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Review

Role Of Copp In Pharmaceutical Export

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Abstract

This review includes basics of CoPP, origin of CoPP, types, types of drug includes in CoPP, procedure to obtain CoPP, requirement for CoPP, applicant, examples, format and content and benefits of CoPP. A CoPP is given by the drug regulator not before conducting an inspection of the manufacturing plant. Proper documentation is essential in almost every aspect of the pharmaceutical industry. Whether for product registration, factory inspection, or internal quality control, Adva Care employs the latest technologies to streamline and process information. All facilities possess up-to-date Good Manufacturing Practice (GMP), CE, TUV, and/or ISO certificates that reflect high quality standards and WHO rules and regulations. Essential product registration documents, such as the Certificate of Pharmaceutical Product (COPP), Free Sales Certificate (FSC), Certificate of Origin (COO), and Marketing Authorizations are among the many documents our registration department frequently submit for registration purposes.

Keywords: Pharmaceutical Industry, COPP, GMP, COO, Drug Regulator.

INTRODUCTION

Certificate of pharmaceutical product[1]

The certificate of pharmaceutical product (abbreviated: CPP) is a certificate issued in the format recommended by the World Health Organization (WHO), which establishes the status of the pharmaceutical product and of the applicant for this certificate in the exporting country. It is issued for a single product, because manufacturing arrangements and approved information for different pharmaceutical forms and strengths can vary.[2]

Scope

The Certificate of a Pharmaceutical Product is needed by the importing country when the product in question is intended for registration (licensing, authorisation) or renewal (prolongation) of registration, with the scope of commercialisation or distribution in that country. Certification has been recommended by WHO to help undersized drug regulatory authorities or drug regulatory authorities without proper quality assurance facilities in

importing countries to assess the quality of pharmaceutical products as prerequisite of registration or importation.

In the presence of such CPP, WHO recommends to national authorities to ensure that analytical methods can be confirmed by the national laboratory, to review and if necessary to adapt product information as per local labelling requirements, and to assess bio equivalence and stability data if necessary.[3]

However, regulatory practices often vary in importing countries. Thus, in addition to CPP, assessment of application dossiers to support drug registrations, with different levels and complexity of requirements are considered necessary to satisfy full assurance on the appropriate quality of drugs.[4]

Content and format

The content of CPP consists of the following main data:

- Exporting (certifying) country
- Importing (requesting) country
- Name, dosage (pharmaceutical) form and composition of the product [active ingredient(s) and amount(s) per unit dose]
- Information on registration (licensing) and marketing (presence on the market) status of the product in the exporting country
- Number of product licence (including licence holder details, licence holder's involvement in manufacturing if any) and date of issue, if applicable
- Appended summary of technical basis on which the product has been licensed (if required by the issuing authority)
- Appended current product information
- Details on the applicant for the CPP
- If marketing authorisation is lacking in the exporting country, information about reasons

When applicable, information if the manufacturing site is periodically inspected by certifying authority and if the manufacturing site complies with Good Manufacturing Practice (GMP) as recommended by WHO.

Although issuing authorities claim that their CPP conform to WHO format (a statement to confirm whether or not the document is issued in the format recommended by WHO should be included in the certificate), their format and content may vary from an issuing country to another. Also, some authorities do not issue CPP if the respective drug is not licensed in the exporting country (e.g. Italy). In this last case, a Certificate of Exportation is issued instead, with a format and content similar to those of CPP.

Special considerations in importing countries

Most competent authorities in importing countries require CPP to be issued by the country of origin.Also, even though this certificate is released in its original form, addressed to a specific importing country and stamped with the seal of issuing authority on each page, many authorities in importing countries may unnecessarily request authentication of such a document in the form of legalisation by their embassy in the exporting country or by apostillation ("Abuse of scheme"). Proper documentation is essential in almost every aspect of the pharmaceutical industry. Whether for product registration, factory inspection, or internal quality control, AdvaCare employs the latest technologies to streamline and process information. All facilities possess up-to-date Good Manufacturing Practice (GMP), CE, TUV, and/or ISO certificates that reflect high quality standards and WHO rules and regulations. Essential product registration documents, such as the Certificate of Pharmaceutical Product (COPP), Free Sales Certificate (FSC), Certificate of Origin (COO), and Marketing Authorizations are among the many documents our registration department frequently submit for registration purposes. Likewise, technical files are repeatedly checked for consistency and accuracy for both internal quality control purposes and in preparation of inspections. Adva Care is highly specialized in the export process and has vast experience with documentation for product registration. Our customers realize the value in registering our products - the value of quality, time, and reliability.[5]

