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VITALITY OF COPP IN PHARMACEUTICAL EXPORTS

J. Balasubramanian*, G. A. Nandhini, S.Hariram, N. Radhika

Aeon Formulations Pvt Ltd, Ramapuram, Chennai- 600 089

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For Correspondence:

Dr. J. Balasubramanian

Aeon Formulations Pvt Ltd,

Ramapuram,

Chennai- 600 089

E-mail:

hippocratesbala@gmail.com

ABSTRACT

When registering a pharmaceutical product overseas, the Government body in charge of approving the application will usually require a Certificate of Pharmaceutical Products (COPP) to ensure that the product is being sold as a commercial finished product in the country that is producing it. A certificate issued by the Inspectorate establishing the status of the pharmaceutical, biological, radiopharmaceutical product listed and the Good Manufacturing Practices (GMP) status of the fabricator of the product. This certificate is in the format recommended by the World Health Organisation (WHO). Every country has its own system and requirements in order to register a pharmaceutical product. Although the required documents and procedures vary quite a bit most have many similar requirements for documents in order to ensure that the product being registered meet their standards for efficacy, safety and quality. To ensure quality standards are met, the appropriate regulatory authority in the intended drug market may request documents about the drug in question such as the COPP. The COPP is the legal document that declares a certain manufacturing company is legally allowed to sell their pharmaceutical product in the country they are producing. The COPP is mandatory in many countries that require WHO accreditation for pharmaceutical products being imported. As laid down by the WHO, the GMP certification is also necessary for the same. The WHO has time and again expressed concerns on the implementation of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce.

INTRODUCTION:

Certificate of pharmaceutical product is a scheme developed by the WHO in response to the request of WHO Member States to facilitate international trade in pharmaceutical products between Member States. It was first developed in 1975. Since then it has been revised in 1988, 1992and in 1997.[1]

As the pharmaceutical industries throughout the world are moving ahead towards becoming more and more competitive, these are realizing that the real battle of survival lies in executing the work by understanding the guidelines related to variousactivities carried out to give an assurance that the process is under regulation.[2]Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue guidelines for drug development, licensing, registration, manufacturing, marketing and labelling of pharmaceutical product. The production, import, storage, distribution, sales and supply of drug must be regulated. [3]Therefore, the certificate of pharmaceutical product (abbreviated: COPP or CoPP) is a certificate in the format recommended by the WHO and is issued for export or registration in countries outside the European Community. This certificate describes the characteristics of the medicinal product approved in the exporting country, includes information about the applicant of the certificate and is according with the model recommended by the World Health Organization.[4] This certificate is intended to define the status of the pharmaceutical product and its manufacturer in the exporting country. It is issued by the competent authority in the exporting country in accordance with the requirements of the competent authority of the importing country. It may be required by the importing country at the time of the first importation and subsequently if confirmation or updating is required.[5]This is a certificate issued by the Inspectorate establishing the status of the pharmaceutical, biological, radiopharmaceutical or veterinary product listed and the GMP status of the fabricator of the product.[6]

SCOPE OF COPP:

The COPP is the legal document that declares a certain manufacturing company is legally allowed to sell their pharmaceutical product in the country they are producing. When registering a pharmaceutical product overseas, the Government body in charge of approving the application will usually require a COPP to ensure that the product is being sold as a commercial finished product in the country that is producing it.[7]

The Certificate of a Pharmaceutical Product is needed by the importing country when the product in question is intended for registration (licencing, 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 COPP, 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 labeling requirements, and to assess bioequivalence and stability data if necessary. However, regulatory practices often vary in importing countries. Thus, in addition to COPP, 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.[8]

NEED & IMPORTANCE OF COPP:

To obtain global marketing approval for any pharmaceutical product (whether intended for animal/human use) one of the key documents required is a COPP, which has been recommended by the WHO.[9]

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

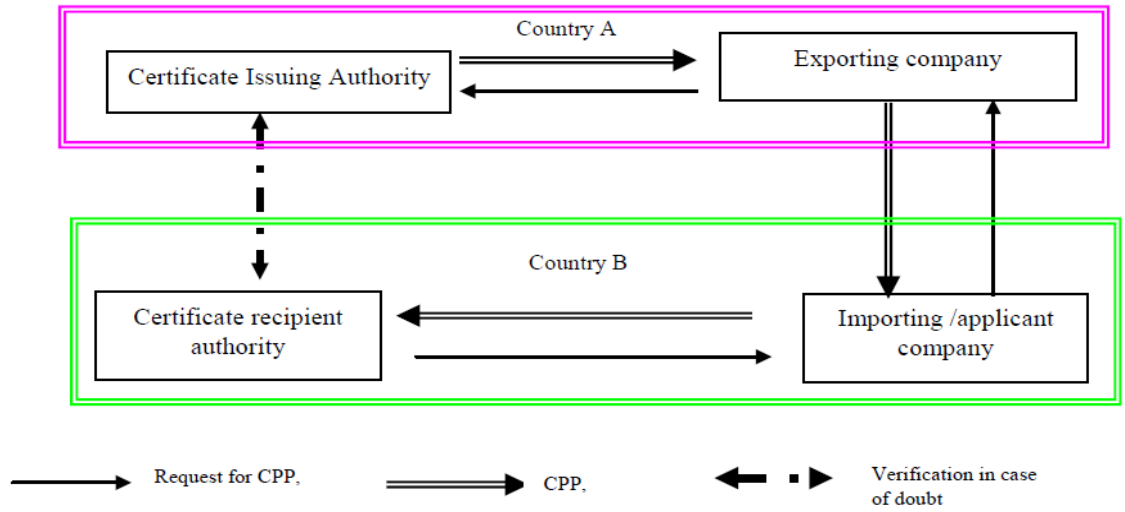
- when a pharmaceutical product is under consideration for a product license/marketing authorization that will authorize its importation and sale in the importing country;
- when administrative action is required to renew, extend vary or review such license.[1]

