
- Drugs Information Association (DIA)

148. In addition, as mentioned under Chapter 5.4 (Networking), direct informal contacts could be established between PIC/S and international industry associations on a regular basis (see proposal of a regular "PIC/S GMP Forum" at paragraph 128).

Other organisations

149. Regarding other organisations (ICH, EDQM[23], etc.), the PIC/S Committee must closely watch initiatives and developments at ICH, notably with regard to the "Q series" process, which aim at improving quality systems and lessening the risk of quality problems of medicinal products before they go into full scale production. However, as long as some Members of the PIC/S Committee remain actively involved in the ICH process, this can be done without greater involvement.

150. Relations with EDQM have been recently established, notably with the unit responsible for certificates of suitability for APIs. Some PIC/S Participating Authorities have actively assisted EDQM in carrying out GMP inspections in PIC/S countries as well as in non-PIC/S countries under the Pilot Program of the Certification Unit. Although there is a potential of development in the relations between the two organisations, it is still too early to say how relations will evolve. The only certainty is that the key element in the relations will be continued assistance with the inspection of manufacturers of APIs.

Goal:	Ensure the support of relevant international industry associations and professional organisations to PIC/S.
Means:	Invite industry and professional associations as well as other relevant organisations to the "PIC/S GMP Forum" (see networking).
Actions:	By 2010: Organise first "PIC/S GMP forum" (see networking).

7. Secretariat and Finances

151. For historical and practical reasons, the Secretariat services for PIC and then PIC/S were entrusted to the EFTA Secretariat between 1971 and 2003. The Secretariat's main task was to deal with the services and meeting facilities for the Committee and sub-committees.

[23] European Directorate for the Quality of Medicines

152. The appointment of the EFTA Secretariat was revoked in principle at the 65th meeting of the Committee in Geneva on 23-24 April 2002. In 2004, PIC/S became an independent organisation with the status of an Association under the Swiss law and an independent Secretariat.

153. On the basis of a Memorandum of Understanding, signed on 3 October 2003, with the Convention on the Control and Marking of Articles of Precious Metals (Hallmarking Convention), previously serviced by the EFTA Secretariat, PIC/S agreed to provide Secretariat services to the Hallmarking Convention against the payment of an annual fee (to be paid by each Contracting State of the Hallmarking Convention).

154. PIC/S Participating Authorities contribute to the cost of Secretariat in equal parts. The contribution amounts to CHF 8,100 a year. In 2005, the Secretariat had two permanent staff members and a budget of CHF 390,000.

155. If the membership fee remains unchanged, the budget should grow by around 30% by 2015 to reach CHF 520,000. The increase will be exclusively financed by new Members (around 10 new Members for PIC/S; 6 new Contracting States for the Hallmarking Convention). Provided that overall conditions remain unchanged, no increase in the annual membership fee may be necessary.

156. To secure a stable income to the budget, PIC/S must maintain good relations with the Hallmarking Convention, whose contribution represents around one-third of the PIC/S budget. Accounts will have to be professionally audited in the future to eliminate the risk of mismanagement. Finally, one of the main inconveniences, linked to the status of an Association under the Swiss law, will have to be resolved by negotiating a tax exoneration agreement with the Swiss Government.

157. PIC/S will have to consider the level of the fees paid by non-Members to attend PIC/S Seminars and Expert Circle meetings. Professional organisation such as PDA and ISPE discriminate against non-Members by requesting a fee, which is between 15 and 20% higher than the Members' fee. At PIC/S, non-Members are only requested to pay an additional € 50 when registering to Seminars (nothing in addition for Expert Circle meetings). This non-Member tax represented around 10% of the registration fee at the 2005 Seminar.

158. As the membership is growing and activities increase, a slow expansion of the Secretariat staff may have to be considered in the longer term.

Period	PIC/S Members	Staff Member
1970 – 1994	10 → 18	1 → 1.5
1995 – 2005	18 → 28	1.5 → 2
2006 – 2015	28 → 38 *(e)*	2 → ?

e = estimate

Goal:	Maintain an efficient and flexible Secretariat; Ensure a good co-operation with the Hallmarking Convention; Keep membership fees stable (circumstances permitting).	
Means:	Provide professional secretariat services; Spend funds in a conservative and transparent manner.	
Actions:	By 2006:	Audit PIC/S accounts on a yearly basis by an independent, reputable professional.
	By 2007:	Negotiate tax agreement with Switzerland.
	By 2015:	Hire additional staff unit at the Secretariat (if necessary).

8. Action Plan

159. The following is a plan of all the actions to be taken by PIC/S in order to meet the various goals identified in the present document. For each goal, a number of actions have been defined as well as a maximum deadline (e.g. 2013 means by the end of 2013 at the latest). Long-term goals (e.g. integrating 10 new Members by 2015) have been subdivided into short-term goals (e.g. integrate one new Member every year). The deadlines have been chosen in such a way that their implementation does not (i) disrupt PIC/S traditional activities and (ii) overload the bodies in charge of preparing or executing the various actions (Committee, Bureau, Secretariat, etc.). An earlier implementation of the action is always possible and should be encouraged.