Certificate of a pharmaceutical product (CPP)

The Medical Products Agency (MPA) issues export certificates on request to assist exporters of medicinal products to satisfy the import requirements of other countries. The format of the certificates complies with that specified by the World Health Organization (WHO), except point 1.3 "Is this product actually on the market for use in the exporting country?" which is not included, as the MPA does not have access to that information. The certificate can be ordered from the MPA using the form available on the website (see hyperlink to the right). The certificate of a pharmaceutical product (CPP) will provide details about a single named medicinal product for human or veterinary use. A certificate can be issued for a medicinal product for which a Marketing Authorisation application is under consideration or refused or for a medicinal product which is licensed or withdrawn in Sweden. The certificate provides detailed information about the product including the Marketing Authorisation Holder (MAH), the complete composition and the manufacturing site(s).

The MAH or a representative of the MAH can apply for the certificate. The certificate is issued in English

only. Certificates for medicinal products applied for through the centralised procedure are only issued by the EMA. The MPA will issue a certificate within 30 days of the arrival of the request. The certificate is issued on specific certificate paper with an MPA stamp assigned. The requesting company is responsible for the legalisation of the certificate when needed; this is not done by the Medical Products Agency. The fee for issuing one CPP is 950 SEK. The MPA will send an invoice to the applicant after the delivery of the certificate.

The medicinal product may have a different name in the importing country. If so, a statement of this can be attached to the certificate. The statement has to be written on the company's headed paper, be signed and dated and should state the trade name, pharmaceutical form and strength in both the exporting and the importing country. If the Summery of Product Characteristics (SmPC) is to be attached to the certificate, the applicant is responsible for the translation of the latest approved Swedish SmPC from Swedish to English. The translated version should be enclosed to the request of the certificate. If the medicinal product is authorised through the mutual or decentralised procedure with Sweden as Reference Member State (RMS), the latest approved English SmPC is already available at the MPA and can be attached to the certificate.[6]

Importance of COPP

It is needed ny the importing country when the product is intended for registration (licencing, authorisation), or renewal(prolongation) of registration. Certificate has been recommended by WHO to help undersized drug regulatory authorities without proper quality assurance facilities in importing countries to acess the quality of pharmaceutical products as prerequisite of registration or importation.

WHO

The application for the grant of WHO GMP certificate of pharmaceutical product shall be made to respective zonal officers as per the requirement. The CIOPP will be issued by the zonal officers on behalf of Drugs Controller General (India) after inspection and satisfactory clearance by CDSCO officers as per WHO-GMP guidelines .

General requirements for the submission of application for issue of COPP

- A application letter shall be addressed to DDC(1) / ADC(1) of respective CDSCO zonal/ subzonal offices with copy of covering letter and product summary sheet to DCG(1) by authorised person only .
- Application should clearly indicate for fresh(Grant) or reissue of products applied , accordingly it will be scrutinized for the products applied .
- Applications will be reviewed by CDSCO officers and completed applications in all respects would be accepted for inspection on first come first serve basis.
- The forwarding letter or application shall be accompained with the list of products applied for grant of COPP, along with the product permission copy (manufacturing liscence issued by SLA) and notarised product summary sheet, site master file as per WHO-GMP requirements .
- List of major/master documents like master validation plan , quality manuals , specifications , master formula records maintained by firm and list of SOP'S (to indicate the documentation system of firm).
- Manufacturing layout
- List of personnel (with designation, quqlification and experience) , list of equipments , instruments , utilities along with make and model and capacity.
- List of primary and secondary impurity and reference standards /cultures available with the firm(relevant to the applied products for the grant of COPP).