A COPP is issued for human drugs (pharmaceutical, biological and radiopharmaceutical) as well as for veterinary drugs (food producing animals and non food producing animals).[10]For each medicinal product (Trade Name / Pharmaceutical Form / Strength) is issued a certificate stating the country to export. These Certificates are issued to the marketing authorizations holders (MAH) for medicinal products (with valid Marketing Authorization) or their representatives, manufacturers (without Marketing Authorization and with manufacturing authorization valid) or wholesale distributor authorized by the MAH to consult the information for the medicinal product(s).[4]

REQUESTING A CERTIFICATE:

As the COPP is classified as a confidential document, it can only be issued by the Competent Authority (CA) if the applicant (and MAH, if different to the applicant)apply for the certificate and give their permission to provide a COPP for a specific finished medicinal product to the requesting Health Authority (HA). Usually the applicant will forward the COPP, issued by the CA, to the local affiliate in the requesting country in order to send the COPP. Applications are usually made by pharmaceutical companies with commercial interests. The CA of the Country of Origin (CoO) or any other country, eligible to issue a COPP according to the WHO Certification Scheme for a locally registered finished medicinal product, will issue the COPP on application of the MAH in the issuing country. The MAH or applicant will afterwards send the COPP to the requesting HA in the importing and requesting country. This is usually done via the local MAH of the importing/recipient country. This process is also depicted below.[11]

Figure-1.0: Process of COPP Application (World Health Organization, 2010)[11]



PHARMACEUTICAL PRODUCTS COVERED UNDER THE WHO CERTIFICATION SCHEME:

a) Finished Pharmaceutical Products (FPP)s intended for administration to human beings;
b) pharmaceutical products intended for administration to food-producing animals;
c) active pharmaceutical ingredients (APIs).

There is now a separate scheme called the WHO pharmaceutical starting materials certification scheme (SMACS) which has guidelines on importation of APIs.[1]

STANDARD FORMAT FOR COPPs:

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

- The standard WHO format for COPPs facilitates understanding and review by the recipient authority. It obliges certifying authorities to disclose important information to the importing country.
- Recipient authorities should refrain from obtaining data other than in the WHO standard format or in addition to the standard COPP format.
- Certifying authorities should not issue the outdated "free sales certificates". These have been replaced by the WHO format COPP.[1]

INFORMATION CONTAINED WITHIN THE COPP:

- Details of the market (importing country) and the national authority of the exporting country
- Pharmaceutical information about the product, including; dosage, form and composition (including all ingredients making up the drug)
- Marketing Authorisation Holder information and date of issue of the product licence in the export market
- GMP inspection and approval, including manufacturing licence number and term of manufacturing licence. To obtain a COPP, a request is made by the MAH to the exporting country's health authority. An authorised person issues the COPP and returns it to the MAH. Other documents required to obtain a CPP include; an Application for Export Certificate form, evidence of a GMP certificate (if applicable), Manufacturing Licence and the last approved SPC (Summary of Product Characteristics).[9]

COST OF COPP:

There is a cost of issuing a COPP for a product, for example in Ireland a standard request is 147 Euro and a fast track request 277 Euro. Once a COPP is issued by a national agency, there may be special requirements from the importing market which can include embassy legalisation or apostillation (acceptance of international notarised documents) and consularisation.[9]

A THROW ON QUALITY,SAFETY& EFFICACY OF THE PRODUCT AND GMP DECLARATION IN COPP:

The COPP is based on the assumption that the authorities issuing a COPP have the capacity to assess the quality, safety, and efficacy (QSE) of the product they approve for marketing.[1] As a part of economical growth, there may be shortcomings and at times conflicting interests within the pharmaceutical industry when dealing with public health concerns arising from drug safety issues.[12] Adverse drug reactions are problematic in that they cause significant morbidity & mortality. Knowledge of causative factors and an increase in patient education may help prevent adverse drug reactions. [13] The industry needs to overcome weaknesses in

safety monitoring during clinical trials and post-marketing surveillance. Manufacturers should take a more proactive approach to drug safety rather than maintaining defensive tactics.[12]Based on the intention of the Scheme, a recipient authority could require a COPP when it does not undertake a full review of QSE data submitted for registration, and evidence of approval in another country isrequired.[1]A COPP demonstrates to Regulatory Authorities in the exporting country in question that the imported medicine is of the appropriate standard of quality, safety and efficacy to allow marketing in their market, having undergone rigorous testing and examination. The certificate also demonstrates that the product follows the correct guidelines and procedures of GMP, increasing the level of safety and indeed quality of the product. [9]

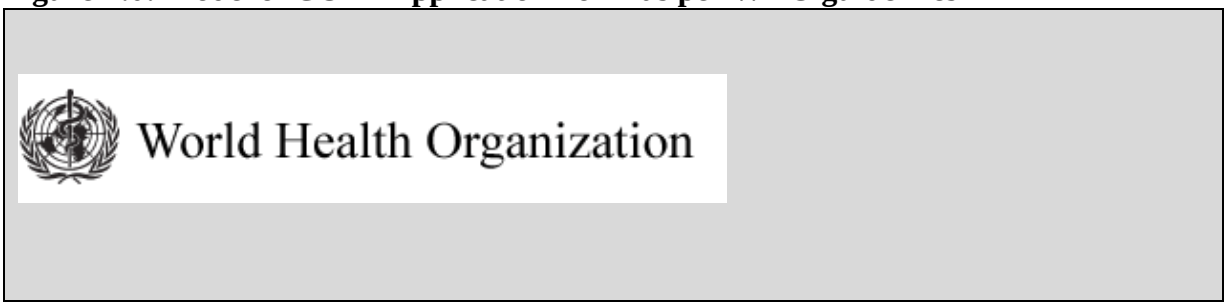
The GMP declaration in the COPP refers to assurance of GMP for the product approved in the certifying country at the stated manufacturing site. In addition, certificates from national medicine regulatory authorities(NMRAs) party to the Pharmaceutical Inspection Co-operation Scheme(PIC/S) and International Conference on Harmonisation (ICH) regions (USA, Japan, and EU) provide evidence of GMP status.[1]While the COPP can provide information on the GMP status, some HAs accept the COPP as alternative to additionally providing a GMP certificate of the relevant manufacturing site, for example CFDA in China and HA in Russia, but they ask for the inspection date to be included to the COPP. Other HAs in countries like Argentina, Brazil, Uruguay and Malaysia will not accept the COPP as compensatory to the GMP certificate. The GMP certificate will be requested as another mandatory document for NDA.[11]

Table No.1: CERTIFICATES REQUISITION FOR REGISTRATION

Country	**Registration unit**	**Certificates requested**
China	CFDA	COPP*
Russia	HA	COPP*
Argentina	HA	GMP certificate
Brazil	HA	GMP certificate
Uruguay	HA	GMP certificate
Malaysia	HA	GMP certificate

*The COPP acts as alternative to additionally providing a GMP certificate, but they ask for the inspection date to be included to the COPP.