160. For some actions the number of hours per man has also been estimated. The estimate represents the effective additional work to be carried out by Participating Authorities (e.g. assessing a new Authority, drafting guidelines, etc.) but excluding the preparatory work by the Executive Bureau and Secretariat.

161. From all actions, the most labour intensive activity is the assessment of an applicant authority. The Action Plan foresees the assessment in parallel of six Applicants per year corresponding to a total annual work load of around 480 hours/man. This estimate is based on past experience according to which the assessment of a membership application requires 80 hours/man/year over a period of maximum 6 years or 480 hours in total (see detail below):

Task	Days x Man	Hours / Man
Assessment by Rapporteur	30 days x 1 man	240hours/man
Assessment by Co-Rapporteur	15 days x 1 man	120 hours / man
On-site inspection by Delegation (excl. Rapporteur and Co-Rapporteur)	5 days x 3 men	120 hours / man
Total Assessment		480 hours / man
Total Assessment per year		**80 hours / man**

NB: 8 working hours per day

162. The second most labour intensive activity is the reassessment of a Participating Authority, which is normally carried out within 12-18 months. 12 reassessments will have to be carried out before 2015 (i.e. one per year). A distinction has been made between a full reassessment (8 Authorities) and a partial reassessment (4 Authorities) which is based on other audit reports:

Task	Full Reassessment	Partial Reassessment
Submission of documents by audited Authority	40 hours / man	-
Assessment by Team Leader	40 hours / man	20hours/man
On-site inspection by Team (3)	120 hours / man	-
Reporting (incl. evaluation of corrective action)	80 hours / man	20hours/man
Total Assessment	**280 hours / man**	**40 hours / man**

163. The work load presented by other tasks (drafting guidelines, elaborate modules, etc.) is evaluated as follows: 3-day work for 3 inspectors or 72 hours / man. Guidelines to be drafted by the Secretariat or Executive Bureau are not taken into consideration.

164. The Action Plan is the following:

ACTION PLAN
(in chronological order)

YEAR	ACTION	PARA	HOURS
2005	The Joint Visits Programme is opened up to GDP inspectors	75	
	IMID is made dormant	Page 34	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Total		480
	Total / Participating Authorities (28)		17
2006	The PIC/S Chairman to meet with the Commission, write to the EU Heads of Agencies, ASEAN, etc	49	
	The Executive Bureau to adopt its own Rules of Procedure	54	
	PIC/S, in co-operation with its Expert Circles, to propose which guidance documents should be given priority	92	
	Audit of PIC/S accounts on a yearly basis by an independent, reputable professional	156	
	Update the PIC/S web site to include membership benefits	61	

YEAR	ACTION	PARA	HOURS
2006 (cont'd)	The PIC/S Committee to agree on an information brochure (to be drafted by Secretariat / Executive Bureau)	61	
	The PIC/S Committee to decide which way to go with regard to WHO (invite WHO to reapply for Observer Status or negotiate a MoU)	144	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority (MHRA)	122	240
	Partial reassessment of 2 Participating Authorities	122	80
	Total		800
	Total / Participating Authorities (29)		28
2007	Harmonise JRP and assessment tools, draft a forward plan for the reassessment of PIC/S Authorities	124	
	Steering Committees of Expert Circles to consider how to improve presentations given at Circle meetings	110	
	The PIC/S Committee to consider how to improve presentations given at Seminar (various options)	98	
	The Committee to consider whether to elaborate common standards in GDP and set up a Working Group to draft such standards (3 Members)	75	72
	Target "key players" which have no or limited contact with PIC/S (Brazil, China, India, Japan, Korea, Mexico, Russia, Turkey, etc.) and encourage them to apply to join PIC/S (action to be repeated in 2012)	39	
	Possible visit of the Chairperson to the ASEAN Secretariat (in the margins of the 2007 Seminar)	49	
	Negotiate tax agreement with Switzerland	156	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Partial reassessment of 2 Participating Authorities	122	80
	Total		872
	Total / Participating Authorities (30)		29
2008	Encourage all PIC/S Participating Authorities to have at least one inspector involved in the Joint Visit Programme	114	
	Coached inspections are introduced by the Working Group on Training (Guidelines to be elaborated by Chairman)	114	
	Update Joint Consultation Procedure with the EMEA	49	
	Include a regional training module in PIC/S Seminars (if needed)	99	72
	Include a regional training module in Expert Circles (if needed)	109	72

YEAR	ACTION	PARA	HOURS
2008 (cont'd)	Finalise concept of PIC/S "think-tank" and put in place review mechanism on co-operation	51	
	Finalise "Questions & Answers" project on GMP interpretation	93	72
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		936
	Total / Participating Authorities (31)		30
2009	Review the situation regarding the IMID and if necessary re-activate the IMID following a revision of its Statute	Page 34	
	Elaborate guideline on PIC/S requirements	117	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		720
	Total / Participating Authorities (32)		23
2010	Organise the first "PIC/S GMP forum"	128	72
	Review co-operation with ASEAN, EU Heads of Agencies, Commission and EMEA	49	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		792
	Total / Participating Authorities (33)		24
2011	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		720
	Total / Participating Authorities (34)		21
2012	Target "key players" which have no or limited contact with PIC/S (Brazil, China, India, Japan, Korea, Mexico, Russia, Turkey, etc.) and encourage them to apply to join PIC/S	39	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		720
	Total / Participating Authorities (35)		21

