



Certification Scheme for a Certificate of Pharmaceutical Product (CPP)

IFPMA CPP Network
Training Toolkit

September 2021

External Training Package



Why is training needed?



Training modules

CPP Overview

CPP Scenario FAQ

eCPP



IFPMA position papers and articles



Reference and Glossary



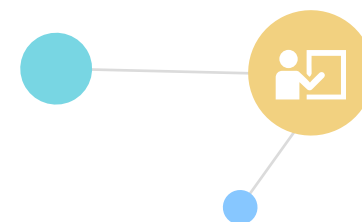
Appendix – WHO CPP Template





Why is training needed?

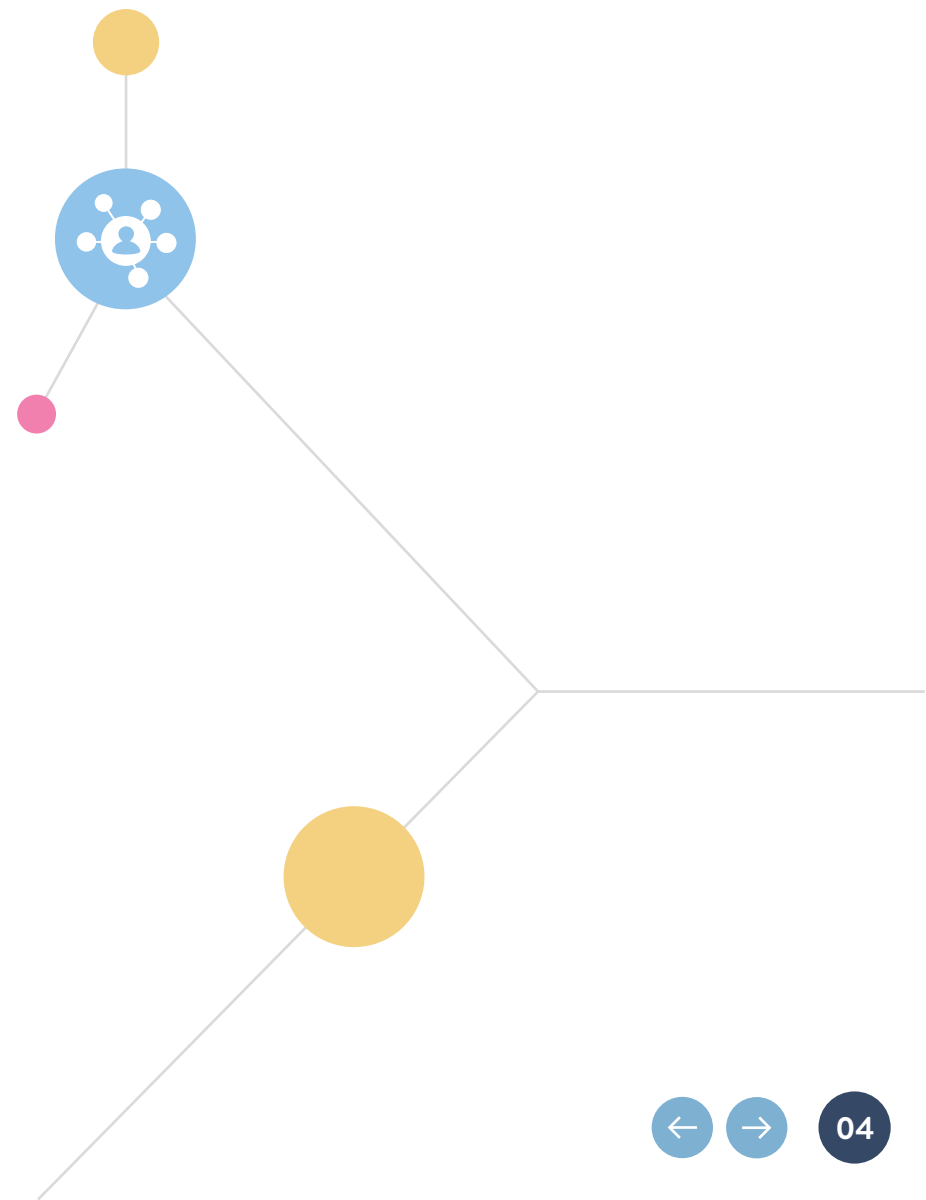
- Under the WHO Certification Scheme, the CPP is a key document that aims to accelerate patient access to medicines, especially in countries that do not have the infrastructure or capabilities to complete a full Quality, Safety and Efficacy (QSE) review themselves.
- Despite the original aim of the WHO Scheme since 1997, i.e. to provide a standard process, the regulatory procedures among countries have varied significantly and different approaches and interpretations of the CPP Scheme have applied from one country to another.
- This training toolkit should be used in conjunction with the current WHO guidelines and relevant local legislative requirements.
- This training toolkit aims at providing a greater understanding of the current process, as well as, highlighting the challenges and opportunities needed to improve and modernize the regulatory procedures that will ultimately accelerate patient access to medicines.