Procedure For Acceptine The Application For Issue Of Copp

- Applications forwarded by before 1-10-2009 will be considered provided they should resubmit the application in the revised format with forwarding letter , notarised product summary sheet and other documents which were not submitted earlier as per requirment on first come first serve basis .
- A ll applications received will be scrutinized by CDSCO officials after receipt and query letter will be sent to applicant , if any or otherwise will be considered for inspection .
- Inspection will be carrid out by CDSCO officers ads per WHO GMP guidelines of TRS 822/902 for sterile products and other relevent guidelines in TRS937 , TRS 929 , TRS 863 etc. as applicable from time to time .
- Self apprisal cheklist should be filled and submitted to CDSCO officer before inspection .
- inspection team verify the checklist at the time of inspection .
- Inspectors brief the inspection findings at the exit meeting .
- The report should clearly define defeciencies as per WHO GMP guidelines .
- Respective zonal/subzonal certifying authority prepare "Review Report" based on review of observations of checklist and written inspection report as per WHO GMP guidelines .

- Firm may reapply if required after proper compliance after 5 months from date of rejection.
- If the same firm applies after 5 months , scrutiny of such application should be asked for earlier compliance with documentary evidences in addition to the usual general requirements for submission of application for issue of COPP .

Types of CoPP

1) WHO 1975 type CoPPThe WHO 1975 version is a certificate to be issued byexporting country regulatory authority stating:
   a) the authorized product has to be placed on themarket for its use in the country also, the permit numberand issue date, or
   b) that the nonauthorized product has placed on themarket for its use in the country and also add the reasonswhy it is needed;
   Also, that;
   a) As recommended by World Health Organization,the manufacturer of product conforms to GMPrequirements.
   b) only within the country of origin the products to besold or distributed ;orc) To be exported to manufacturing plant where theproduct is produced and at suitable intervals subject to inspections .

2) WHO 1988 type CoPP Unlike the WHO 1975 version, the competent authorityof the exporting country should have:
   - All labelling copies.
   - Product detailed information in the country of origin

3) WHO 1992 type CoPPThis is intended for use by the competent authority of animporting country in two situations:
   - When the question arises related to importation andsale license; and
   - For license renew, extend, review or changes.

The following information required for the certificate:
- Whether a licensed product is required to be placed onthe market or not.
- Also if the satisfied information submitted by theapplicant that the certifying authority of the manufactureof the product undertaken by another party
- Inspection have been carried out of the manufacturerof product;
- If the certificate is provisional or permanent;
- Is the dosage forms, packages and/or labels of afinished dosage form manufactured by an independent company or by the applicant;
- states the names of the importing and exporting(certifying) countries

Here besides three types of CoPPs also we haveanother specific type of the U.S. FDA CoPPs

The U.S. FDA issued "Pilot- CoPP" for the remainingproducts which are neither exported nor manufactured inthe United States. It is only when no other country hasgiven an approval for the finished medicinal product registration

Certificate of a pharmaceutical product model

The form is suitable for generation by computer. Itshould be submitted as hard copy, with responses printedin type rather than handwritten .

How to obtain CoPP?

To obtain a CoPP, a request is made to the exportingcountry's health authority by the Marketing Authorization Holder (MAH).

An authorized person issues the CoPP and returns itto the MAH. Also other documents required to obtain aCoPP including an application for Export Certificateform, evidence of a GMP certificate (if applicable),Manufacturing License and the last approved SPC(Summary of Product Characteristics.

Content and format

- Importing country
- Exporting country
- Name, form of dosage and its composition of theproduct (API per unit dose).
- Registration Information (licensing)
- Marketing status of the product in the exportingcountry.

- license no. of product (containing license holderdetails; involvement of license holder in manufacturingif any) and also add date of issue,
- Summary of technical basis on which the producthas been licensed (if required by the issuing authority)
- Currently marketed product's information
- Details about the product's applicant
- If lacking is there in the exporting country, need tomention the information about reason

Certificates May Be Issued

- Legally marketable drug in the country.
- Nonauthorized drugs for distribution in the countrywhich are legally exported to a foreign country.
- For a foreign manufactured drug.Exportation for Personal Use
- Awareness is necessary for the drugs that are legalin some countries may be illegal in other countries.Importation for Personal Use
- Risky to health, such drugs are prevented fromimportation.
- Also Enforcement actions have been taken domestically

Types of drugs for which CoPPs may be issued

- Approved drug products
- Active pharmaceutical ingredients (API)
- Over the counter drug (OTC) products
- Unapproved drug products
- Homeopathic drugs

Who can apply for CPP?