Figure-2.0: Model of COPP Application Form as per WHO guidelines [14]



Certificate of a Pharmaceutical Product[1]

No. of Certificate.....
Exporting (certifying) country:
Importing (requesting) country:

Proprietary name (if applicable) and dosage form:

Active ingredient(s)[2] and amount(s) per unit dose:[3]

1. Is this product licensed to be placed on the market for use in the exporting country?[4] If yes, complete box A. If no, complete box B.

A
Product-licence holder:
Status of licence holder:[5]
a ☐ b ☐ c ☐ d ☐
Number of product licence[6] and date of issue:
Is an approved technical summary appended?[7]
yes ☐ no ☐
Is the attached product information complete and consonant with the licence?
Yes ☐ no ☐ not provided ☐
Applicant for certificate if different from the licence holder:[8]

B
Applicant for certificate:
Status of applicant:[5]
a ☐ b ☐ c ☐ d ☐
Why is authorization lacking?
not required ☐ requested under consideration refused ☐ ☐
Remarks:[9]

2. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced?	yes ☐	If no, proceed to question 3
	no ☐	
Periodicity of routine inspections (years):		
Has the manufacture of this type of dosage form been inspected?	yes ☐	no ☐
Do the facilities and operations conform to GMP as recommended by the World Health Organization?[10]	yes ☐	no ☐

3. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party?"

yes ☐ no ☐ If no, explain:

Address of certifying authority:	Name of authorized person:
	Signature:

Telephone/fax numbers:	Stamp and date:

This certificate conforms to the format recommended by the World Health Organization *(General instructions and explanatory notes overleaf)*

General instructions

Please refer to the guidelines for further information on how to complete this form and on the implementation of the Scheme.

Forms should be completed using a typewriter to ensure legibility.

A cross should be placed in boxes as appropriate to indicate which options apply.

Additional sheets should be appended, as necessary, to accommodate remarks and explanations.

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 Nonproprietary Names (INNs) or national nonproprietary names.

[3] A qualitative listing of other ingredients contained in the dosage form should be appended.

[4] When applicable, append details of any restriction applied to the sale, distribution, or administration of the product that is entered on the product licence.

[5] Specify whether the person responsible for placing the product on the market:

(a) manufactures the active ingredients and the finished dosage form;

(b) manufactures the finished dosage form;

(c) packages and/or labels a finished dosage form manufactured by an independent company; or

(d) is involved in none of the above.

[6] Indicate, when applicable, if the licence is provisional, pending technical review.

[7] This refers to the document, prepared by certain national regulatory authorities, that summarizes the technical basis on which the product has been licensed.

[8] In this circumstance, permission for issuance of the certificate is required from the product-licence holder.

[9] Please indicate the reason 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.

[10] The requirements for good practices in the manufacture and quality control of drugs referred to in the certificate are those adopted by the Twenty-eighth World Health Assembly in its resolution WHA28.65 (see WHO Official Records, No. 226, 1975, Annex 12, Part 1). Proposals for the amendment of these requirements are included in the Thirty-second Report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (WHO Technical Report Series, No. 822, 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).

[11] This section is to be completed when the product-licence holder or applicant conforms to status (c) or (d) as described in note 5 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 to indicate the extent and nature of any controls exercised over each of these parties.

CERTIFICATE OF A PHARMACEUTICAL PRODUCT:

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.

The COPP provides the information of the following:

1. **Certificate number of COPP:**

The certificate number of COPP should be enclosed in the specified format recommended by WHO.

2. **Name of exporting country i.e. (certifying country):**

The name of the country (certified country) to which the product is being exported must be mentioned in the certificate.

3. **Name of importing country i.e. (requesting country):**

The name of the countries (requesting countries) from which the product is being imported from certified country must be mentioned in the certificate.

4. **Name and dosage form of the product:**

Table No.2: ESSENTIALS OF PRODUCT

Active ingredient	➢ International Non-proprietary Names (INNs) or national non-proprietary names.
Amount per unit dose	➢ The formula (complete composition) of the dosage form should be given on the certificate or be appended.
Complete composition including excipients	➢ Details of quantitative composition are preferred but their provision is subject to the agreement of the product-license holder.
Is this product licensed to be placed on the market for use in the exporting country?(yes/no)	➢ When applicable, append details of any restriction applied to the sale, distribution or administration of the product that is specified in the product license.

5. Status of the product actually on the market in the exporting country:

If the product is actually marketed in the exporting country, the COPP should be provided with the following details:

➢ Number of product license and date of issue:

Indicate, when applicable, if the license is provisional, or the product has not yet been approved.

➢ Product license holder (name and address):

➢ Status of product license holder:

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.

➢ For categories b and c the name and address of the manufacturer producing the dosage form is

This information can only be provided with the consent of the product-license 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 license. If the production site is changed, the license has to be updated or it is no longer valid.

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

This refers to the document, prepared by some national regulatory authorities, that summarizes the technical basis on which the product has been licensed.

➢ Is the attached, officially approved product information complete and consonent with the license?(yes/no/not provided)

This refers to product information approved by the competent national regulatory authority, such as Summary Product Characteristics (SPC).