Training modules

- 1 → CPP Overview
- 2 → CPP Scenario FAQ
- 3 → eCPP





CPP overview

- What is a CPP and what is its purpose?
- Which Regions require a CPP and why?





What is a CPP and what is its purpose?

The WHO Certification Scheme for a Certificate of Pharmaceutical Product (CPP) is an international voluntary agreement to provide assurance to countries participating in the Scheme, about the quality of pharmaceutical products moving in international commerce.

- Guidelines are located on the WHO website www.who.int*
- The CPP template (contents) are provided in the [Appendix](#)

The CPP Scheme supports the regulatory review in countries without sufficient capability to conduct a full dossier review themselves. Ideally, a CPP should not be required in countries that have the capabilities to conduct full reviews (QSE).

The CPP should be used when a pharmaceutical product is under consideration for a product license / marketing authorization, or when administrative action is required to renew, extend or vary such a license.

The CPP contains, but is not limited to, the following information:

- Confirmation of approval of QSE in the issuing country
- A snapshot of the license (only includes information registered in the issuing country)
- Confirms product approval, license holder and Good Manufacturing Practices (GMP) status

The Scheme ensures:

- The CPP issuer meets a comprehensive system of quality assurance through independent inspection that all manufacturing operations are carried out in conformity with GMP

* WHO Expert Committee on Specifications for Pharmaceutical Preparations 55th report, Section 9.2 WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce





What is a CPP and what is its purpose?



Which Regions require a CPP and why?

Content of the CPP

A CPP has two DISTINCT parts:

- Evidence of QSE Review
- Evidence of Compliance with GMP





What is a CPP and what is its purpose?



Which Regions require a CPP and why?

Key challenges of the interpretation of the CPP scheme

- Difference in product names between certifying and requesting countries.
- The CPP confirms GMP status, additional GMP certificates should not be necessary or requested.
- The CPP is a legal document and additional apostille and/or legalization should not be requested. (Note: Align with WHO recommendations)
- Requirements for the 'country of origin' or 'source country' have multiple definitions and should be clarified as it could refer to the country of any one of the following: final approval or marketing, manufacture, packaging, final release, or main headquarters of the pharmaceutical company.
- The CPP provides evidence of a positive QSE review in the issuing country. A full dossier is not recommended to be requested by CPP requesting country.
- The scheme refers only to the manufacturer of the dosage form but some importing countries require additional manufacturers to be listed.
- The issued CPP is a snapshot of the Market Authorization (MA) in the issuing country and may not necessarily reflect the entire situation in the importing country.





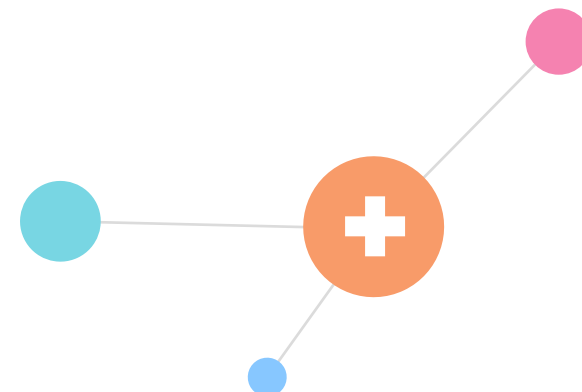
What is a CPP and what is its purpose?



