



**WHO CERTIFICATION SCHEME ON THE QUALITY OF
PHARMACEUTICAL PRODUCTS MOVING IN
INTERNATIONAL COMMERCE:
Questions and answers (Q & A)**

The WHO Certification Scheme for finished pharmaceutical products is an international voluntary agreement to provide assurance to countries participating in the Scheme, about the quality of pharmaceutical products moving in international commerce (World Health Assembly resolution WHA22.50 (1969), World Health Assembly resolution WHA28.65 (1975), World Health Assembly resolution WHA41.18 (1988), World Health Assembly resolution WHA45.29 (1992), World Health Assembly resolution WHA50.3 (1997). The primary document of the Scheme was the Certificate of Pharmaceutical Product (CPP). The WHO Expert Committee on Specifications for Pharmaceutical Preparations, during its forty-third meeting, recommended that the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce should be **reviewed** in light of the changing environment, including the rapid globalization of the pharmaceutical manufacturing sector coupled with changes in the make-up of both the regulators and the groups involved in procurement.

In addition, as an interim measure, it also requested that a questions and answers (Q & A) document on the function of the Scheme should be prepared (see WHO Technical Report Series, No. 953, pp. 47-48 (2009). The Q & A document, version 1, is found below.

Comments and suggestions to improve this document should be sent by 30 July 2010 to Dr Samvel Azatyan, Medicines Quality Assurance Programme, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or e-mail: azatyans@who.int.

**WHO CERTIFICATION SCHEME ON THE QUALITY OF
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INTERNATIONAL COMMERCE:
Questions and answers (Q & A)**

Q1 What is the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce?

A1 It is a Scheme developed by the World Health Organization (WHO) in response to the request of WHO Member States to facilitate international trade in pharmaceutical products between Member States.

Q2 When was the Scheme developed?

A2 It was first developed in 1975. Since then it has been revised in 1988, 1992 and in 1997.

Q3 How can it facilitate trade in pharmaceutical products?

A3 The Scheme is an administrative instrument that requires a participating Member State (a certifying country), upon application by a commercially interested party (the applicant company), to certify/attest to the competent authority of another participating Member State (the recipient country) that:

- a specific pharmaceutical product is authorized for marketing in the certifying country, or if not, the reason why authorization has not been accorded;
- the manufacturing facilities and operations conform to good manufacturing practices (GMP) as recommended by WHO.

Q4 Why is it called the WHO Certification Scheme?

A4 It is called the WHO Certification Scheme because it was developed by WHO in response to the request of Member States.

Q5 How does the Scheme operate?

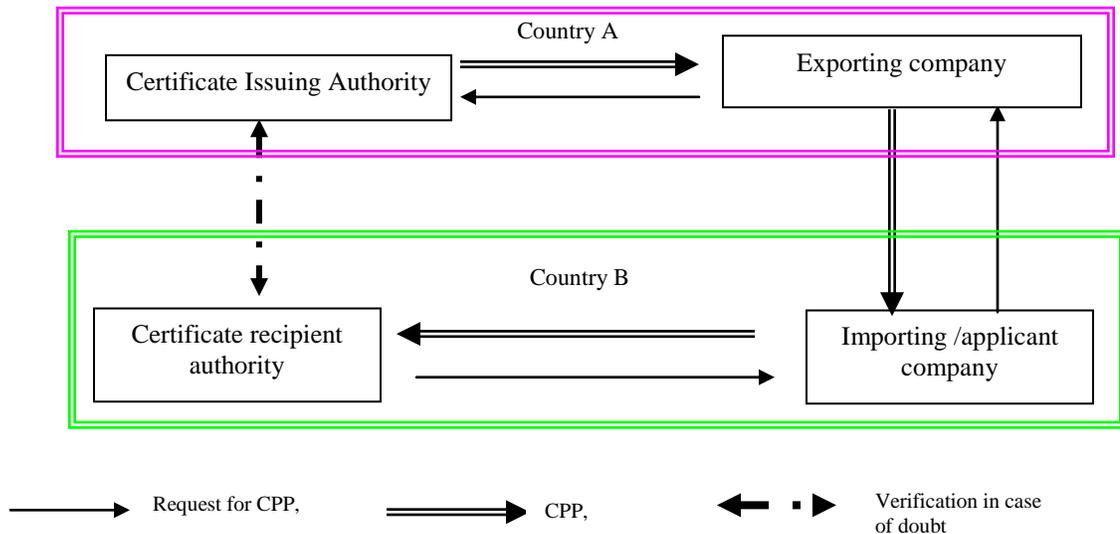
A5 The Scheme operates as follows:

1. The certificate recipient authority has *in its national medicine legislation or guidelines a requirement* for the submission of a Certificate for a Pharmaceutical Product (CPP) for products being imported into the country as a support to ensure the quality of the product being imported. *(In some countries the CPP forms part of the dossiers to be submitted to the national*

medicine regulatory authority (NMRA) to have a product registered by the authority).

2. The applicant/importing company *requests* a CPP from the **certifying authority** through the exporting company.

3. The certifying authority *issues* a CPP to the importing/applicant company via the exporting company. (At the time of the development of the Scheme the understanding was that a CPP would be sent directly to the recipient authority by the issuing authority. The practice at present is as shown in the diagram.)



Q6 Is the Scheme mandatory?

A6 No, the Scheme is not mandatory. It is a voluntary agreement devised to enable countries with limited medicine regulatory capacity obtain partial assurance from exporting countries concerning the quality, safety and efficacy of the pharmaceutical product they plan to import.

Q7 Can any one issue a Certificate for a Pharmaceutical Product (CPP)?

A7 No, it is only countries and regional organizations such as the European Medicines Agency (EMA) that are party to the Scheme who can issue a CPP.

Q8 How can a WHO Member State or regional organization be eligible for participation in the Scheme?

A8 Any WHO Member State or regional organization intending to participate in the Scheme may do so by notifying the Director-General of WHO in writing, of its willingness to participate in the Scheme; any significant reservations it intends to observe relating to this participation; and by providing the names and address of its NMRA or other competent authority.

- Q9 Where can one find the list of organizations and countries party to the Scheme?
- A9 WHO publishes the names and addresses of Member States party to the Scheme. The list is available on the WHO web site: http://www.who.int/entity/medicines/areas/quality_safety/regulation_legislation/certification/contacts/en/index.html. A hard copy of the list is also published and distributed to Member States. The list is updated from time to time.
- Q10 Does the list of Member States and organizations party to the Scheme provide the names and addresses of those government organizations authorized to sign and issue a Certificate for a Pharmaceutical Product (CPP)?
- A10 Yes, the list provides the names and full addresses of those government organizations authorized to sign and issue a CPP. NMRAs receiving a CPP can use this list to check and verify if the certificate they are receiving has been issued by the authorized organization.
- Q11 Is there any written document that provides detailed information on the WHO Certification Scheme?
- A11 Yes, there are published guidelines called “Guidelines for implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce”. One can access these guidelines by going to the WHO website: http://www.who.int/entity/medicines/areas/quality_safety/regulation_legislation/certification/guidelines/en/index.html.
- Q12 What should Member States and regional organizations possess in order to issue a Certificate for a Pharmaceutical Product (CPP) to support the export pharmaceutical products?
- A12 Member States and regional organizations should have the following to issue a CPP:
- an effective national licensing system for pharmaceutical products, manufacturers and distributors;
 - GMP requirements consonant with those recommended by WHO to which all manufacturers of finished pharmaceutical products (FPPs) are required to conform;
 - effective controls to monitor the quality of pharmaceutical products registered or manufactured within the country, including access to an independent quality control laboratory;

- a national pharmaceutical inspectorate having the technical competence experience and resources to assess whether GMP and other controls are effectively implemented and legal power to conduct appropriate investigations;
- the administrative capacity to issue the required certificates, to institute inquiries in the case of complaint associated with a potentially serious quality defects or other hazard and to notify WHO and other concerned parties.