➢ Applicant for certificate, if different from license holder (name and address)

In this circumstance, permission for issuing the certificate is required from the product-license holder. This permission has to be provided to the authority by the applicant.

If the product is actually marketed in the exporting country, the COPP should be provided with the following details:

- Applicant for certificate (name and address):
- Status of applicant:

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.

A. For categories (b) and (c) the name and address of the manufacturer producing the dosage form is:

This information can only be provided with the consent of the product-license 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 license. If the production site is changed, the license has to be updated or it is no longer valid.

B. Why is marketing authorization lacking?

Mention the status of marketing authorization by specifying the following catergories:
(not required/not requested/under consideration/refused)

C. Remarks

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 origin;
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.

6. Periodic inspection of the manufacturing plant by the certifying authority:

If the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced, the following details were to be included in the COPP.

- Periodicity of routine inspections (years):
- Has the manufacture of this type of dosage form been inspected? (yes/no)
- Do the facilities and operations conform to GMP as recommended by the World Health Organization?(yes/no/not applicable)

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).

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.

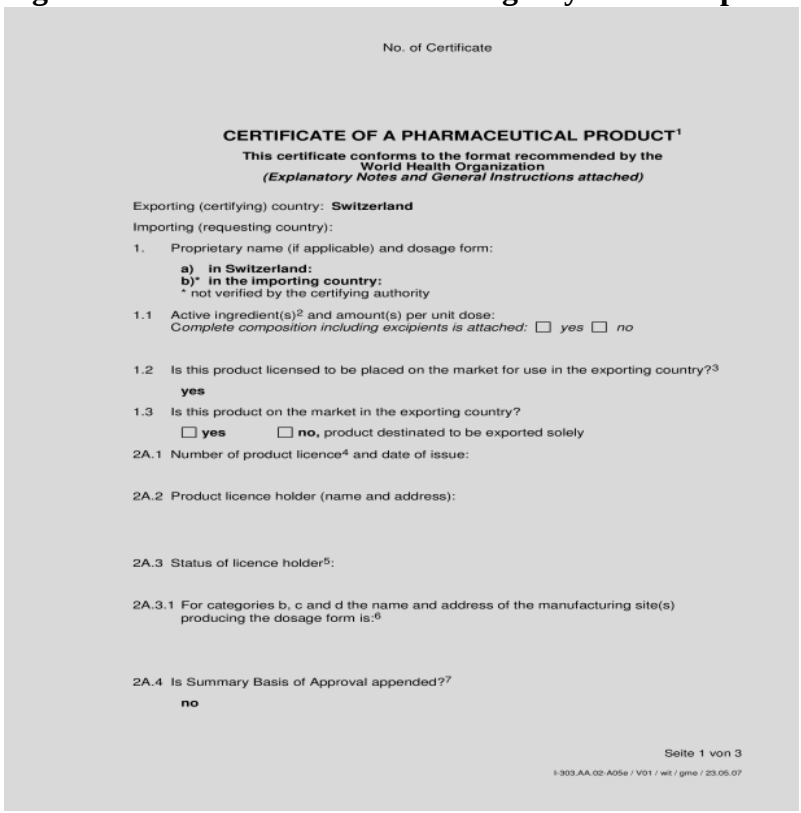
7. **The information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party:**
   This section is to be completed when the product-license holder or applicant conforms to status (b) or (c) as described in note above. It 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.
8. **Other details of Manufacturing premises:**
   The following details which is to be enclosed in the COPP are,
   - Address of certifying authority
   - Telephone
   - Fax
   - Name of authorized person
   - Signature
   - Stamp and date

General instructions:

- Please refer to the guidelines for further information on how to complete this form and on the implementation of the Scheme.
- Forms should be completed using a typewriter to ensure legibility.
- A cross should be placed in boxes as appropriate to indicate which options apply.
- Additional sheets should be appended, as necessary, to accommodate remarks and explanations.[5]

MODEL FORMAT OF COPP:

Figure-3.0: Model COPP of Swiss Agency for Therapeutic Products(Switzerland)[15]



No. of Certificate

CERTIFICATE OF A PHARMACEUTICAL PRODUCT[1]

This certificate conforms to the format recommended by the World Health Organization
(Explanatory Notes and General Instructions attached)

Exporting (certifying) country: **Switzerland**

Importing (requesting country):

1. Proprietary name (if applicable) and dosage form:

a) in Switzerland:
b)* in the importing country:
* not verified by the certifying authority

1.1 Active ingredient(s)[2] and amount(s) per unit dose:
Complete composition including excipients is attached: ☐ *yes* ☐ *no*

1.2 Is this product licensed to be placed on the market for use in the exporting country?[3]

yes

1.3 Is this product on the market in the exporting country?

☐ **yes** ☐ **no,** product destinated to be exported solely

2A.1 Number of product licence[4] and date of issue:

2A.2 Product licence holder (name and address):

2A.3 Status of licence holder[5]:

2A.3.1 For categories b, c and d the name and address of the manufacturing site(s) producing the dosage form is:[6]

2A.4 Is Summary Basis of Approval appended?[7]