Which Regions require a CPP and why?

Advantages of the scheme

- Provides the standard format that is expected to be used.
- Enables recipient CPP countries to gain assurance on the QSE of the product in the issuing country.
- Obliges certifying authorities to disclose important information to the importing country.
- Facilitates patient access to quality medicines, by relying on the review and approval of reference regulatory authorities.





What is a CPP and what is its purpose?



Which Regions require a CPP and why?

Authorities issuing WHO-type certificates should satisfy the following criteria

- An effective marketing authorization, vigilance and market surveillance and control systems for pharmaceutical products, including the responsible manufacturers and licensing of distributors.
- GMP requirements, consistent with those recommended by WHO in accordance with its current publication, to which all manufacturers of finished pharmaceutical products (FPP) are required to conform.
- Effective controls to monitor the quality of pharmaceutical products registered or manufactured within its country or region, including access to an independent medicine testing laboratory.
- A pharmaceuticals inspectorate, operating as an arm of the national or regional medicines regulatory authority, and having the technical competence, experience and resources to assess whether or not GMP and other controls are being effectively implemented, and the legal power to conduct or to coordinate appropriate investigations to ensure that manufacturers conform to these requirements by, for example, examining premises and records and taking samples; and
- An efficient surveillance system, administrative capacity and good regulatory practices compliance to issue the required certificates efficiently, to detect and institute inquiries in the case of complaint, and to expeditiously notify WHO and, when possible, the competent authority in the Member State or region known to have imported a specific product, or publish the information on the website about the product that is associated with a potentially serious quality defect or other hazard in a timely manner.





What is a CPP and what is its purpose?



Which Regions require a CPP and why?

Which Regions require CPPs and why?

Most non-ICH Countries

The CPP may be required to support a regulatory submission.

- This can be submitted at the beginning of or during the NRA review, throughout the lifecycle of a product.

- According to the WHO Scheme, CPPs should not be required in countries that require full ICH CTD dossiers and have the capability to conduct full QSE reviews. Requirement for CPP should be removed if it is not used as its original intent to replace partial or full review.

- Issuing NRA should not require CPPs for their regulatory submission.





CPP scenario training

- 1 → CPP applications are not harmonized
- 2 → The CPP only reflects the registered information of the certifying NRA
- 3 → Authentication of CPP
- 4 → CPP may still be requested even when the NRA is completing a full dossier QSE review





1

Scenario:
CPP applications are not harmonized

2

Scenario

3

Scenario

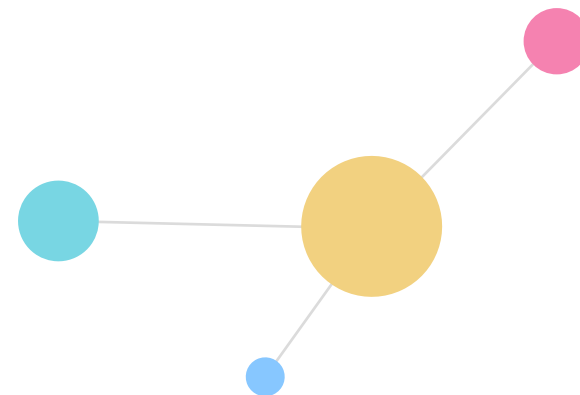
4

Scenario

CPP Applications are not harmonized

Each certifying authority has its own system:

- Requests to NRAs can be submitted as hard copy or preferably electronically.
- Different levels of detail are required by different NRAs.
- Timeline for issuing CPP is not standardized, some NRAs provides opportunity to Fast Track a request.
- Issuing authorities may not perform quality check; it is advised that a quality check be done by the CPP recipient.