Q13 Does WHO issue Certificates for a Pharmaceutical Product (CPP)?

A13 No, WHO does not issue CPPs or any of the certificates described under the Scheme.

Q14 Should a CPP issued by Member States bear the WHO emblem or the acronym “WHO”?

A14 No, certificates should not bear the WHO emblem or the acronym “WHO”. The use of the emblem or acronym creates the impression that the certificate is issued or endorsed by WHO. It is an illegal act and countries receiving such CPPs should reject them and report to WHO.

Q15 What products are covered under the WHO Certification Scheme?

A15 Pharmaceutical products covered under the Scheme are:

- FPPs intended for administration to human beings;
- pharmaceutical products intended for administration to food-producing animals;
- active pharmaceutical ingredients (APIs).

There is now a separate scheme called the WHO pharmaceutical starting materials certification scheme (SMACS) which has guidelines on importation of APIs.

Q16 What are the different types of Certificates that can be requested within the scope of the Scheme?

A16 Three types of certificates can be requested within the scope of the Scheme:

- a Certificate for a Pharmaceutical Product (CPP) or Product Certificate (PC);
- a Statement of Licensing Status of Pharmaceutical Product(s) (SLSPP);
- a Batch Certificate of Pharmaceutical Product (BCPP).

Q17 By whom and when is a Certificate for a Pharmaceutical Product (CPP) issued?

A17 A CPP is issued by the authorized body of the exporting country and is intended for use by the competent authority within an importing country:

- when a pharmaceutical product is under consideration for a product license/marketing authorization that will authorize its importation and sale in the importing country;
- when administrative action is required to renew, extend vary or review such license.

Q18 When and by whom is a Statement of Licensing Status of Pharmaceutical Product(s) (SLSPP) issued?

A18 An SLSPP is issued by the competent authority of the exporting country and is intended for use by importing agents when considering bids in an international tender. It is requested by the importing agent as a condition for bidding.

Q19 What is a Batch Certificate?

A19 A Batch Certificate is a certificate that accompanies and attests to the quality and expiry date of a specific batch or consignment that has already been licensed/approved for marketing in the importing country.

- A batch certificate is usually issued by the manufacturer.
- In case of biological products, a lot certificate is issued by the competent authority of the exporting country.

Q20 Is there a standard format for CPPs?

A20 Yes, there is a standard format. The WHO standard format was last agreed by WHO Member States in 1997 (reference: WHO Guidelines, Section 3.2).

- The standard WHO format for CPPs facilitates understanding and review by the recipient authority. It obliges certifying authorities to disclose important information to the importing country.
- Recipient authorities should refrain from obtaining data other than in the WHO standard format or in addition to the standard CPP format.
- Certifying authorities should not issue the outdated "free sales certificates". These have been replaced by the WHO format CPP.

Q21 Is the Certificate for a Pharmaceutical Product (CPP) evidence of quality, safety, efficacy review and approval?

A21 Yes, the CPP is based on the assumption that the authorities issuing a CPP have the capacity to assess the quality, safety, and efficacy (QSE) of the product they approve for marketing.

Based on the intention of the Scheme, a recipient authority could require a CPP when it does not undertake a full review of QSE data submitted for registration, and evidence of approval in another country is required.

Q22 Does the CPP provide evidence of good manufacturing practices (GMP)?

A22 Yes, the GMP declaration in the CPP refers to assurance of GMP for the product approved in the certifying country at the stated manufacturing site.

In addition, certificates from national medicine regulatory authorities (NMRAs) party to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and International Conference on Harmonisation (ICH) regions (USA, Japan, and EU) provide evidence of GMP status.

Q23 What is the difference between approval of the quality data in the submission and evidence of GMP?