no

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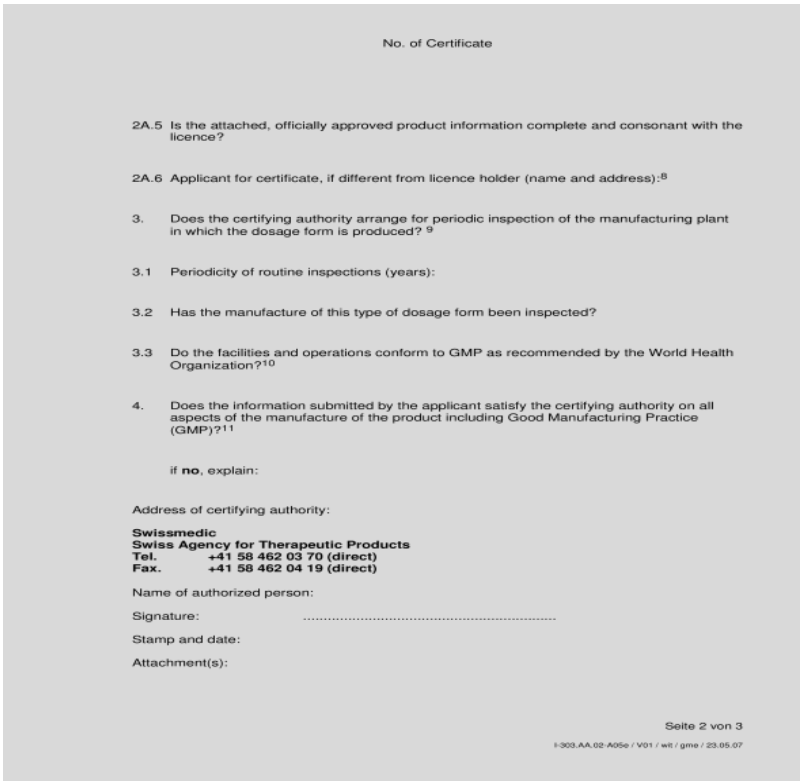
Figure-3.1:



No. of Certificate

2A.5 Is the attached, officially approved product information complete and consonant with the licence?

2A.6 Applicant for certificate, if different from licence holder (name and address):[8]

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? [9]

3.1 Periodicity of routine inspections (years):

3.2 Has the manufacture of this type of dosage form been inspected?

3.3 Do the facilities and operations conform to GMP as recommended by the World Health Organization?[10]

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product including Good Manufacturing Practice (GMP)?[11]

if **no**, explain:

Address of certifying authority:

Swissmedic
Swiss Agency for Therapeutic Products
Tel. +41 58 462 03 70 (direct)
Fax. +41 58 462 04 19 (direct)

Name of authorized person:

Signature: .....

Stamp and date:

Attachment(s):

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Figure-3.2:

No. of Certificate

General Instructions

Please refer to the guidelines for full instructions on how to complete this form and information on the implementation of the scheme.

The forms are suitable for generation by computer. They should always be submitted in type face.

Additional sheets should be appended, as necessary, to accommodate remarks and explanations.

Explanatory Notes (Type A)

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 nonproprietary names (INNs) or national nonproprietary names.

3 When applicable, append details of any restriction applied to the sale, distribution or administration of the product that is entered into the product licence.

4 Indicate, when applicable, if the licence is provisional, or the product has not yet been approved.

5 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;
(c) is involved in none of the above; or
(d) manufactures the dosage form and further manufacturing sites for the dosage form may be involved

6 This information can only be provided with the consent of the product licence holder or, in the case of nonregistered products, the applicant. Non-completion of this section (2A.3.1) 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.

7 This refers to the document, prepared by some national regulatory authorities, that summarizes the basis on which the product has been licensed.

8 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.

9 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.

10 The requirements for good practices in the manufacture and quality control of drugs referred to in the certifcate are those in the report of the Thirty-second Expert Committee on Specifications for Pharmaceutical Preparations, WHO Technical Report Series No. 823, 1992. Recommendations specifically applicable to biological products have been formulated by the WHO Expert Committee on Biological Standardization and are published in the WHO Technical Report Series.

11 This section is to be completed when the product licence holder or applicant conforms to status (b), (c) or (d) as described in note 5 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.

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Figure-4.0:[Model COPP of Food and Drugs Administration (United States)](#)[16,17,18]

United States Food and Drug Administration

Center for Drug Evaluation and Research (CDER)
10903 New Hampshire Avenue, Silver Spring, MD 20993, USA
Email: CDERExportCertificateProgram@fda.hhs.gov Telephone: (301) 796-4950

Certificate of a Pharmaceutical Product- Unapproved

Certificate Issue Date: XXXXXXX
Certificate No: XXXXXXXXXX

Certificate Expiration Date: XXXXX
Exporting Country: United States of America
Importing Country: XXXXX

1. International or National Nonproprietary Name (if applicable) and dosage form:
1.1 Active Ingredient(s) and amount(s) per unit dose (complete quantitative composition is preferred): Trade name (generic name) dosage and potency: See Attachments
1.2 Is this product licensed to be placed on the market for use in the exporting country? NO - See Block A
1.3 Is this product actually on the market in the exporting country? No

A	B
2A.1 Number of product-license and date of issue:	2B.1 Applicant for certificate (name and address): XXXXXXXXXXX
2A.2 Product-license holder:	2B.2 Status of Applicant: XXXXXXXXXX
2A.3 Status of product-license holder:	2B.3 Why is authorization lacking? not required / not applicable / under consideration / refused
2A.4 Is an approved summary basis appended? No	2A.3.1 or 2B.2.1 Manufacturer name and address: XXXXXXXXXXXXXXXXXXXXXXXXXX
2A.5 Is the attached product information complete and consonant with the license? Yes	2B.4 Remarks: [redacted]
2A.6 Applicant for certificate if different from the license holder (name and address):	

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? Yes
3.1 Periodicity of routine inspection (years): Pursuant to Section 510(h)(3) of the Federal Food, Drug, & Cosmetic Act, inspections will occur in accordance with a risk-based schedule.
3.2 Has the manufacture of this type of dosage form been inspected: Yes
3.3 Do the facilities and operations conform to GMP as recommended by the WHO* (GMP including 21 CFR Parts 210, 211 or ICH Q7A) Yes, at time of inspection, site complies with U.S. CGMP
4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party? Yes

This certificate conforms to the format recommended by the World Health Org[redacted]997. Website: www.who.int

[redacted]
Huascar Batista, Chief
Drug Imports and Exports Compliance Branch
Office of Drug Security, Integrity & Recalls

Figure-4.1:

United States Food and Drug Administration

Center for Drug Evaluation and Research (CDER)
10903 New Hampshire Avenue, Silver Spring, MD 20993, USA
Email: CDERExportCertificateProgram@fda.hhs.gov Telephone: (301) 796-4950

