21 September 2020

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

Key Messages

- **IFPMA encourages the issuing and the acceptance of electronic CPPs** (eCPPs) to facilitate acceleration of submission and approval by health authorities for Marketing Authorization and other activities in the product lifecycle that require a CPP.
- The eCPP should be fully integrated with **other digital systems used for dossier submission and review**, including e-signatures and electronic dossier submissions.
- **Appropriate international security standards for electronic signatures should be in place** to ensure **authenticity** of digital documents, including eCPP. Additional Legalization of the eCPP (by the Consulate or Embassy) is discouraged[1].
- Using **digital technologies such as eCPPs will aid faster access of medicines to patients** and contribute to **conserving environmental resources**.

Introduction

Increasing number of regulatory agencies require or allow the electronic submission of a full dossier or certain defined sections for the assessment of a pharmaceutical product's quality, safety and efficacy (QSE) attributes. In many cases, these are the same National Regulatory Authorities (NRAs) who issue Certificates of Pharmaceutical Product (CPP) for other countries that require or base their regulatory approval on the initial evaluation conducted by these CPP-issuing authorities.

The need for regulators to maintain business continuity, make fast decisions and stay well connected to an overwhelmingly digital world was proven critical during the SARS-COV-2 public health situation. Rapid adaptation and use of available digital technologies by the regulators during the unprecedented pandemic situation have provided opportunities to modernize the regulatory ecosystem. Data collected by IFPMA and EFPIA in May 2020 from 80 countries demonstrated that almost 90% of countries' NRAs have accepted eCPPs to facilitate lifecycle management submissions of products on the market or new product approvals (Figure 1). From these NRAs, almost 30% are already fully accepting eCPP and the rest is accepting eCPP with the commitment to obtain paper copies once feasible (either for all or some product categories). Additionally, as more CPP-dependent countries start implementing electronic submissions overall, more dossiers and CPPs can be submitted electronically. This, in the long-term, can ensure more innovative treatments are available faster to patients in need.

This paper provides the position of the biopharmaceutical industry on the possibilities to improve and modernize current use of CPPs and provide recommendations for implementing an electronic version of the CPP (eCPP). eCPP, in the context of this paper, refers to the electronic version of the CPP securely requested by and securely delivered to the requestor and/or the agency via electronic means (e.g. email, web link, or portal).

Recommendations

1. **eCPP should be accepted as the preferred mode of document, or as equivalent to a hard copy document.**

Currently, eCPP is not explicitly covered in the WHO Certification Scheme nor in country-specific regulations. As there are no legal or regulatory requirements to prohibit use of eCPP, we encourage applicants and regulators to implement the use of eCPP as an equivalent to the paper copy CPP. Keeping in line with the digitalization of most administrative information in the pharmaceutical field, eCPP should be considered as an improved and preferred option. Therefore, where applicable, we encourage the removal of barriers for acceptance for electronic certificates and appropriate changes to related regulations to allow eCPP acceptance.

2. The eCPP should aid accelerating the overall assessment process and also favor **interoperability with other digital systems.**

Some technical prerequisites to allow acceptance and processing of eCPP are welcome in the requesting country, but these should not be a barrier for the acceptance of eCPP, e.g. there could be a phasing in the approach of adopting digital strategy from simple to complex system (e.g. accepting eCPP via email, direct access from issuing CPP NRA). As a natural evolution, each country should implement a comprehensive digital strategy that ensures interoperability between systems used for dossier submission and review, including e-signatures and electronic dossier submissions, where available. This will accelerate the overall review process. Moreover, once these technical prerequisites are met, requirements for providing hard copy documents should be waived. In addition, Health Authorities should harmonize electronic signature software acceptance such as DocuSign, to enable this to work effectively. The acceptance of electronic signature is a must in the new digitalized world.

3. **Appropriate international security standards for electronic signatures should be in place** to allow authentication of exchanged documents, including eCPP.

Recognition and implementation of international security standards is paramount. Once implemented, additional requirements for the legalization of the eCPP (by the Consulate or Embassy) should be discouraged[1]. Every requesting authority should in addition assess the requirements for wet signatures, original hard copies, and additional verification measures and adjust their requirements to allow electronic signatures when possible. These additional requirements are not only resource-demanding, but also redundant.