1

Scenario:
CPP applications are not harmonized

2

Scenario

3

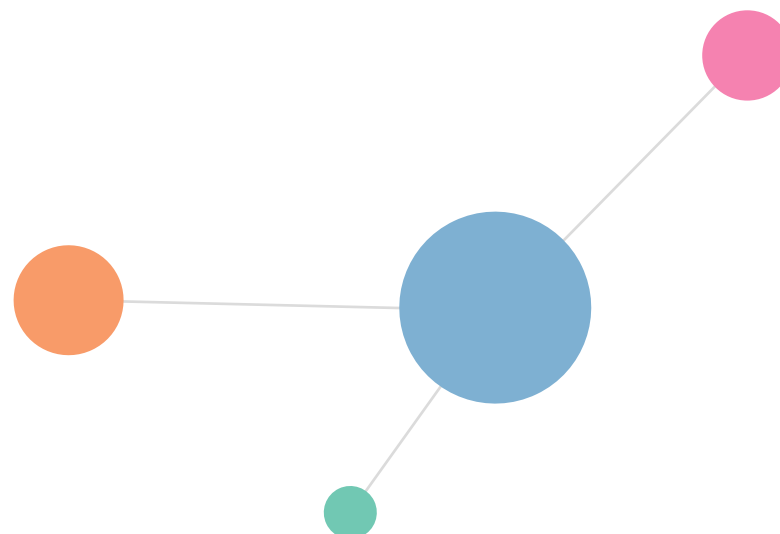
Scenario

4

Scenario

Example of lack of harmonization

- There is a requirement to submit a CPP for registration of a new indication.
- The first issuing HA to approve will only issue eCPPs, however there is no digital signature!
- The recipient HA will only accept legalised CPPs, however this is not possible to obtain with a digital/wet ink signature!





1

Scenario:
CPP applications are not harmonized

2

Scenario

3

Scenario

4

Scenario

Suggestions to improve harmonization

Work towards harmonization and a standard electronic submission, such as the approach with electronic Common Technical Document (eCTD). Harmonization among regulatory agencies will enable a faster, compliant and simplified issuing process. e.g. Introduction of eCPP already provide improvements in this regard.

Issuing NRAs should be aware that the CPP issuing times can significantly impact registration timelines.

Issuing NRAs should ensure adequate communication to industry of changes to CPP application and/or issuing processes to make sure that all involved stakeholders are aware and can prepared for implementation.

Patient access to medicines will be enhanced by recipient NRA's willingness to accept CPPs during the review rather than at the time of submission, as well as to accept alternatives to CPP (e.g. public assessment report or approval letter), when applicable.

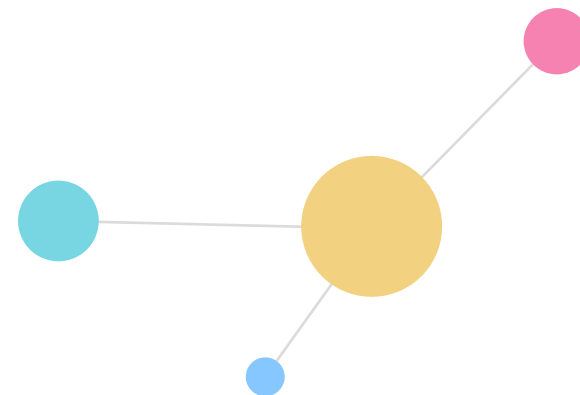
Appropriate issuing of eCPP (i.e. with electronic signature), and acceptance of eCPPs by requesting NRAs.





CPP only reflects the registered information of the certifying NRA

- For the approval of product with an unmet medical need, the NRA requires submission of CPP within the initial application.
- To accelerate the submission timelines, the company's regulatory team provides the CPP, based on the first approval, so that they can begin the submission procedure as quickly as possible.
- The recipient CPP NRA rejects the submission as CPP does not reflect the information that has been provided within the module 3 as it contains a different manufacturing site.
- How can the global regulatory submission team, issuing and recipient NRAs work together to overcome this issue?





Suggestions to ensure content of CPP meet NRA's requirements

- Most recipient authorities expect that the drug product they will receive mirrors that which has been approved by the authority issuing the CPP.