Certificate of a Pharmaceutical Product

Certificate Issue Date: XXXXXXX
Certificate No: XXXXXXXXXX

Certificate Expiration Date: XXXXX
Exporting Country: United States of America
Importing Country: XXXXX

1. International or National Nonproprietary Name (if applicable) and dosage form:
1.1 Active Ingredient(s) and amount(s) per unit dose (complete quantitative composition is preferred): Trade name (generic name) dosage and potency: See Attachments
1.2 Is this product licensed to be placed on the market for use in the exporting country? YES - See Block A
1.3 Is this product actually on the market in the exporting country? Yes

A	B
2A.1 Number of product-license and date of issue: XXXXXXXXXXXX	2B.1 Applicant for certificate (name and address):
2A.2 Product-license holder: XXXXXXXXXXXXXX	2B.2 Status of Applicant:
2A.3 Status of product-license holder: XXXXXXX	2B.3 Why is authorization lacking? not required / not applicable / under consideration / refused
2A.4 Is an approved summary basis appended? No	2B.3.1 or 2B.2.1 Manufacturer name and address: XXXXXXXXXXXXXXXXXXXXXXXXX
2A.5 Is the attached product information complete and consonant with the license? Yes	2B.4 Remarks:
2A.6 Applicant for certificate if different from the license holder (name and address):	

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? Yes
3.1 Periodicity of routine inspection (years): Pursuant to Section 510(h)(3) of the Federal Food, Drug, & Cosmetic Act, inspections will occur in accordance with a risk-based schedule.
3.2 Has the manufacture of this type of dosage form been inspected: Yes
3.3 Do the facilities and operations conform to GMP as recommended by the WHO* (GMP including 21 CFR Parts 210, 211 or ICH Q7A): Yes, at time of inspection, site complies with U.S. CGMP
4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party? Yes

This certificate conforms to the format recommended by the World Health Organization for [illegible] 1997. Website: www.who.int

[redacted]
Huascar Batista, Chief
Drug Imports and Exports Compliance Branch
Office of Drug Security, Integrity & Recalls

Figure-4.2:

United States Food and Drug Administration

Center for Drug Evaluation and Research (CDER)
10903 New Hampshire Avenue, Silver Spring, MD 20993, USA
Email: CDERExportCertificateProgram@fda.hhs.gov Telephone: (301) 796-4950

Certificate of a Pharmaceutical Product- Foreign Manufacture

Certificate Issue Date: XXXXXXX
Certificate No: XXXXXXXXXX

Certificate Expiration Date: XXXXX
Exporting Country: United States of America
Importing Country: XXXXX

1. International or National Nonproprietary Name (if applicable) and dosage form:
1.1 Active Ingredient(s) and amount(s) per unit dose (complete quantitative composition is preferred): Trade name (generic name) dosage and potency: See Attachments
1.2 Is this product licensed to be placed on the market for use in the exporting country? Yes - See Block A
1.3 Is this product actually on the market in the exporting country? Yes

A	B
2A.1 Number of product-license and date of issue: XXXXXXXXXX	2B.1 Applicant for certificate (name and address):
2A.2 Product-license holder: XXXXXXXXX	2B.2 Status of Applicant:
2A.3 Status of product-license holder: XXXXXXXXXXXXX	2B.3 Why is authorization lacking? not required / not applicable / under consideration / refused
2A.4 Is an approved summary basis appended? No	2B.3.1 or 2B.2.1 Manufacturer name and address: XXXXXXXXXXXXXXXXXXXXXXXXX
2A.5 Is the attached product information complete and consonant with the license? Yes	2B.4 Remarks: [redacted]
2A.6 Applicant for certificate if different from the license holder (name and address):	

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? Yes
3.1 Periodicity of routine inspection (years): Pursuant to Section 510(h)(3) of the Federal Food, Drug, & Cosmetic Act, inspections will occur in accordance with a risk-based schedule.
3.2 Has the manufacture of this type of dosage form been inspected: Yes
3.3 Do the facilities and operations conform to GMP as recommended by the WHO* (GMP including 21 CFR Parts 210, 211 or ICH Q7A): Yes, at time of inspection, site complies with U.S. CGMP
4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party? Yes

This certificate conforms to the format recommended by the World Health Organization for [illegible] 1997. Website: www.who.int

[redacted]
Huascar Batista, Chief
Drug Imports and Exports Compliance Branch
Office of Drug Security, Integrity & Recalls

Figure-5.0:Model COPP of Federal Public Service (FPS) Health, Food Chain Safety and Environment (Belgium)[19]

FEDERAL AGENCY FOR MEDICINES AND HEALTH PRODUCTS

CERTIFICATE OF A PHARMACEUTICAL PRODUCT[1]

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

(General Instructions and explanatory notes attached)

N° of Certificate:

Exporting (certifying) country: BELGIUM

Importing (requesting) country:

1. Name and dosage form of the product:

1.1 Active ingredient(s)[2] and amount(s) per unit dose[3]:
Complete composition including excipients: see below[4] or see attached[4]

1.2 Is this product declared to be placed on the market for use in the exporting country[5]? Yes/no

1.3 Is this product actually on the market in the exporting country? Yes/no

2A.1 Number of product declaration[7] and date of issue:

2A.2 Product-declaration holder:

2A.3 Status of product declaration holder[8]: a/b/c

2A.3.1 For the categories b and c name and address of the manufacturer producing the dosage form[9]:

2A.4 Is summary basis of approval appended?[10]yes/no

2A.5 Is the attached, officially approved product information complete and consonant with the declaration?[11]yes/no/not provided

