GUIDELINES FOR PROCESSING OF APPLICATION FOR CERTIFICATION UNDER WHO–GMP SCHEME FOR PHARMACEUTICAL PRODUCTS

Introduction:

The first World Health Organization (WHO) draft text on Good Manufacturing practices (GMP) was prepared at the request of Twentieth World Health Assembly in 1967 by a Group of Consultants. The text was discussed by the WHO Expert Committee on specification for Pharmaceutical Preparations in 1968.

When the World Health Assembly recommended the first version of the WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce in 1969, it accepted at the same time, the GMP text as an integral part of the Scheme. The revised versions of both the certification scheme and GMP text was adopted in 1975.

Since then the certification scheme has been extended to include certification of:

- Veterinary products administered to food producing animals.
- Starting materials for use in dosage form.
- Information on safety and efficacy.

The Director General of WHO invited the member States to participate in the Scheme. The Drugs Controller of India informed WHO that India had decided to participate in the certification scheme. The issue was discussed in the 20th Meeting of Drugs Consultative Committee held at New Delhi on 4th & 5th July 1978.

The silent features of WHO Certification Scheme were discussed and it was decided that the inspection of firms intending export of drugs be

thoroughly inspected and ensured that they observe the necessary control on quality during and after manufacture of pharmaceutical products and follow Good Manufacturing Practices before a certificate is issue in their favour.

It was also decided to follow following guidelines-

(1) Joint Inspection of manufacturing firms by the officers of the State Drugs Control Organization and Zonal Officer from Central Drugs Standard Control Organization should be carried out before issuing certificates under the Scheme.

(2) It should be ensured that the firm is observing – Good Manufacturing Practices and have checks on controls exercised.

Since the Licensing Authority for the State of Maharashtra was the Commissioner, FDA, he was issuing the certificates under the WHO certification scheme till 1990. The powers of the Licensing were decentralized, hence, in 1988, the guidelines for grant of GMP Certificate as per WHO guidelines were issued and 1990 onwards the said Certificates were issued by the Divisional Joint Commissioners. From 1998 onwards, the certificates were issued by the Joint Commissioner (H.Q.) Mumbai, as single Certifying Authority as required by WHO.

Since many of the provisions and guidelines issued by the WHO have been upgraded, the revised guidelines on the subject were issued by the Commissioner, FDA vide circular no. WHOGMP/शुल्कवाढ/1083-03/11, dated 17 November, 2003. Since July 2003, Commissioner, Food and Drug Administration, Maharashtra State authorized Joint Commissioner (Law) to sign and issue the certificate/s under WHO certification scheme. The procedure to be adopted for the application

processing received for grant of WHO-GMP Certification was issued vide circular no., डब्लुएचओजीएमपी/मार्गदर्शक तत्वे/१३६४-२०११/११, dated 13.7.2011. Further as per Commissioner's circular no. आस्था/कवज/औषधे/२५०/१३/२, dated 25/02/2013, the Joint Commissioner (HQ) and Controlling Authority were authorized for signing the WHO-GMP Certificate and other Certificate under WHO-GMP certification Scheme w.e. from 01/05/2013.

Whereas, there have been revision in the WHO – GMP guidelines and the procedures to be followed in Certifying the unit, the existing guidelines are revised. Henceforth the revised guidelines for the issue of Certification under WHO-GMP guidelines will be as follows;

PROCEDURE TO BE FOLLOWED IN THE STATE OF MAHARASHTRA

(A) RECEIPT OF APPLICATIONS

1. The applicant will make an online application on the *URL* ***https://fdawhogmp.maharashtra.gov.in*** for Certification under WHO–GMP Guidelines Scheme on the letter head of the company, along with the Site Master File and other relevant data in the office of the Assistant Commissioner depending on the location of the factory. The fees should be remitted against each appliaction online through ***https://gras.mahakosh.gov.in*** using the office code WHO-GMP Authority. The applicant should upload the following enclosures along with the said application.
   a. An undertaking that the manufacturing site is ready for inspection at the time of the application.
   b. The details of the sections with list of products to be covered under certification.

c. Photocopies (in PDF) of licenses and the list of approved products.