However, companies are operating in the global environment and having the global supply chains, where the same product (of the same quality, safety and efficacy) is being manufactured at multiple manufacturing sites. As long as the sameness (e.g. through comparability studies) can be confirmed, flexibility should be allowed related to the justifiable differences, e.g. different manufacturing sites.
- When developing a global submission strategy, CPP requirements are considered early during the planning phase. If required, NRAs should be open to discussion in advance of the regulatory submission to give advice and agree on the content of the submission including the CPP to move forward as quickly possible.
- Issuing NRAs are indeed adequately qualified to conduct certification in all aspects. CPP is foreseen to certify not only QSE assessment performed by issuing NRA, but also that WHO GMP requirements of manufacturing sites are met.
- When the CPP replaces a partial QSE, the CPP would be a condition of approval and should not be required at 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 thus not delaying patient access to medicines.



Authentication of CPPs

- A CPP is an official document that is issued by a certifying NRA at the request of the marketing authorization holder.
- Once prepared, it is provided to the requesting authority as part of the regulatory submission package.
- When any doubt arises about the authenticity of a CPP, the requesting authority should verify the CPP direct with the certifying authority, as referenced within the WHO Scheme guidelines: Section 4.3.
- Where the requesting NRA insists on the CPP being authenticated, the applicant is responsible for this step, however, this is discouraged by the WHO in the new CPP scheme, as reference within the WHO Scheme guidelines: Section 6.6.
- Acknowledging that falsified CPP is a challenge, eCPP listed in the official website can secure authenticity of the CPP.
- Issuing NRA should provide digital signature for authentication purposes when required.

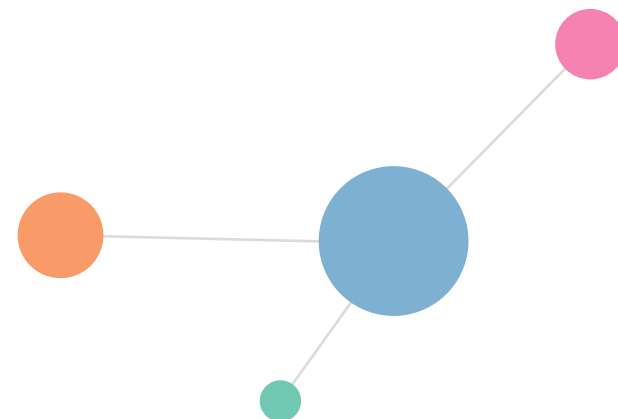
Note: There are various approaches from CPP issuing Authorities to support authenticity of the CPP, e.g. [EMA Verification tool of the electronic CPP](#)





CPP may still be requested even when NRA is completing a full dossier QSE review

- Country X requires a CPP to be submitted as part of the initial registration dossier.
- During submission preparation it is noticed that the legislative requirements for the dossier consist of submitting a full ICH CTD dossier (Modules 2, 3, 4 & 5).
- It is not understood why the full ICH CTD dossier is being requested in addition, to a CPP. According to the WHO scheme, the CPP should replace the QSE review.
- Upon consultation with the NRA of country X, it is explained that the CPP is required as reassurance of an approval by a stringent NRA rather than to replace the QSE review.





QSE evaluation

According to WHO Scheme, CPPs should not be required in countries that require full ICH CTD dossiers and have capabilities of conducting full QSE reviews. However, CPP requirements are often legislatively driven and necessitates legislative changes to remove this requirement. Countries' NRAs should reconsider undertaking steps towards removing such unnecessary burdens.

Increase flexibility in providing the CPP during the review or prior to approval, not at the time of submission, to enable earlier dossier submission and allow faster patient access to innovative treatments.

Alternatives should be considered by the NRA when they move to a full or partial ICH CTD assessment, to overcome the inappropriate use of the CPP, e.g. use of an approval letter or a public assessment report.

Also, relevant recommendations for the appropriate documents requirements depending on the assessment procedure performed are given in the Appendix 5: Example of a national regulatory authority reliance model approach: information, documentary evidence and assessment activity of the WHO "Good practices of national regulatory authorities in implementing the collaborative registration procedures for medical products"



QSE evaluation (cont.)