4. When **any doubt arises about the status or the authenticity** of the CPP, the competent Authority within the requesting country should **request a copy directly from the issuing Health Authority.**

Requesting NRAs are strongly encouraged to directly contact the issuing authority in case of any concerns, and issuing authorities are encouraged to allow direct and transparent communication, to

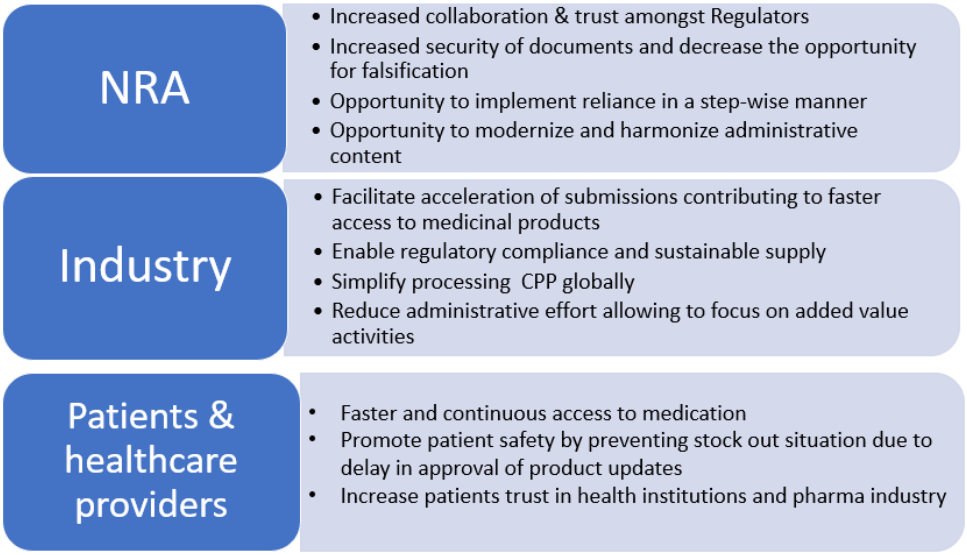
[1] IFPMA Position on the Use of a Certificate of Pharmaceutical Product (CPP)

prevent any misuse of the issued certificates[2,3]. In case of exchange of new electronic documentation, the Marketing Authorization Holder (MAH) should also be informed.

5. Use of eCPP digital technology will contribute to **conserving environmental resources.**

In a progressively digital world where reliable information transfer can be increasingly done in a sustainable way, the use of eCPP digital technology can contribute to the reduction of the environmental footprint.

Potential Benefits of eCPP submission to all Stakeholders



Proposal for implementing a complete eCPP process

1. **Definition of eCPP**

The overarching definition, content and procedural aspects of the eCPP should be recognized by WHO and implemented in the appropriate regulations in the CPP-issuing and CPP-requesting countries.

Electronic CPP (eCPP), in the context of this paper, refers to the electronic version of the CPP that is securely, electronically requested and delivered to the requestor and/or the agency accessing the CPP via electronic means (e.g. email, web link, or portal).

2. **Legislative Prerequisites** – related to the CPP requesting and issuing aspects

Regulatory framework addressing the issuance and acceptance of CPP should be adjusted to allow use of electronic documents through secured and validated platforms, recognizing authenticity of provided electronic documents. Any redundant manual activities related to the authenticity verification have to be avoided.

[2] EMA Information note on the format and validity features of electronic certificates for medicines issued by the European Medicines Agency

[3] WHO: Use of e-signature for Certificates using the WHO Certification Schemes

3. Administrative prerequisites

CPP-issuing health authorities have unique procedures for processing CPPs. Those procedures should be adjusted to correspond to the scope and the requirements of the WHO Certification Scheme.

Health authorities should perform updates to the information technology infrastructure to enable automated CPP request processing, and the system should be compatible with systems used by other health authorities for consistency and interoperability.

4. Technical Prerequisites

Most technical prerequisites and basic infrastructure are already available. A new eCPP-processing system could potentially be set up based on existing example such as the Extended Eudravigilance Medicinal Product Dictionary (XEVMPD) or the EUDRA GMP database. Another method for authentication and ensuring security in global supply chains is provided with pdf documents where each certificate contains an advanced electronic signature from a trusted provider fully compliant with e-signature regulations, which would be a good model for authenticating eCPPs. There are technologies available that can provide an extra level of authenticity that would protect from counterfeit eCPPs without the need for legalization.

5. Adaptation of the CPP template to an electronic format solution

The current WHO CPP format would require adaptation in the text and in the related explanatory notes to enable changes to make an electronic version from the paper version. A potential solution would be to have open access to one part of the CPP and a closed section which would be confidential to the public. This approach is similar to what is used for the Drug Master File system. The product owner/sponsor grants access or authorization for the requesting authority to download confidential information such as the full quantitative composition.

6. Clarification of responsibilities

Responsibilities of the product owner/sponsor, eCPP-issuing authorities and eCPP-requesting authorities should be clearly defined to ensure an efficient eCPP request, procurement and delivery process is in place.