2. Second copy of the application along with its enclosures should be submitted *within* two (02) days by the applicant to the Office of the Deputy Drugs Controller (I), C.D.S.C.O., (West Zone), Mumbai.

(Note: The incomplete applications or applicant whose site is not ready for Inspection shall be liable for rejection and fees shall be forfeited.)

(B) <u>INSPECTIONS.</u>

1. The District Office shall sent a letter within 4 working days with the request for the Joint Inspection, with the tentative dates of Inspection, to the Office of the Deputy Drugs Controller (I), C.D.S.C.O., (West Zone) under intimation to the Divisional Joint Commissioner.
2. The Joint Commissioner (HQ) and licensing Authority WHO-GMP Certification within 2 working days upon receipt of the online application will send a request letter to the Dy. Drugs Controller (I) CDSCO, West Zone, Mumbai for joint inspection.
3. The joint inspection shall be carried out in accordance with the latest WHO GMP Guidelines as published time to time in various WHO-TRS.
4. The Joint inspection may be carried out within 30 days from the receipt of the application.
5. The joint inspection team as far as possible shall prepare the inspection report in the prescribed format at the time of the inspection and the copy of the same shall be given to the applicant.

(C) <u>RECOMMENDATIONS</u>

1. The detailed inspection report in the prescribed Proforma shall be submitted within 4 working days to the Assistant Commissioner with the recommendations by the concerned drugs inspector of FDA.
2. The Assistant Commissioner shall submit the said report with his comments and recommendations to the Licensing Authority within 4 working days.
3. The Licensing Authority shall decide on the said application preferably within 4 working days. In case of compliance of the observations noted in joint inspection shall be informed to the applicant within 2 working days. The period given for the compliance to the applicant shall not exceed 1 month from the date of information.
4. After receipt of the inspection report with recommendation and compliance, if any, to the Divisional Licensing Authority, shall decide on the said application preferably within 2 working days. The Licensing Authority shall forward the said application online with recommendation to the Certifying Authority i.e. the Joint Commissioner (HQ) and Controlling Authority, FDA, Mumbai. The Divisional Licensing Authority before forwarding the online application to the Certifying Authority must ensure that the application is accompanied with all necessary documents viz. complete joint inspection report, recommended product list dully signed, compliance report/compliance verification report (s), if any, opinion and recommendation in the online application and any other information, documents as per requirement.
6. The Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai, shall decide on the said application within 15 working days from the receipt of the said application, with the assistance of

Drugs Inspector, Assistant Commissioner (Drugs) of WHO-GMP cell of the HQ.

7. The application for the certification from the receipt of application, joint inspection, compliance report submission, compliance verification inspection and certification may be disposed off preferably within the period of 3 months from the date of application.
8. The application which is found to be pending for 3 month or more periods without any action or justified reason will automatically rejected and the fees will be forfeited.

(D) VARIOUS CERTIFICATES TO BE ISSUED UNDER THE SAID SCHEME

The office of the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai i.e. WHO- GMP Cell at Head Quarters of FDA, may issue, following certificates to the manufacturers on their request.

1. Certificate of Pharmaceutical Product(s).
2. Model Statement of Licensing Status of Pharmaceutical Product(s).
3. Unit WHO GMP Certificate along with the list of products for which Certificate of Pharmaceutical Products have been granted.