Pathway	Assessment approach	Documentary evidence (supporting documentation)	Example of products	Comments
Recognition	No scientific assessment	<ul style="list-style-type: none"> • Certificate of pharmaceutical product (CPP) from reference stringent regulatory (SRA) • Public assessment and inspection reports • Assessment and inspection reports 	<ul style="list-style-type: none"> • Products prequalified by the World Health Organization (WHO) • National regulatory authority (NRA) may specify the NRA(s) or institutions whose decision it recognizes 	CPP is not applicable for prequalified products similarity between the local context information for this pathway / approach
Reliance				
Reference SRA	Combination of verification and abridged review	<ul style="list-style-type: none"> • Signed agreements/consent • QIS-SRA(crp) – endorsed by SRA • Bridging report, if applicable • SRA assesment reports, inspection reports • Public assessment and inspection reports (publicly available) 	Products approved by SRA and marketed in SRA market	Information may be shared by the applicant/ manufacturer; SRA approvals do not necessarily consider use in other settings



electronic CPP





Evolution of CPPs

With the increasing number of CPPs required for regulatory submissions generating an administrative burden for both Regulators and Industry, the next step in the modernization of the CPP is the evolution to an electronic CPP (eCPP). Moving in the era of digitalization as CPP-dependent countries start to implement electronic submissions, dossiers and CPPs submitted electronically should be more widely accepted.

- Currently, several NRAs accept electronic CPP applications and some NRAs' have already taken the next step to issue eCPPs e.g. EMA, Health Canada, Swissmedic, MHRA, etc.
- In keeping with the increasing number of electronic submissions, the provision and acceptance of an electronic CPP should be considered by all NRAs.





Modernization of the Certificate of Pharmaceutical Product (CPP)

- The issuance and acceptance of electronic CPPs (eCPPs) to facilitate accelerated submission and approval of a Marketing Authorization or other activities in the product lifecycle has been endorsed by WHO.
- Notarization or Legalization of the eCPP (by Apostille or Consulate/ Embassy) is discouraged.

Use of eCPPs will

- Increase collaboration & trust amongst Regulators
- Increase security of documents and decrease the opportunity for falsification
- Opportunity to modernize and harmonize administrative content
- Facilitate acceleration of submissions contributing to faster access of medicinal products
- Enable regulatory compliance and sustainable supply
- Simply processing CPP globally
- Contribute to conserving environmental resources

- International security standards for electronic signatures is recommended to allow authentication of exchanged documents, including eCPP.

- It is recommended, when any doubt arises about the status or the authenticity of the eCPP, the competent Authority within the requesting country should request a copy directly from the issuing NRA.

Note: The use of eCPP during the COVID-19 pandemic has already demonstrated that the electronic version of CPP is valuable to facilitate regulatory business continuity.





IFPMA Position Paper and Articles



Modernization of the Certificate of Pharmaceutical Product (CPP) - IFPMA position on the use of Electronic CPP - 2020



IFPMA Position on the Use of a Certificate of Pharmaceutical Product (CPP) – 2018



Modernization of the Certificate of Pharmaceutical Product (CPP) - Process: Facts and Vision



WHO Certification Scheme On The Quality Of Pharmaceutical Products Moving In International Commerce: Q&A



US Certificate of Pharmaceutical Product Questions and Answers (Q&A)



Article: How has the evolution of the global pharmaceutical market affected the use of WHO Certificates of Pharmaceutical Product (CPP)?



All documents can be found on [IFPMA website](#)





References

WHO TRS 1033, 55th report

- 1 WHO Guideline on the implementation of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce (Annex 9, page 205)
- 2 WHO Good reliance practices in the regulation of medical products: high level principles and considerations (Annex 10, page 237)
- 3 WHO Good regulatory practices in the regulation of medical products (Annex 11, page 269)
- 4 Paper from CIRS on CPP use <https://link.springer.com/article/10.1007/s43441-020-00196-2>
- 5 APEC KPI paper published: <https://link.springer.com/content/pdf/10.1007/s43441-021-00285-w.pdf>
- 6 WHO Guidelines on CRP (PQ and SRA)
- 7 Good practices of national regulatory authorities in implementing the collaborative registration procedures for medical products: https://www.who.int/medicines/areas/quality_safety/quality_assurance/WHO_TRS_1019_Annex6.pdf?ua=1