- A complete application for export certification mustbe submitted by the person/company who exports thedrug.
- The certification is intended for a drug which :meets the applicable requirements of the Act or Food Drug and Cosmetic Act 801(e)(1) requirements [21U.S.C.381(e)(1)]

Process to apply for a

a)Submit Form no. 3613b– Located on the FDA internetwww.fda.gov/downloads/AboutFDA/Reports ManualsForms/Forms/UCM052388

b) Requirements for CoPP application:

- Applicant Contact Information
- Trade name (the drug product's brand name)
- Bulk Substance Generic Name
- Name of Applicant
- Status of Product License holder
- Listing of manufacturing location on CPP
- Complete Manufacturing Facility Address
- Facility Registration Number
- Importing countries
- Authorization to Release Information
- Number of certificates requested
- Certification Statement
- Billing contact
- Marketing Status in the Exporting Country

CoPP Fee Schedule

- First Certificate (original) – ($175.00) 11025Rs/-
- Second Certificate – ($90.00) 5670 Rs/-
- Third and subsequent certificates –($40.00)2520Rs/

Expiration of CPP

- Certificate expires on 2 years from the notarizationdate or as noted.
- After expiry date, a new CoPP application has to besubmitted.[8]

General Certificates of Pharmaceutical Product Information

Firms exporting FDA-regulated articles are often asked by foreign customers or foreign governments to supply a certification relating to articles subject to the Federal Food, Drug, and Cosmetic Act (FD&C Act) and other laws FDA administers. Section 801(e)(4)(A) of the FD&C Act, as amended by the FDA Export Reform and Enhancement Act of 1996 (Public Law 104-134) provides that FDA may issue certificates for food, drugs, animal drugs, and devices within 20 days of receipt of a request for such a certificate. FDA issues export certificates for approved or licensed drugs and for unapproved drugs that meet the requirements of Sections 801(e)(1) or 802 of the FD&C Act. Certificates of Pharmaceutical Product (CPPs), the only export certificate issued by CDER, are issued for drugs typically exported from the U.S. directly to the requesting country. CPPs conform to the format established by the World Health Organization (WHO) and are intended for use by importing countries when considering whether to license the product in question for sale in that country. CDER only issues CPPs for human drugs that it regulates. Certificates expire 24 months from the date of issuance, after which a new application must be submitted. Certificates cannot be reissued. CPPs issued for drugs exported from the U.S. are printed on security paper and contain the signature of the authorized CDER Official, embossed federal seal, and ribbon.[9]

India's Drug Controller General to Take Over COPP and GMP Drug Certification

The Certificate of Pharmaceutical Products (COPP) and Good Manufacturing Practice (GMP) under World Health Organization (WHO) certification will be taken over by the Drug Controller General of India (DCGI). Previously, State Drug Controllers were responsible for issuing these two certificates. However, the WHO has expressed concern on the implementation and the quality of pharmaceutical products entering international commerce. The DCGI of the Centre of Drug Standards Control Office (CDSCO) took over this certification process in October 2009. The COPPs will be issued after inspection of manufacturing facilities by CDSCO regulatory officials. Facilities must comply with WHO-GMP guidelines. The COPP will be issued only in the format recommended by the WHO. COPPs already issued are valid until expiration. The application forms will include details such as a product summary sheet, site master file as per WHO-GMP requirements, a list of master documents such as quality manuals and master validation plan, manufacturing layout, personnel list, etc. The main purpose of the COPP establishes the status of the pharmaceutical product and of the applicant in the exporting country. Therefore, a country importing a COPP-certified Indian drug can be assured that the product complies with WHO mandated GMP certification.[10]

1. "Site Master File" has to be submitted as recommended in the WHO technical report series.
2. The Department of AYUSH, in consultation with Drugs Controller General (India) will fix the date of inspection.