(E) FEES

1. A fee of Rs 5000/- per Section/Dosage form of the manufacturer, as an inspection fee, to be remitted online through URL gras.mahakosh.gov.in
2. In case of application by a Loan Licensee, a fee of Rs 5000/- per Section/Dosage form of the own manufacturer, as an inspection fee, to be remitted online through URL gras.mahakosh.gov.in

3. A fee of Rs. 500/- for per copy of Certificate of Pharmaceutical Products shall be remitted by the applicant for a specific single country for the product, which the Unit WHO GMP Certificate or COPP has been already granted.
4. A fee of Rs. 1000/-for per copy of Certificate of Pharmaceutical Products shall be remitted by the applicant for multiple countries or country annexure or any other annexure such as excipients, formula, etc.
5. A fee of Rs. 1000/- for per copy of Certificate of Pharmaceutical Products without annexure shall be remitted by the applicant for a product for which the Unit WHO GMP Certificate or COPP has not been previously granted and have applied with the data such as Validation, Stability, etc. Additional Rs 500/-per product shall be remitted by the applicant in case the said certificate is required with the annexure.
6. A fee of Rs. 1000/- for per list of ten (10) products is to be remitted by the applicant for Model Statement of Licensing Status of Pharmaceutical Product(s).
7. A fee of Rs. 1000/-for per list of ten (10) products is to be remitted by the applicant for grant of Unit WHO - GMP Certificate.

(F) ISSUE OF CERTIFICATES UNDER THE SCHEME

1. Joint Commissioner (HQ) is authorized by Commissioner, Food & Drug Administration, Maharashtra State, to sign & issue the certificates under the WHO-GMP certification scheme online.
2. After approval from the Joint Commissioner (HQ), the Certificate of Pharmaceutical Products or other certificates under Scheme shall be issued in the prescribed format to the manufacturer.

3. The validity of certificates shall be two years from the date of grant of the Certificate.

(G) CERTIFICATE OF PHARMACEUTICAL PRODUCTS (CoPPs) FOR ADDITIONAL PRODUCTS AFTER GRANT OF WHO-GMP CERTIFICATE

A manufacturer may apply for grant of Certificate of Pharmaceutical Products for additional product(s) to the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai. Such application shall be accompanied by the following documents.

1. Stability data of the product as per WHO GMP guidelines.
2. Process validation of the product as per WHO GMP Guidelines.
3. In cases where there are no WHO GMP guidelines on stability studies, other international guidelines, such as ICH guidelines shall be applicable.

(H) APPROVAL OF ADDITIONAL SECTION / CATEGORY OF PHARMACEUTICAL PRODUCTS

The proposal of approval of additional category of product whose section was not approved in earlier proposal has to be considered as a fresh proposal and is to be approved after carrying out joint inspection and by following procedure for grant of WHO-GMP Certificate.

(I) GRANT OF WHO-GMP CERTIFICATES TO LOAN LICENSEE

1. The application shall be submitted online through the URL as mentioned in clause A by the loan licensee after the grant of WHO-

GMP certificate to the own manufacturer for only such dosage form granted to the own manufacturer in WHO-GMP certification.

2. The loan licensee application shall be directly processed by the office of the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai, to avoid the delay in the processing.
3. The loan licensee's proposal shall be considered only for the category(s)/section(s) of formulations / API as that has been recommended/granted for the own licensee.
4. Wherever required the application shall accompany the data about stability data, process validation as per WHO GMP guidelines.
5. The date of validity of certificate of Pharmaceutical Product issued to the loan licensee will be the same as that assigned to the own manufacturer.
6. A copy of the contract should be submitted between the contract giver (Loan Licensee) and the contract acceptor (own license) which specifies their respective responsibilities relating to manufacture, quality control, quality assurance, stability, procedures to be followed, etc. pertaining to the products. This contract should be as per the conditions laid under WHO GMP guidelines.
7. The fees to be paid in case of such applications will be same as prescribed for the own licensee holding the WHO GMP Certificate.
8. If the Loan Licensee applies for the fresh certification at the time of the extended period of Validity of the Own Licensee's Certification, then it shall be supported with the proper justification for the same.

(J) INFORMATION ABOUT THE STATUS TO THE JOINT COMMISSIONER (HQ)

All the divisional Licensing Authority shall inform to the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai periodically about:

1. The details of the applications received / pending for the grant of WHO-GMP Certificates
2. The details of the NSQ reports received and actions thereof pertaining to the WHO – GMP Certificate holders.
3. The details of the action such as license / product suspension, cancellation, etc. taken on the GMP – GMP Certificate holders.