A23 The approval of the quality information in a submission is an approval of how the applicant company proposes to manufacture and control the quality of the product at the time of manufacture and throughout the product's life. Evidence of GMP compliance shows that the applicant company has been able to demonstrate that the manufacturing site fulfils the underlying GMP principles.

Q24 When would a CPP be required?

A24 When the CPP replaces either a full or partial quality, safety and efficacy (QSE) review, the CPP would be a condition of approval and it would not be required at the time of submission.

If local legislation stipulates provision of a CPP at the time of submission, the authority review should be a "verification" procedure with published, communicated timelines that should be short and thus not delaying patient access.

Q25 Are there any alternatives to a CPP as evidence of approval by a national medicine regulatory authority (NMRA)?

A25 Outside the WHO Certification Scheme other forms of evidence include:

- product approval letters (or copies of licenses) from well-established national medicine regulatory authorities (NMRAs), e.g. Australia, Canada, People's Republic of China, Denmark, Finland, Germany, India, Japan, Norway, Republic of Korea, Spain, United Kingdom, United States of America;
- positive scientific opinion from the European Medicines Agency (EMA);
- decisions of the European Commission;
- licensing/approval information on regulatory authority web sites; and
- evidence of approval on the United States Food and Drug Administration (US FDA) web site.

Q26 Is it a must that a pharmaceutical product has to be exported from the same country as the certifying authority?

A26 No, it is not necessary for the product to be exported from the certifying country as long as a declaration of GMP assurance appears on the Certificate for a Pharmaceutical Product (CPP).

The Scheme was established on the basis that the certifying country was also the country where finished product manufacture took place and was, therefore, the exporting country. Subsequent revisions to the Scheme have introduced scope for CPPs to be issued by other reference authorities. Most certifying authorities currently provide CPPs when the finished product is not manufactured in the certifying country on the basis that GMP is assured.

Moreover many authorities assume that certifying authorities issue CPPs even when finished product manufacture does not occur in the certifying country. Strict adherence to the above assumption potentially limits licensing and registration options and can delay the introduction, or affect the continued supply, of important medicines.

Q27 Is it possible to obtain a CPP from a certifying authority that is not the country where the manufacture of the finished product takes place?

A27 Yes, the GMP declaration in the CPP will refer to assurance of GMP for the product approved in the certifying country at the stated site, even if the manufacturing site is in a different country than the issuing authority.

The Scheme has a provision that when manufacture takes place in a country other than that where the product certificate is issued, an attestation that such manufacture complies with GMP may still be provided as an attachment to the product certificate, on the basis of inspections undertaken for registration purposes.

Q28 Is it necessary for the Certificate for a Pharmaceutical Product (CPP) to come from the country where finished product manufacture takes place?

A28 No, although the Scheme was set up assuming that the certifying country was also the country where finished product manufacture takes place, there is scope within the Scheme for CPPs to be issued by other authorities that can provide independent assurance of the GMP compliance status.

There needs to be an appreciation of the complexity of manufacturing and sourcing routes currently employed by companies operating internationally. WHO Member States define the “source” differently:

- country of finished product manufacture;
- country of final packing;
- country of final release; and
- country of main headquarters of the pharmaceutical company, etc.

The critical element is the confirmation that all production/manufacturing/quality operations are carried out according to GMP.

Due to complex modern, sourcing routes, together with varying local regulatory processes, the approval in the country where finished product manufacture takes place may be later than in other countries. In this case it is a matter of judgment as to whether it is necessary for the CPP to be issued from the country where finished product manufacture takes place. The preference, in order to speed up patient access, would be to accept the CPP from the earlier approving country – in order to approve the product the certifying authority must also be assured of GMP.