3. Drugs Controller General (India) will constitute inspection team /Committee comprising
    i. Expert from Department of AYUSH,
    ii. Nominee of DCG(I), and
    iii. State Drugs Controller/ Licencing Authority,

5. Inspection team/Committee will make inspection as per Check list and submit report to department of AYUSH with a copy to DCG(I)
6. The recommendation of the Inspection team/ committee, will be examined by DCG(I) and if found suitable, DCG(I) will issue Certificate of Herbal Pharmaceutical Products.

Explanatory notes

1. This certificate, which is in the format recommended by WHO, establishes the status of the pharmaceutical product and of the applicant for the certificate in the exporting country. It is for a single product only since manufacturing arrangements and approved information for different dosage forms and different strengths can vary.
2. Use, whenever possible, International Non proprietary Names (INNs) or national non proprietary names.
3. The formula (complete composition) of the dosage form should be given on the certificate or be appended.
4. Details of quantitative composition are preferred but their provision is subject to the agreement of the product-licence holder.
5. When applicable, append details of any restriction applied to the sale, distribution or administration of the product that is specified in the product licence.
6. Sections 2A and 2B are mutually exclusive.
7. Indicate, when applicable, if the licence is provisional, or the product has not yet been approved.
8. Specify whether the person responsible for placing the product on the market:
    a. manufactures the dosage form;
    b. packages and/or labels a dosage form manufactured by an independent company; or
    c. is involved in none of the above.

9. This information can only be provided with the consent of the product-licence holder or, in the case of non-registered products, the applicant. Non-completion of this section indicates that the party concerned has not agreed to inclusion of this information. It should be noted that information concerning the site of production is part of the product licence. If the production site is changed, the licence has to be updated or it is no longer valid.
10. This refers to the document, prepared by some national regulatory authorities, that summarizes the technical basis on which the product has been licensed.
11. This refers to product information approved by the competent national regulatory authority, such as Summary Product Characteristics (SPC)
12. In this circumstance, permission for issuing the certificate is required from the product-licence holder. This permission has to be provided to the authority by the applicant.
13. Please indicate the reason that the applicant has provided for not requesting registration.
    a. the product has been developed exclusively for the treatment of conditions — particularly tropical diseases — not endemic in the country of export;
    b. the product has been reformulated with a view to improving its stability under tropical conditions;
    c. the product has been reformulated to exclude excipients not approved for use in pharmaceutical products in the country of import;
    d. the product has been reformulated to meet a different maximum dosage limit for an active ingredient;
    e. any other reason, please specify.
14. Not applicable means the manufacture is taking place in a country other than that issuing the product certificate and inspection is conducted under the aegis of the country of manufacture.
15. The requirements for good practices in the manufacture and quality control of drugs referred to in the certificate are those included in the thirty-second report of the Expert Committee on Specifications for Pharmaceutical Preparations, WHO Technical Report Series No. 823, 1992, Annex 1. Recommendations specifically applicable to biological products have been formulated by the WHO Expert Committee on Biological Standardization (WHO Technical Report Series, No. 822, 1992, Annex 1).
16. This section is to be completed when the product-licence holder or applicant conforms to status (b) or (c) as described in note 8 above. It is of particular importance when foreign contractors are involved in the manufacture of the product. In these circumstances the applicant should supply the certifying authority with information to identify the contracting parties responsible for each stage of manufacture of the finished dosage form, and the extent and nature of any controls exercised over each of these parties.

Guidance document on the application for a certificate of a pharmaceutical product(GUI- 0024)
Purpose

This document clarifies the requirements to be met for the issuance of a Certificate of a Pharmaceutical Product (CPP) and describes the procedure for the request of a CPP.

Background

In 1967, the Twentieth World Health Assembly requested in resolution WHA20.34 that a draft text be prepared on good manufacturing practices (GMP). The text was subsequently submitted to the Twenty-first World Health Assembly in 1968, under the title "Draft requirements for good manufacturing practice in the manufacture and quality control of drugs and pharmaceutical specialities". In 1969, the Twenty-second World Health Assembly endorsed these requirements for "Good Practices in the Manufacture and Quality Control of Drugs" (resolution WHA22.50). These requirements have since been revised: the first revision was adopted by the World Health Assembly in 1975 (resolution WHA28.65) and the most recent revision is included in the Thirty-seventh report of the World Health Organization (WHO) Expert Committee on Specifications for Pharmaceutical Products.