2A.6 Applicant for certificate[12]: see 2A2

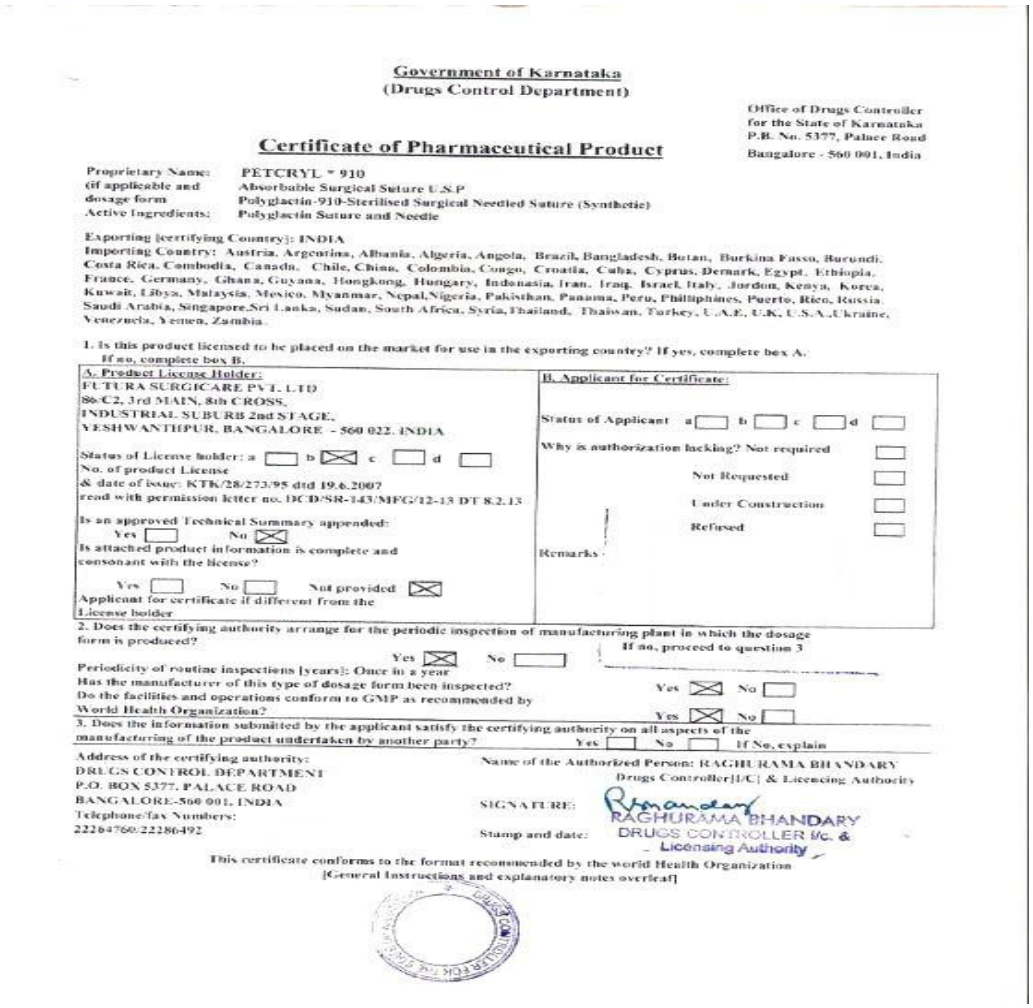
2B. Not applicable [6]

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced?[14] yes/no/not applicable

3.1	Periodicity of routine inspections: 2 years/not applicable
3.2	Has the manufacture of this type of dosage form been inspected? Yes/no/not applicable
3.3	Do the facilities and operations conform to GMP as recommended by the World Health Organization?[15] Yes/no/not applicable
4.	Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product?[16] yes

Address of certifying authority:	FEDERAL AGENCY FOR MEDICINES AND HEALTH PRODUCTS, EUROSTATION II, Victor Hortap 40, 1060 BRUSSELS (BELGIUM)	
Telephone n°: +32 2 524.82.97 / +32 2 524.82.98 / +32 2 524.80.61		Fax n°: +32 2 524.83.01
Date:		Name of authorized person: Xavier De Cuyper Chief Executive Officer
Stamp:		

Figure-6.0:Model COPP of Central Drugs Standard Control Organisation (India)[20]



Government of Karnataka
(Drugs Control Department)

Office of Drugs Controller
for the State of Karnataka
P.B. No. 5377, Palace Road
Bangalore - 560 001, India

Certificate of Pharmaceutical Product

Proprietary Name: PETCRYL ® 910
(if applicable and dosage form: Absorbable Surgical Suture U.S.P
Active Ingredients: Polyglactin-910-Sterilised Surgical Needled Suture (Synthetic)
Polyglactin Suture and Needle

Exporting [certifying Country]: INDIA
Importing Country: Austria, Argentina, Albania, Algeria, Angola, Brazil, Bangladesh, Butan, Burkina Fasso, Burundi, Costa Rica, Cambodia, Canada, Chile, China, Colombia, Congo, Croatia, Cuba, Cyprus, Demark, Egypt, Ethiopia, France, Germany, Ghana, Guyana, Hongkong, Hungary, Indonasia, Iran, Iraq, Israel, Italy, Jordon, Kenya, Korea, Kuwait, Libya, Malaysia, Mexico, Myanmar, Nepal, Nigeria, Pakisthan, Panama, Peru, Philliphines, Puerto, Rico, Russia, Saudi Arabia, Singapore, Sri Lanka, Sudan, South Africa, Syria, Thailand, Thaiwan, Turkey, U.A.E, U.K, U.S.A, Ukraine, Venezuela, Yemen, Zambia.

1. Is this product licensed to be placed on the market for use in the exporting country? If yes, complete box A. If no, complete box B.

