Policy Position

August 17, 2018

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

Key Messages

IFPMA endorses the following ideas that:

1. Certifying authorities issue CPPs in accordance with the WHO CPP criteria and format.
2. Timing of the proof of approval by Reference Agency (CPP or alternative) provision by the sponsor in the context of an approval process should be kept flexible and ideally lead to accelerated abridged or reliance-based assessments.
3. Independently of where the product is manufactured, released and exported, a CPP should be available for issue as soon as the product is approved by the certifying authority.
4. The CPP should be considered as a valid alternative of a Good Manufacturing Practices (GMP) certificate as the GMP status is already indicated in the document.

Introduction[1,3,4]

The WHO Certification Scheme[2] for 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. The CPP is a document issued by a National Regulatory Authority (NRA, called '"certifying authority") at the request of a product owner/sponsor to support submission and verify GMP compliance of a pharmaceutical product to another NRA ("requesting authority").

The CPP was introduced as a tool to facilitate the regulatory review and to essentially replace a full dossier evaluation of the Quality, Safety and Efficacy (QSE) in the CPP-requesting country. The CPP confirms:

- the referenced NRA's approval was based on a full evaluation of the product's QSE;
- the product is manufactured under GMP conditions; and/or
- the registration and marketing status of the product in the certifying country.

The Scheme was originally endorsed as a powerful instrument to assist NRAs in sharing information and avoiding duplication. When used in such a context, it has the potential to facilitate the review and accelerate patient access to newly-registered products.

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In line with the original concept of the WHO Scheme, a CPP can be issued as soon as the product is approved in a country, independently of where it is manufactured, released or exported. Adherence to this principle will then allow products to be registered within shorter time frame in the recipient markets, allowing patients to access the medicines earlier.

As the requirements from the recipient authorities and the restrictions from the issuing authorities increase, the processing time for a CPP can range from a few days to several months. These differences often depend on how individual NRAs interpret the CPP Scheme and can lead to delays in approvals, renewals and sometimes even to failure to renew a licence.

Detailed recommendations to be considered when utilizing CPP are given below.

Recommendations

In order to adhere to the original concept of the WHO Scheme[5] and utilize the CPP according to its initial purpose (i.e. to enable facilitated and faster access for patients to medicines), we are proposing the following approach for the CPP-requesting NRA:

1. ***CPP should not be required if the NRA is performing a full ICH CTD dossier review (QSE, according to the WHO Scheme[5]) under a standard registration pathway.***

It is recommended that NRAs adapt their requirements based on the assessment process they are performing[4]:

- Full or abridged registration pathways that require a full QSE dossier review: a CPP should not be requested at all, since NRAs intend to conduct an independent review;
- Abridged pathway review with acceptance of abbreviated dossiers, e.g. Modules 1 & 2 only: a CPP should not be required at the time of dossier submission, but should be provided before the end of the review process (i.e. before approval);
- Reliance pathway review: a CPP is submitted at the time of dossier submission, as timelines for assessment are shorter than with standard review process.

Providing a CPP should lead to either an accelerated review process, or an abbreviated reliance/recognition procedure of an assessment already conducted by a former Stringent Regulatory Authority (SRA)[11] and future WHO-listed Authority[10]***.***

Many countries require provision of the CPP in addition to carrying out their own full or abridged QSE review, thus increasing the time for approval and delaying patient access. The CPP provides confirmation that a full review of quality, safety and efficacy has already been carried out.

Therefore, to reaffirm the original intention of the CPP, i.e. to support countries with “limited drug regulatory capacity”, countries capable of carrying out a full or abridged QSE evaluation based on a complete QSE dossier should be advised to review their regulatory requirements and cease to require a CPP as a mandatory element for approval.

CPP can nonetheless be requested, in the event that countries decide to leverage the evaluation of former SRA[11] and future WHO-listed[10] Authorities (i.e. reliance pathway) to expedite review, and hence accelerate patient access to newly-registered medicines.

2. ***Issuance of CPP by NRAs that rely on a CPP for review should not be accepted: CPP should only be accepted if it is issued by former a SRA[11] or future WHO-listed Authorities[10] in accordance with the WHO CPP criteria and format (which could define competent NRA full adoption of ICH)***

As manufacturing can be outsourced and the capacity of emerging countries to manufacture pharmaceuticals is increasing at great speed, there is a growing demand for CPPs to be issued by countries that also rely on a CPP for their own review processes. This situation is also complicated by the issuance of certificates that are not in the WHO CPP format.

WHO lists the requirements for an authority to issue a CPP within the Scheme. As this approach is self-regulated and not enforced by the WHO, it can lead to the situation where a NRA that relies on a CPP for review also issues CPPs, so that thorough QSE assessment of the product has never been performed.