These requirements also provide the basis for the WHO Certification Scheme on the Quality of the Pharmaceutical Products moving in International Commerce, recommended initially in resolution WHA22.50. The WHO Certification Scheme, an international voluntary agreement, enables countries with limited drug regulatory capacity to obtain partial assurance from exporting countries that the pharmaceutical products, which they plan to import, are safe, effective and of good quality.

All Member States of the WHO are urged to adopt and to apply these GMP standards as recommended by WHO. Canada, represented by the Health Products and Food Branch Inspectorate (HPFB Inspectorate), adopted the WHO Certification Scheme on May 1, 1996. Prior to this date, Certificates of Free Sales were used to attest that the pharmaceutical products were fabricated in compliance with GMPs. These types of certificates are no longer issued. They have been replaced by Certificates of a Pharmaceutical Product (CPP) and are issued as a service to the industry when required by an importing country.

Scope

A CPP is issued for human drugs (pharmaceutical, biological and radiopharmaceutical) as well as for veterinary drugs (food producing animals and non food producing animals). Since the Food and Drugs Act and Regulations apply also to veterinary pharmaceuticals intended for non food producing animals, they must be fabricated according to GMP requirements and consequently, Health Canada chooses to issue CPPs for these pharmaceutical products. Products falling under the Natural Health Products (NHP) framework are excluded from the scope of this document.

Procedure

A CPP, in the format recommended by the WHO, establishes the status of the pharmaceutical product listed on the certificate, and the GMP status of the fabricator of the pharmaceutical product, in the exporting country. The Inspectorate issues a CPP to one of the following applicants:

- the Drug Identification Number (DIN) owner of the pharmaceutical product; **or** in the case of radiopharmaceuticals the party to which an NOC has been issued
- the fabricator of the pharmaceutical product, if it is located in Canada and GMP compliant; or
- a third party that submits, along with the application, a written authorization for the issuance of the CPP from the DIN owner of the pharmaceutical product. (To be updated annually)

Requirements for issuance of a Certificate

When the pharmaceutical product is fabricated and packaged/labelled in **Canada**, a CPP is issued if all the following requirements are met:

- the fabricator and packager/labeller are GMP compliant;
- the pharmaceutical product has a valid DIN and a valid date of notification;
- **or** in the case of radiopharmaceuticals an NOC has been issued and the product has a valid date of notification
- the pharmaceutical product is sold on the Canadian market;
- the applicant must be located in Canada.

*Please note: If the fabricator is other than the DIN owner, their subsidiary or legal agent, confirmation is required from the fabricator that they fabricate the product.

*Please note: the application form requests the "date of notification" and this is inserted in the field, on the certificate, identified as the date of issue. The date of notification indicates the date of issuance of the product on the market.

When the pharmaceutical product is fabricated in a **foreign country** and packaged/ labelled in **Canada** or fabricated in **Canada** and packaged/ labelled in a **foreign country**, a CPP is issued if all the following requirements are met:

- the packager/labeller and the fabricator are GMP compliant;
- the foreign establishment is GMP compliant and is listed on the Canadian Drug Establishment Licence (DEL);
- the pharmaceutical product has a valid DIN or an NOC and a valid date of notification;
- the pharmaceutical product is sold on the Canadian market

When the pharmaceutical product is fabricated and/or packaged/labelled in Canada but **not marketed in Canada**, a CPP is issued if the following conditions are met:

- the fabricator and/or packager/labeller are/is GMP compliant;
- a DIN or an NOC has been issued, (that is the drug product has market authorization).

When the pharmaceutical product is **fabricated in Canada and not sold on the Canadian market, but the drug submission is under review**, a CPP is issued if the fabricator is GMP compliant and if the applicant submits information on the formulation and active ingredients of the pharmaceutical product. Furthermore, the CPP issued will carry the following statement: "The product is manufactured for export only. The Health Products and Food Branch of Health Canada is currently reviewing an application to permit the marketing of this product in Canada."