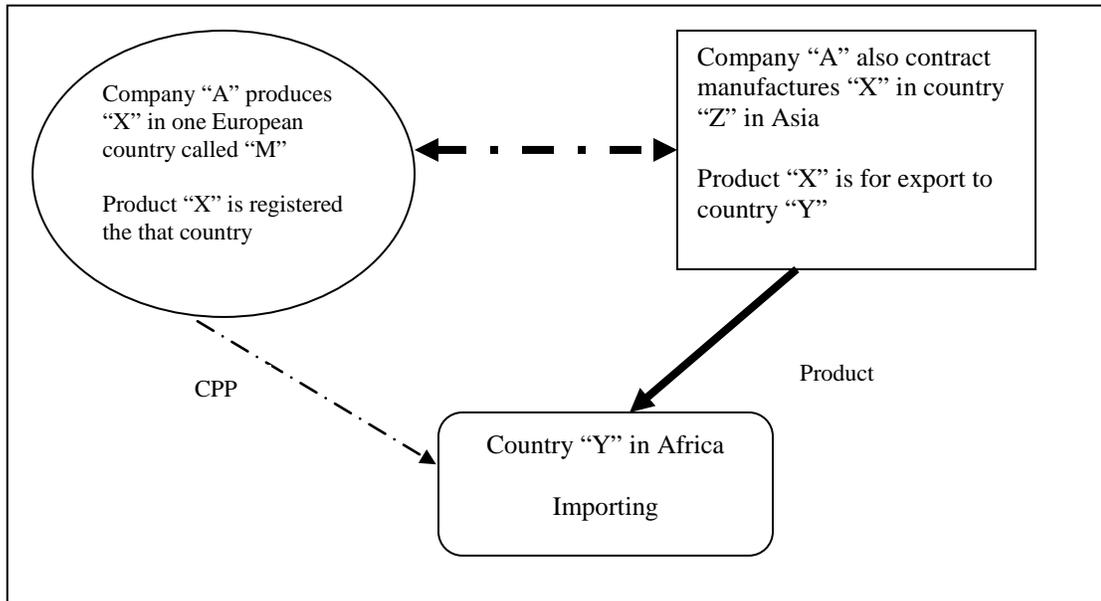
Implementation and compliance with GMP ensures quality of product irrespective of source. Requirement of an additional CPP for the release site if it is different from the product manufacture site, delays patient access since multiple CPPs provide no additional value.

Q29 What is the significance of the declaration of marketing status (i.e. whether the product is actually on the market in the exporting country)?

A29 Declaration of marketing authorization approval is the aim of the CPP. It is true that the WHO format CPP includes information on marketing status (if the product is actually on the market of the exporting country), but the Scheme also has a provision where the issuing authority can indicate why the product may not be marketed. In circumstances where the product is not actually on the market the issuing authority can indicate that in the certificate.

The actual presence on the market of the product depends on many other factors. The recipient authority should not require that a product be marketed in the certifying country.

- Q30 Should recipient authorities require a Certificate for a Pharmaceutical Product (CPP) from more than one certifying authority?
- A30 No, they should not require a CPP from more than one certifying authority. A WHO-format CPP from a single certifying authority should provide appropriate evidence of approval and GMP status.
- Q31 Is it necessary for recipient authorities to require GMP certificates in addition to a CPP?
- A31 No, the CPP includes a GMP declaration so additional GMP certificate is not necessary.
- Following the introduction of the WHO CPP some authorities no longer issue GMP certificates (e.g. US-FDA).
 - In the CPP context separate GMP certificates are redundant and are, therefore, discouraged. CPPs should be accepted (in particular from PIC/S and ICH regions) as evidence of GMP status.
 - Outside of the Scheme, there are occasions when it is appropriate to require a GMP certificate.
- Q32 When a CPP forms part of a regulatory review, is it necessary to conduct a site inspection as well?
- A32 An inspection should not be necessary when the GMP declaration on the CPP covers the product to be approved in the recipient country.
- Inspections outside of this condition are a matter of judgment and decision by the recipient country. Membership of PIC/S, ICH or other means of recognizing inspections by other authorities is encouraged to reduce unnecessary inspections.
 - CPPs should be accepted (in particular from PIC/S and ICH regions) as evidence of GMP status. The decision to inspect should be made after a risk-based assessment of the facility, taking into account GMP and inspection status from other authorities.
- Q33 Imagine a situation in which company “A” in one European country called “M” produces a pharmaceutical product called “X” and the product is authorized for marketing in that country. Company “A” also produces “X” under contract manufacturing in country “Z” in Asia and wants to export it to country “Y” in Africa. The authority in the importing country “Y” requires a CPP to approve importation. The questions are:



Q33.1 Is contract manufacturing accepted?