3. ***Additional Legalization (by the Consulate or Embassy) should not be required[4], as it is beyond the international rules for the exchange of certificates/documents and it does not provide any enhanced evidence of authenticity***

The CPP is a legal document that adheres to the principles of WHO that are endorsed by the majority of countries. Consulate legalization is sometimes required, which is beyond the international rules for the exchange of certificates and documents as it does not provide any enhanced evidence of authenticity and does not provide additional value to patient safety.

However, care must be taken to provide accepting authorities with timely and appropriate verification of the validity of certificates issued. For example, appropriate maintenance of membership[6] of NRAs participating in the WHO Scheme is of utmost importance for preventing its misuse.

In addition, required legal authentication leads to delays in CPP availability, impacting registration timelines and the availability of newly-registered medicines to patients. Where a country requires a CPP prior to the approval of a product, Consulate/Embassy legalization should therefore not be required since the CPP was issued by the NRA in accordance with the adopted WHO requirements.

In addition, it is recommended to establish a concept of having CPPs issued for all NRAs who may require the CPP, rather than issuing CPPs for single, specified countries. The cost and resources used for obtaining CPPs have to be carefully managed in terms of ensuring timely access to safe medications.

Where NRAs publish approvals online, details of approval on the official NRA's website can be used as proof of approval.

4. ***CPP issuance should not be dependent upon where the product is manufactured or exported, but on the basis that the product has been approved by a CPP issuing authority***

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 or exporting country. The focus of the CPP is to ensure that a full review has been undertaken by the NRA to ensure QSE.

5. ***Additional GMP certificates should not be requested, since the GMP statement is included in the CPP***

An additional aim of the WHO Scheme is to certify that the respective facilities and operations conform to GMP as recommended by WHO, as appropriate. WHO clearly discourages the request of an additional GMP certificate since the GMP statement is already included in the CPP.

If the requirement for provision of a CPP is related solely to confirmation of GMP status, then it is advised that the NRA accepts only GMP certificates, as they could be more readily available.

Glossary

Abridged review registration pathway[8,9]: This model relies on assessments of scientific supporting data that has been reviewed and accepted by former SRA[11] and future WHO-listed[10] authorities, but includes an 'abridged' independent review of a certain part of the registration dossier of the product (e.g. relevant to use under local condition). This might include a review of the pharmaceutical quality (CMC) data in relation to climatic conditions and distribution infrastructure and a benefit-risk assessment in relation to use in the local ethnic population, medical practice/culture and patterns of disease and nutrition. As for the verification procedure, there needs to be the assurance that the product is equal or similar to that approved by the reference agency.

Reliance[7]**:** the act whereby the NRA in one jurisdiction may take into account and give significant weight to – i.e., totally or partially rely upon – evaluations performed by another NRA or trusted institution in reaching its own decision. The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others.

Recognition[7]**:** the routine acceptance by the NRA in one jurisdiction of the regulatory decision of another NRA or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B. Recognition may be unilateral or multilateral, and may be the subject of a mutual recognition agreement.

References

1. IFPMA Position paper: "Modernization of the Certificate of Pharmaceutical Product (CPP) Process: Facts and Vision"
2. WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce: Questions and answers (Q & A).
3. "How has the evolution of the global pharmaceutical market affected the use of WHO Certificates of Pharmaceutical Product (CPP)?" Elaine Whiting, TOPRA Regulatory Rapporteur – Vol 9, No 4, April 2012
4. "The WHO CPP Scheme in today's regulatory environment – is it time for change?" WHO Drug Information Vol. 29, No. 4, 2015
5. Use of the WHO Certification Scheme On The Quality Of Pharmaceutical Products Moving In International Commerce, World Health Organization, WHO/DAP/94.21, Action Programme on Essential Drugs (DAP) Original, Geneva January 1995
6. Proposal For Revision Of The WHO Certification Scheme On The Quality Of Pharmaceutical Products Moving In International Commerce - Working document QAS/18.768, April 2018, Draft document for comment
7. Good Regulatory Practices: Guidelines for National Regulatory Authorities for Medical Products, Working document QAS/16.686, October 2016, Draft for comment Prepared by EMP/RSS
8. Lawrence Liberti, Globally Applicable Facilitated Regulatory Pathways to Improve Equitable Access to Medicines. July 2017.
9. EFPIA White paper on reliance and expedited registration pathways in emerging markets, November 2017
10. WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fifty-second report
11. Model quality assurance system for procurement agencies (WHO Technical Report Series (TRS), No. 986, Annex 3, 2014. 137