If the request for a Certificate is not specific for a pharmaceutical product, a GMP certificate is issued when the fabricator is GMP compliant. In this particular case, the certificate that is issued indicates the dosage forms only, instead of the product information.

DISCUSSION

Master of Drug Regulatory Affairs

Within the WHO Certification Scheme the Certificate of a Pharmaceutical Product (CPP) will be the focus topic in this thesis. Not only will the requirements given by Health Authorities from countries outside of "The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals

for Human Use (ICH)" be discussed, but also the experiences from Local Regulatory Affairs Managers (LRAMs) worldwide will be evaluated. Therefore, a short questionnaire was sent to several country affiliates requesting their personal 'every day working experience' on the demand and benefit of submitting a CPP to their Health Authority during the Life Cycle Management (LCM) of a finished medicinal product (MP). This could be either during new drug applications (NDA) or during maintenance activities, for prescription drugs (Rx) or over the counter (OTC) products. The strategic use and benefits of a CPP for a Health Authority as well as for a pharmaceutical company will be addressed during the evaluation of the data. This master thesis will analyze the value, need and importance of a CPP for countries outside of the ICH. The CPP was created within the WHO Certification Scheme on the quality of pharmaceutical products described by the World Health Organization (WHO) funded by the United Nations (UN). Differences in the use by local HAs and the WHO recommendation will be evaluated and discussed. The need of the CPP will be analyzed regarding useful transfer reflected to the view of the HAs, patient groups and pharmaceutical companies.

Who is "WHO"? – History, origin and relevance of the World Health Organization

Since the United Nations (UN) was formed in 1945, one of their goals was to set up a global health organization. Therefore, the United Nations Organization, which currently has 193 member states (WHO, An introduction to the World Health Organization, 2013), created the World Health Organization (WHO) whose constitution came into force on 7th April 1948. Today the WHO is the authority directing and coordinating functions around health topics within the UN system. The responsibility of the WHO covers discussions on global health topics in general, research on health issues, providing norms and standards for research and health industry as well as the creation of guidelines available for all countries worldwide. The WHO also provides technical support to countries worldwide and further monitoring of health trends including their assessment. The WHO coordinates the responsibility for all industrial countries to make pharmaceutical products and essential care accessible for all humans worldwide and further to provide a defense against transnational threats like epidemic diseases (WHO, An introduction to the World Health Organization, 2013). Several resources of knowledge can be utilized and accumulated using the structure of the WHO with many participating countries. Single countries or single resources could not provide so much support on the different areas of work represented by the WHO. The vision of the WHO "is that people everywhere have access to the essential medicines and health products they need" and further "that the medicines and health products are safe, effective and of assured quality; and that medicines are prescribed and used rationally…" (WHO, Medicines; About us, 2013).

WHO Guidelines

The WHO issues different guidelines and recommendations on the health sector. The aim of the WHO is to provide guidelines and to strengthen their medicines strategy for worldwide access to medicine. One is the provision of scientific or medicinal support and ensures quality and safety of medicinal products worldwide. Guidelines created by the WHO are approved by the Guidelines Review Committee (GRC). The GRC (including content experts, methodologists, target users, policy makers, with gender and geographical balance) reviews initial proposals for guideline development before creating final versions for publication. Guideline developments are supposed to meet the WHO requirements described in the WHO handbook for guideline development (WHO, Guideline Review Commitee (GRC), 2013). The development of global guidelines, recommendations or certification schemes is relevant for the appropriate use of healthcare with suitable evidence and seen as one important function of the WHO. In general the recommendations given by the WHO with possible impact upon health policies or clinical interventions are considered guidelines for WHO purposes (WHO, World Health Organisation, 2013). Internationally recognized standards are adopted by the WHO and the methods used for guideline development ensure that guidelines are free from bias. Public health need is supposed to be addressed and recommendations are based on a wide-ranging and independent assessment of the available evidence (WHO, WHO Handbook for Guideline Development, 2012).