A33.1 Yes, contract manufacturing is accepted under GMP.

Q33.2 In case of a contract-manufactured product, from which country should the authority in the importing country (receiving authority) accept the Certificate for a Pharmaceutical Product (CPP)?

A33.2 Country "Z" can issue a CPP if the product is registered by the authority of that country "Z". If the product is not registered in "Z" then the authority in "Z" cannot issue the CPP.

- If the contract-manufactured product is also authorized for marketing in the European country then the European country can issue certificate.
- If the product is not registered in both countries then the only feasible country that can issue certificate will be the European country "M". The authority of the European country will issue the CPP after it has satisfied itself that the product under contract manufacture is the same in all aspects as the one produced in its own country and that the product is produced in compliance with GMP.

Q34 Can a CPP also be used to provide evidence of an administrative review and approval (e.g. as certification of acceptability of a company name change)?

A34 Yes, the CPP can also provide evidence of an administrative review and approval (e.g. as certification of acceptability of a company name change);

for a name change of the owner of a manufacturing or production site), which often happens in the context of company mergers and acquisitions.

For administrative approvals that now involve a QSE review, recipient authorities should use alternatives to a CPP as a preferred and quicker option (see Question 9).

Issues related to manufacturing company name change ("administrative review") may indeed create various practical difficulties for exporters–importers, but are not associated directly with safety/quality concerns and should be given less prominence (moved from item 5 towards the end of the document).

Q35 Imagine a situation in which a product is authorized for marketing in the country of manufacture but is not actually available on the market. Can the competent authority of the exporting country issue a CPP to support export?

A35 Yes, it can issue a CPP. What it should do is explain why it is not on the market. One reason for not being on the market could be that the disease/health problem for which the product is indicated may not be prevalent in the country.

Q36 Sometimes a country may wish to import a special dosage form, strength or formulation of a certain known product and this particular product may not be registered in the manufacturing country. Under such circumstances can the authority of the exporting country issue a CPP?

A36 Yes, it can issue a CPP but it should explain on the certificate that the particular product is not authorized for marketing in the exporting country, and that it has been produced based on the request of the importing country, and that the manufacturing is in compliance with GMP.

Q37 Is it necessary to legalize the CPP?

A37 No, legalization is not part of the WHO Scheme and this is not considered to provide additional assurance of authenticity. Approval statuses in key reference countries are currently available as public information.

Legalization should not be necessary since an official governmental authority of the certifying country signs the CPP.

Legalization delays availability of the CPP and, therefore, delays access to medicines for patients. If a recipient authority has any doubts about the validity of a CPP it should contact the certifying authority directly.

Q38 What should receiving countries do in case of any doubt about a Certificate of Pharmaceutical Product (CPP)?

A38 In case of any doubt the competent authorities of receiving countries should communicate directly with the authorized body that has issued the certificate or contact WHO to clarify the matter.

Q39 Are certifying authorities penalized if they issue CPPs, but do not meet WHO requirements for self-certification and subsequent issue of CPPs?

A39 No, there is no system to penalize them. WHO does not have the power to certify, inspect or penalize certifying authorities.

Q40 What are the main problems encountered in the application of the Scheme?

A40 A number of problems have been encountered in the use of the Scheme, which include:

- countries not party to the Scheme issue certificates;
- authorities that do not meet the requirements stated in the guidelines for the Scheme issue certificates;
- some issuing authorities put the WHO emblem, logo or acronym on the certificate, thereby creating the impression that the certificate is authenticated by WHO.