YEAR	ACTION	PARA	HOURS
2013	Conclude assessment of new application by WHO / Sign MoU with WHO	144	
	Create a Special Interest Group e.g. on dispensing in the wards	107	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		720
	Total / Participating Authorities (36)		20
2014	Review PIC/S values and principles	51	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		720
	Total / Participating Authorities (37)		19
2015	Review PIC/S mission and goals	68	
	Terminate PIC Convention	53	
	Review Terms of Reference of existing Expert Circles, establish SIG and increase the number of Expert Circles from 5 to 8	107 108	3 x 72
	Evaluate whether the PIC/S, EU and other GMP Guides (as the Canadian) have remained equivalent	91	72
	Hire additional staff unit at the Secretariat (if necessary)	158	
	Integrate 1 new Member (and continue to assess 5 other applications in parallel)	35	480
	Reassess 1 Participating Authority	122	240
	Total		1008
	Total / Participating Authorities (38)		27

* * * * * * *

List of PIC/S Participating Authorities

(# = Contracting States to the PIC Convention)

	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[24]	Státní Ústav pro Kontrolu Léčiv *(State Institute for Drug Control)*	SÚKL
	Ústav pro Státní Kontrolu Veterinárních Biopreparátů a Léčiv *(Czech Institute for State Control of Veterinary Medicaments and Biologicals)*	ÚSKVBL
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[25] #	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 Farmaco	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

cont'd

[24] SÚKL and ÚSKVBL count as two distinct Participating Authorities.

[25] BMGS and ZLG count as one Participating Authority.

	Participating Authority	Acronym
Norway. #	Norwegian Medicines Agency	NOMA
Poland	Main Pharmaceutical Inspectorate[26]	MPI
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

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[26] On 1 January 2006, Poland's MPI will become PIC/S' 29th Participating Authority.

List of Mutual Recognition Agreements (MRAs)
between countries whose Regulatory Authorities are PIC/S Members

	AU	CA	CH	EFTA/EEA*	EU	MY	RO	SG
Australia (AU)		X	**	X	X			X
Canada (CA)	X		X	X	X			
Switzerland (CH)	**	X		X	X			
EFTA/EEA*	X	X	X		X			
European Union (EU) #	X	X	X	X				
Malaysia (MY)								***
Romania (RO)								
Singapore (SG)	X					***		

* Iceland, Liechtenstein & Norway

** Under consideration

*** Under negotiation

The EU has also MRAs with non-PIC/S Members: Japan (MRA in force) and USA (MRA not in force).

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Mains Differences between PIC (Convention) and PIC/S (Scheme)

Convention	Scheme
Formal treaty	Informal arrangement
Between States (countries)	Between Health Authorities
With internationally recognised legal status (international treaty)	Without internationally recognised legal status
Legally binding	Non-binding
Mutual recognition of inspections:	Exchange of information:
1) Exchange of GMP certificates	1) Exchange of mainly GMP inspection reports
2) Each party recognises that GMP certificates of the other party are equivalent to its own national certificates.	2) The exchange is on a purely voluntary basis. PIC/S Participating Authorities may rely on these reports in order to facilitate the GMP approval of medicinal products and establishments.
3) No re-inspection	3) Re-inspection is possible
4) Exceptions are possible	

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List of Acronyms used in the Blueprint

(with the exception of acronyms for PIC/S Participating Authorities, see Annex I)

API(s)	Active Pharmaceutical Ingredients
ASEAN	Association of South East Asian Nations
CHF	Swiss Francs
DIA	Drugs Information Association
EC	European Commission
EEC	European Economic Community
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EFTA	European Free Trade Association
EMEA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
FIP	Fédération Internationale Pharmaceutique
GCP	Good Clinical Practices
GCLP	Good Control of Laboratory Practice
GDP	Good Distribution Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practice
ICH	International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use
IFPMA	International Federation of Pharmaceutical Manufacturers Associations
IMID	International Medicinal Inspectorates' Database
ISPE	International Society for Pharmaceutical Engineering
IQ	Installation Qualification
JVP	Joints Visits Programme
MERCOSUR	Mercado Común del Sur
MoU	Memorandum of Understanding
MRA(s)	Mutual Recognition Agreement(s)
NAFTA	North American Free Trade Agreement

cont'd

OECD	Organisation for Economic Co-operation and Development
OQ	Operational Qualification
PA	Participating Authority
PAHO	Pan American Health Organization
PIC	Pharmaceutical Inspection Convention
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PDA	Parenteral Drug Association
RA	Regulatory Authority
QA	Quality Assurance
Q7A	ICH Expert Working Group on Active Pharmaceutical Ingredients
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organization
WTO	World Trade Organization

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