Glossary

- CTD: Common Technical Document
- eCTD: electronic Common Technical Document
- EVMPD: EudraVigilance Medicinal Product Dictionary
- FDA: Food and Drug Authority
- GMP: Good Manufacturing Practices
- ICH: International Council of Harmonization www.ich.org
- IDMP : Identification of Medicinal Products www.idmp1.com
- IFPMA: International Federation of Pharmaceutical Manufacturers and Associations www.ifpma.org
- NRA: National Regulatory Agency
- QSE: Quality, Safety and Efficacy
- TOPRA: The Organisation for Professionals in Regulatory Affairs www.topra.org
- MAH: Marketing Authorization Holder
- MAA: Market Access Authorization
- WHO: World Health Organization www.who.int





Appendix - WHO CPP template

Certificate of a pharmaceutical product

This certificate conforms to the format recommended by the World Health Organization:

- No. of certificate
- Exporting (certifying country)
- Importing (requesting country)

- 1.1 Name and dosage form of the product
- 1.2 Active ingredient(s) and amount(s) per unit dose

Complete composition including excipients is attached to the CPP

- 1.3 Is this product licensed to be placed on the market for use in the exporting country? (yes/no)
- 1.4 Is this product actually on the market in the exporting country?

If the answer to **1.3.** is yes, continue with section **2A** and omit section **2B.**

If the answer to **1.3** is no, omit section **2A** and continue with section **2B.**





Appendix - WHO CPP template (cont.)

2.A.

Product that is authorized for marketing by the certifying authority

2.A.1.

Number of marketing authorisation and date of issue

2.A.2.

Marketing authorisation holder (name and address)

2.A.3.

Status of marketing authorisation holder

2.A.4.

Is a summary basis for approval appended? (yes/no)

2.A.5.

Is the attached, officially approved product information complete and consonant with the marketing authorization? (yes/no/not provided)

2.A.6.

Applicant for certificate, if different from marketing authorization (name and address)





Appendix - WHO CPP template (cont.)

2.A.7. Web-link to the product marketing authorization information (if available)

2.B. Product that is not authorized for marketing by the certifying authority.

2.B.1. Applicant for certificate (name and address)

2.B.2. Why is marketing authorization lacking? (not required/not requested/under consideration/refused /
Withdrawal for commercial reasons/Withdrawal for sanitary reasons (key in as appropriate)

2.B.3. Reason provided by the applicant for not requesting registration.

- A)** The product has been developed exclusively for the treatment of conditions (e.g. tropical diseases – not endemic in the exporting country)
- B)** The product has been reformulated - please specify
- C)** Any other reason, please specify





Appendix - WHO CPP template (cont.)

3.1. List of name and address of the manufacturing site(s) and activities:

- A) manufacturing of all steps of the finished pharmaceutical product (FPP);
- B) manufacturing the bulk finished product; 221 Annex 9
- C) manufacturing of solvent and diluents;
- D) quality control of the FPP;
- E) batch release of the FPP;
- F) primary packaging of the dosage form;
- G) secondary packaging of the product;
- H) other(s) (specify and list in new arrows).

3.2. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? (yes/no/not applicable)

— If not or not applicable, proceed to question 4.

3.3. Periodicity of routine inspections





Appendix - WHO CPP template (cont.)

3.4. Has the manufacturer of this type of dosage form of the FPP been inspected? (yes/no)

3.5. Do the facilities and operations conform to GMP as recommended by the World Health Organization? (yes/no/not applicable)

3.6. It is recommended that for products approved, but not manufactured in the country of the certifying authority, the source of information that assures the GMP compliance of the manufacturer(es) is declared.

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product: (yes/no)
– If no, explain.



Appendix - WHO CPP template (cont.)

- Address of certifying authority
- Telephone
- Website
- Email Address
- Name and job title of authorized person
- Validity of the certificate 4 (optional)
- Signature
- Stamp and date (electronic whenever possible)