(K) EXTENSION OF VALIDITY OF WHO-GMP CERTIFICATE (COPP)

The validity of Certificate of Pharmaceutical product shall be for a period of two years. If after the expiry of the validity of the said WHO GMP Certificate the licensee wants the fresh certificate, the application for the same as prescribed above in (A) shall be made at least 60 days prior to the expiry of the said certificate.

If the said application is pending for Joint Inspection or under process, the certificate holder may apply for the extension of the validity for the period of 6 months of the certificate already granted directly to the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai. In order to avoid the hardships to the manufacturer for registration/export of the products and participation in international/Local tenders, due to delay in conduct of Joint Inspection the extension to the validity by six months may be granted under following conditions.

1. The manufacturer shall submit the fresh proposal to respective office for grant of WHO GMP Certificate (COPP) 60 days before expiry of validity of earlier certificates of Pharmaceutical Products as per the procedure prescribed in above (A).

2. The licensee has to submit the proposal to the Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai along with the proof of the submission of the application as stated above with the photocopy of the receipt of the inspection fees remitted.

3. The extension period shall be for the period of six months from the date of expiry of the certificate previously granted.

4. In case where the inspection is pending for the period more than 6 months the extension period may further be extended to the period of 6 months. But in any case the said period will not extend to more than 12 months from the validity of the initial certificate, with the intimation to the Office of the Deputy Drugs Controller (I), C.D.S.C.O., (West Zone) Mumbai for arranging immediate inspection in the said case.

(L) <u>WITHDRAWL / SUSPENSION / CANCELLATION OF THE CERTIFICATE ISSUED UNDER THE SCHEME</u>

The Certifying Authority i.e. the Joint Commissioner (HQ), FDA, Mumbai, may pass the order of withdrawal, suspension or cancellation of the Certificate after giving the firm an opportunity to show cause why the WHO-GMP certificate and the CoPPs granted there under to the firm should not be withdrawn / suspended / cancelled in case of following circumstances.

1. In case of any serious violations of WHO-GMP guidelines.
2. Any action such as product licences or complete licence suspension / cancellation by the Licensing Authority under Drugs and Cosmetics Act and Rules there under.
3. In case the product is declared as not of standard quality which is covered in the scope of WHO-GMP certification.

4. Depending on the nature of the defect/ non-compliances the WHO-GMP certificate /COPPs may be withdrawn/Suspended/Cancelled or deferred till satisfactory compliance and recommendation from the Licensing Authority.
5. The decision on the explanation submitted by the firm in pursuance of show cause notice issued by the Certifying Authority may be taken after ensuring the compliance verification through joint inspection by the FDA and CDSCO team.

(M) APPEAL AGAINST WITHDRAWL / SUSPENSION / CANCELLATION ORDER OF THE CERTIFICATE ISSUED UNDER THE SCHEME

The firm whose WHO-GMP certificate and Certificate of Pharmaceutical Products (CoPPs) granted has been withdrawn, suspended or cancelled, within 30 days of the date of the order as mentioned in clause L, may prefer appeal against the said order to the Commissioner, Food and Drugs Administration , Maharashtra State, Mumbai, who shall decide the same.

Schedule of Fees

S. No.	Description	Fees / Per copy
1.	Fresh WHO-GMP Certificate – Inspection fee (Own)	5000/- for each section
2.	Fresh WHO-GMP Certificate – Inspection fee (Loan)	5000/- for each section
3.	Unit WHO-GMP Certificate	1000 for every 10 products
4.	First time COPP with Annexure (with Validation & Stability)	1500/-
5.	First time COPP (with Validation & Stability)	1000/-
6.	COPP with any type of Annexure	1000/-
7.	COPP (if WHO – GMP Cert. or COPP already granted)	500/-
8.	Statement of Licensing status	1000 for every 10 products