A. Product License Holder:
FUTURA SURGICARE PVT. LTD
86/C2, 3rd MAIN, 8th CROSS,
INDUSTRIAL SUBURB 2nd STAGE,
YESHWANTHPUR, BANGALORE - 560 022. INDIA

Status of License holder: a ☐ b ☒ c ☐ d ☐
No. of product License
& date of issue: KTK/28/273/95 dtd 19.6.2007
read with permission letter no. DCD/SR-143/MFG/12-13 DT 8.2.13

Is an approved Technical Summary appended:
Yes ☐ No ☒
Is attached product information is complete and consonant with the license?
Yes ☐ No ☐ Not provided ☒
Applicant for certificate if different from the License holder

B. Applicant for Certificate:
Status of Applicant a ☐ b ☐ c ☐ d ☐
Why is authorization lacking? Not required ☐
Not Requested ☐
Under Construction ☐
Refused ☐
Remarks:

2. Does the certifying authority arrange for the periodic inspection of manufacturing plant in which the dosage form is produced? Yes ☒ No ☐ If no, proceed to question 3
Periodicity of routine inspections [years]: Once in a year
Has the manufacturer of this type of dosage form been inspected? Yes ☒ No ☐
Do the facilities and operations conform to GMP as recommended by World Health Organization? Yes ☒ No ☐
3. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacturing of the product undertaken by another party? Yes ☐ No ☐ If No, explain

Address of the certifying authority:
DRUGS CONTROL DEPARTMENT
P.O. BOX 5377, PALACE ROAD
BANGALORE-560 001, INDIA
Telephone/fax Numbers:
22264760/22286492

Name of the Authorized Person: RAGHURAMA BHANDARY
Drugs Controller[I/C] & Licencing Authority
SIGNATURE:
Stamp and date:
RAGHURAMA BHANDARY
DRUGS CONTROLLER I/c. &
Licensing Authority

This certificate conforms to the format recommended by the world Health Organization
[General Instructions and explanatory notes overleaf]

CONCLUSIONS

The review of this paper revealed that the COPP is a mandatory document needed for filing and approval of New Drug Approval (NDA)s and different kinds of supplemental registrations during Life Cycle Management (LCM) of imported finished medicinal product registrations. But the requirement of presenting a COPP often creates a delay on the availability of these products in countries outside of ICH, although the WHO Certification Scheme was meant to accelerate the access to innovative new drug developments worldwide. Therapeutic feasibilities are not available as fast as it might be possible when considering the WHO recommendations more strictly. Countries outside of ICH could gain more advantage out of the WHO recommendations or regulations in order to save resources for other aspects in their authorities. But there is also room for the WHO recommendations to be adapted to the rapidly changing environment of Regulatory Affairs, which should be processed in collaboration with the WHO, Health Authorities and Stakeholders involved in this business. Current developments seem to worsen than to getting better. While having a closer look at the sizes of HAs compared to their average review time needed to grant approvals on registrations the conclusion can be drawn that even a full review by smaller HAs in countries like Uruguay do not need more time or even less time than HAs with more resources due to size and head count working on NDAs(e.g. in Brazil Korea or China). The potential of the WHO Certification Scheme to improve the efficiency of drug evaluation is not fully exploited by HAs in countries outside the ICH.

REFERENCES

1. Available from URL:http://www.who.int/medicines/areas/quality_safety/regulation /qas_2011.pdf.
2. Rajendra Kumar Songara, Pratibhachauhan, Snehlata and Renukalyanwat, Need for the Introduction of Regulatory Affairs, Quality Assurance & Pharmacy Practice in the Pharmacy Curriculum, IJPRD, 2011; Vol 3(3):16, 122 - 135.
3. S.D.Mankar, V.D. Gholap, T.P. Zende, R.S.Dighe, Drug regulatory agencies in India, USA, Europe and Japan-A Review, International Journal of Institutional Pharmacy and Life Sciences,2014; 4(2): 288-297.
4. Available from URL: http://www.infarmed.pt/portal/page/portal/INFARMED/MONITORIZACAO_DO_MERCADO/CERTIFICADOS_MEDICAMENTOS/SIOMS%20-%20User%20Manual%20(EN).pdf
5. Available from URL: http://apps.who.int/medicinedocs/en/d/Jwhozip43e/16.html
6. Available from URL: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/compli-conform/licences/directives/gui-0024-eng.pdf
7. http://www.mercatorpharma.com/index.php/registration/documentation
8. Available from URL: http://en.wikipedia.org/wiki/Certificate_of_pharmaceutical_product.
9. Available from URL: http://www.pharmalinkconsulting.com/blog/blog/certificates-of-pharmaceutical-product-cpps/
10. Available from URL: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/licences/directives/gui-0024_doc-eng.php.
11. Available from URL: http://dgra.de/media/pdf/studium/masterthesis/master_sahl_a.pdf
12. AmitBihan, RishikantPandey, AshishSrivastava, Jitender Joshi, Dr.RajulRastogi and Dr. Hans J. Gamperl,Challenges in Drug Safety: A Review, IJPRD, 2014; Vol 6(07): 006 - 012.
13. PriyaChandel, MeenakshiDhadwal, Saurabh Mittal, Adverse Drug Reactions: A Review, International Journal of Institutional Pharmacy and Life Sciences, 2014;4(2): 95-103.
14. Available from URL: http://apps.who.int/medicinedocs/en/d/Jwhozip43e/18.html.
15. Available from URL: https://www.google.co.in/url?sa=t&rct=j&q=&esrc=s&source=web&cd=5&cad=rja&uact=8&ved=0CDUQFjAE&url=https%3A%2F%2Fwww.swissmedic.ch%2Fbewilligungen%2F00155%2F00242%2F00243%2F00245%2F00246%2F00247%2F01908%2Findex.html%3Flang%3Den%26download%3DNHzLpZeg7t%2Clnp6I0NTU042l2Z6ln1ad1IZn4Z2qZpnO2Yuq2Z6gpJCDdH5%2Cgmym162epYbg2c_JjKbNoKSn6A--

&ei=PJyvVIPBF4TluQTJnIBo&usg=AFQjCNHLM5j-n2BFSr3ogCdt0u0nAZzVhw&bvm=bv.83339334,d.c2E.
16. Available from URL: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ImportsandExportsCompliance/UCM348905.pdf
17. Available from URL: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ImportsandExportsCompliance/UCM348906.pdf
18. Available from URL: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ImportsandExportsCompliance/UCM348907.pdf
19. Available from URL: http://www.fagg-afmps.be/fr/binaries/CPP%20ENGLISH%20D%20WITH%20LOGO_tcm291-27733.doc.
20. Available from URL: http://www.dolphinsutures.com/sites/default/files/copp.jpg.