Conclusion

Reliance is an important concept to improving the efficiency and effectiveness of regulatory operations for the oversight of medical products. The WHO *Certification scheme on the quality of pharmaceutical products moving in international commerce*, introduced by WHO in 1969, is a form of reliance providing assurance to countries participating in the Scheme about the quality of pharmaceutical products[4].

Implementation of eCPP will participate in increasing the efficiency of regulatory systems, being a recognized "tool" for all stakeholders, and will ultimately facilitate faster access to medicinal products to patients.

The use of eCPP during the COVID-19 pandemic has already demonstrated that the electronic version of CPP is valuable to secure regulatory business continuity (ref. to Appendix 1). This experience should be used to swiftly implement eCPP.

[4] WHO Good reliance practices in regulatory decision-making: high-level principles and recommendations

Appendix 1: Current eCPP acceptance (based on the EFPIA and IFPMA Network experiences during COVID-19 pandemic)

In a survey conducted in May 2020 amongst 80 countries, different levels of regulatory agility were observed. It was noted that in some cases, the conditions for accepting eCPP in a country could differ per product category (vaccines versus pharmaceuticals).

Figure 1. eCPP was accepted for pharmaceuticals and/or vaccines products in 89% of the countries assessed.

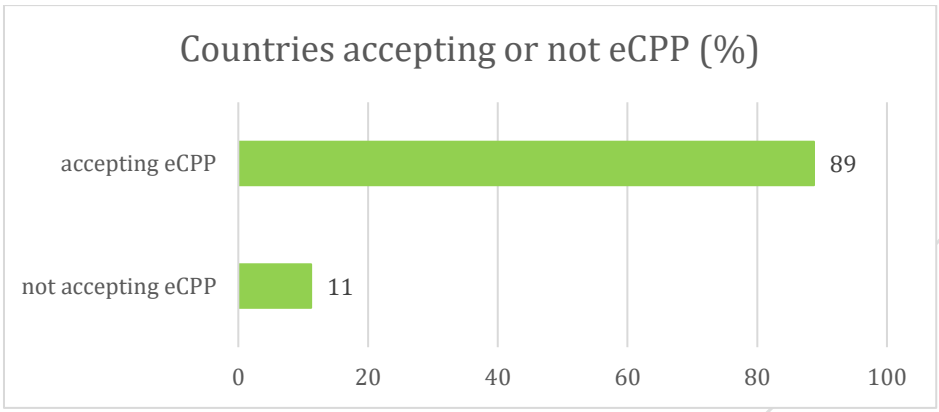


Figure 2 - Some countries/health authorities (n=53) are accepting e-CPP submissions with commitment from the manufacturer to submit the appropriate hard copy documentation after the pandemic: about 7% of them are accepting eCPP for pharmaceuticals products only, 4% are accepting eCPP for vaccines only, and 89% are accepting eCPP for both product categories.

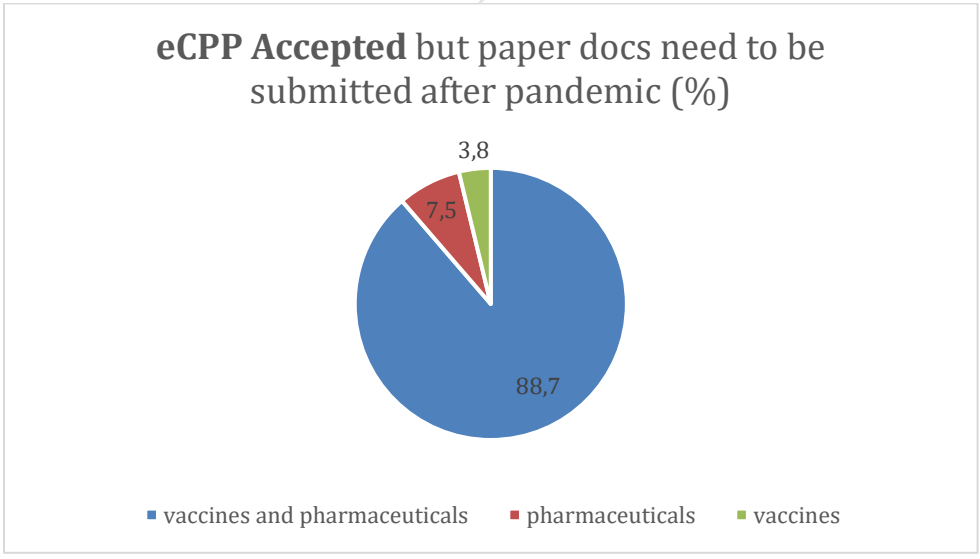


Figure 3: Other countries/health authorities (n=23, 29%) are accepting eCPP with no further documentation required. About 9% of them are accepting eCPP for pharmaceuticals products only, 52% are accepting eCPP for vaccines only, and 39% are accepting eCPP for both product categories.