The WHO has different areas of defined activities. For example, "Medicine access and rational use", "Prequalification of Medicines" or 'Quality and Safety: Medicines' only to mention a few within the part of the WHO strategy on Medicines. Under the topic of 'Regulatory Support' the WHO has two roles. On the one hand they provide support for the development of norms, which are internationally acknowledged, besides standards and guidelines which can be used internationally. On the other hand they provide guidance, technical assistance and training so that countries are supported in the implementation of global guidelines to meet needs and specific regulatory requirements for particular medicinal environments (WHO, World Health Organization - Medicines, 2013).

One of the guidelines created by WHO within this "area of work" is the WHO Certification Scheme on the quality of pharmaceutical products as a "voluntary and non-binding agreement between WHO and their Member States" (Rägo, 2011) in order to provide a "comprehensive system of quality assurance … founded on a reliable system of licensing" (WHO, World Health Organisation - Model certificate of a pharmaceutical product, 2013).

Certificates of the WHO Certification Scheme

Certificates according to the WHO Certification Scheme can be stated as "certificates in conformity" according to the format suggested by the WHO. Overall there are three different documents within the scope of the WHO Certification Scheme using a "standard format" (Rägo, 2011):

1. The statement of licensing status of pharmaceutical product(s),
2. the batch certificate of a pharmaceutical product, and
3. the Certificate of a Pharmaceutical Product (CPP), which is in focus of this master thesis.

The content of certificates according the WHO Certification Scheme can easily be transformed into national templates, as locally preferred by country specific use, in order to provide the information represented by the certification scheme. But the scope of this scheme should not be expanded by supplementing the content of the certificates.

Statement of Licensing Status

The Statement of Licensing Status confirms the information that a license has been issued for a specified finished medicinal product for use in the exporting country. This can be required for participating in tender as a condition of bidding and is meant to be used for this information, only. With respect to the specific use it is possible to include several registration licenses of one Marketing Authorization Holder (MAH) into one Statement of Licensing Status. e. g. in case of an explanation of a name change of a MAH, in order to avoid multiple documents for the same submission.

Batch Certificate

Another certificate within the WHO Certification Scheme is the Batch Certificate of a Pharmaceutical Product providing a reference on a specific batch of a finished medicinal product. Batch Certificates are often requested as a mandatory procurement documents for tender business. This certificate provides information with reference to the quality and expiry date of a specific batch including the specifications of the finished medicinal product at the time of batch release. Usually this certificate is issued by the manufacturer registered for final release of the finished product.

Certificate of a Pharmaceutical Product

The Certificate of a Pharmaceutical Product is a certificate which is presenting several details on a registered finished medicinal product. Annex I lists the content of a CPP according to the recommendation of the WHO Certification Scheme including the explanatory notes as referenced from the WHO-Homepage (WHO, World Health Organisation - Model certificate of a pharmaceutical product, 2013). The intended use of a CPP (which is usually issued by the exporting country or the so-called Country of Origin (CoO*)), in which a Health Authority of an importing country requires a CPP, can usually be separated in different typical sceneries:

1. During the review of a NDA, considering that the product which is to be registered will be imported for sale of the CoO.
2. During supplemental registration submissions, such as renewals or variations to the initial NDA and when a license is reviewed.
3. A third scenario where CPPs are often requested is for the participation and completion of tender-business with governments in countries outside of ICH. This can also be in scope of the WHO Medicines Access to Quality products and prequalification projects. Medicines should also be made available in regions where no registration process is in place, maybe due to political riots and civil wars, or when no social structure for medical care is in place. The WHO has created a list of essential medicines where medicinal products are included to be made available via WHO programs worldwide.

CONCLUSION

Any medicinal agent to be marketed in the United Kingdom has to follow the guidelines and regulations framed by MHRA, a regulatory authority which approves the drug products. The objective of this review article is to highlight information regarding the requirements, the different types of submissions for the registration of a medicinal product in a market in the UK. It also includes all the details about the fee for the application and the time period for the approval of the application after the submission of the application. By knowing the requirements of the MHRA guidelines and regulations, it is easy for a product to get into the UK market. Know the requirements of the importing countryprior to submitting an application while obtaining CoPP.

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