FOOD AND DRUGS AUTHORITY

GUIDELINES FOR LICENSING OF PHARMACEUTICAL AND HERBAL MEDICINES MANUFACTURING FACILITIES

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LIST OF ABBREVIATIONS

cGMP **:** current Good Manufacturing Practices
SMF : Site Master File
CAPA : Corrective and Preventive Action
EPA : Environmental Protection Agency
FDA : Food and Drugs Authority
MFL : Manufacturing Facility License GL : Guidelines
DID : Drug Inspectorate Department
Vmaj : Major Variation
Vmin : Minor Variation

1.0 INTRODUCTION

1.1 In pursuance to **Sections 115, 130 and 131 of the Public Health Act, 2012, Act 851 of the Republic of Ghana,** these Guidelines are hereby made to provide prospective applicants with information on the general requirements for the application of a license for pharmaceutical manufacturing facilities.

1.2 These Guidelines apply to business entities duly registered by the Registrar-General Department with intention to establish manufacturing Industries in Ghana.

1.3 The guidelines also apply to Foreign Manufacturing facilities who intend to obtain marketing authorization for the sale of pharmaceutical products manufactured in the facility.

1.4 The manufacturing process facilities shall be carried out under the supervision of a Pharmacist or a person approved by the Authority as having specialist knowledge in the article to be manufactured (Refer to FDA "Guidelines for Selection of Authorized Person in the Pharmaceutical and Chemical Industry").

1.5 This guideline Is hereby promulgated for information, guidance and strict adherence by all concerned.

2.0 GLOSSARY

2.1 *In this guideline, unless the context otherwise states;*

Applicant
Means the management of the wholesale or distributing entity or the Authorized person or a duly appointed person acting for and on behalf of the authorized person but with limited responsibilities to the technical sections reserved for the Authorized person.

Authority
Means Food and Drugs Authority

Authorized Person
Means any person with a background in the sciences (As defined in the Guidelines for Selection of Authorized Persons in the Pharmaceutical industry)

Quality management system
Means a document with a collection of business processes focused on consistently meeting customer requirement and enhancing their satisfaction. It is aligned with an organization's purpose and strategic direction. It provides a proactive approach to

identifying, evaluating and controlling potential risk to quality. It facilitates continual improvement process performance and maintenance of product quality.

Quality manual

A document stating the company management's intentions for operating the quality system. It includes policies for all areas of the storage, distribution, procedures and facility, affecting or that affect quality of product during distribution.

Standard operating procedures

An authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g. equipment operation, maintenance and cleaning; cleaning of premises and environmental control; sampling and inspection).

Site master file

Means a document prepared by the wholesale distributor containing specific and factual GDP information about the products and/or control of the storage conditions carried out at the site and during distribution process, closely integrated operations at adjacent and nearby building.

Corrective action and preventive action (CAPA) Report

Means a report stating the defects and non-conformances issued by the FDA after a GDP inspection as well as steps taken to eliminate the causes of the nonconformances or other undesirable situations.

Variation

Refer to appendix 2

Notifications means changes that could have minimal or no adverse effects on the overall safety, efficacy and quality of the FPP. Annual notification (AN) do not require prior acceptance but must be notified to FDA within 12 months following implementation of the change.

Minor variation (Vmin)

means changes that may have minor effects on the overall safety, efficacy and quality of the FPP. Applicants must satisfy themselves that they meet all of the prescribed conditions for the change and submit all required documentation with the variation application.

Major variation (Vmaj)

means changes that could have major effects on the overall safety, efficacy and quality of the FPP. The documentation required for the changes included in this reporting type should be submitted. Prior acceptance by FDA is required before the changes can be implemented. A letter of approval will be issued for all major variations if and when the variation is considered acceptable.

3.0 REQUIREMENTS

3.1 Documents

3.1.1 Application documents

3.1.1.1 An application for a license to manufacture pharmaceutical products shall be made in writing to the Food and Drugs Authority Ghana.

3.1.1.2 An application form shall also be completed in accordance with the sequence of appendices provided in the form, and shall be dated, signed and stamped by the pharmacist and owner/authorized representative of the firm

3.1.2 Documentary attachments

3.1.2.1 The application shall be submitted in duplicate together with:

- Copy of a valid business registration certificate showing proof of the business name shall be submitted.
- ✦ Proof of payment of the prescribed fee for licensing of the facility
- ✦ A Site Master File (SMF) of the facility. This shall include a sketch of the location plan of the establishment indicating a clear direction with identified landmarks to locate the facility.
- ✦ A Permit from the Environmental Protection Agency (EPA)
- ✦ Basic floor plan showing plant installations
- ✦ Architectural engineering permit issued by the District, Municipal or Metropolitan Assembly where the facility is located.

3.1.2.2 A copy of the submitted documents shall be endorsed by the FDA and returned to the applicant.

3.2 Evaluating Applications Submitted

3.2.1 Applications shall be reviewed by the FDA officers to ensure compliance with both administrative and technical requirements.

3.2.2 based on the outcome of the evaluation in 3.2.1 additional or supplementary documentation may be requested by the FDA.

3.3 GMP Inspection of the Facility

3.3.1 A successful evaluation of submitted documentation shall be followed by cGMP inspection of the facility by the FDA Ghana.

3.3.2 The cGMP inspection shall be conducted in line with the appropriate guideline based on the categories of medicines manufactured by the facility (guideline FDA/DRID/DID/GL-GMP-P/18/01 for pharmaceutical facilities and guideline FDA/DRID/DID/GL-GMP-H/18/01 for herbal facilities).

3.3.3 Additional documentation shall be required during the cGMP inspection of the facility as follows

- Quality Management System
- Quality Manual and standard operating procedures
- Contract agreement (e.g. Manufacturing, packing, repacking for partners involved in business)
- Qualification and validation documents
- Master and batch production records
- Specifications
- Credentials of other qualified persons
- Proof of ownership /lease agreement of the space/building y the establishment occupied
- Relevant reference materials (GMP guide, standard practice guidelines)
- Other procedure, protocols, records, and reports as required by the relevant guideline with which the cGMP inspection is being subjected to.

3.3.4 A Tentative Recommendations (if any) shall be issued by the inspection team to management of the facility immediately after completion of the cGMP inspection. This shall be followed by issuance of a final recommendation signed by the Chief Executive officer of the FDA Ghana at a later date (see flow chart for timelines).

3.3.5 The applicant shall submit a Corrective Action and Preventive Action Report (CAPA) report in respect of the recommendations issued. This shall be submitted to the FDA not later than 3 working days after receipt of the final recommendations. The CAPA shall indicate among others timelines within which the applicant intends to complete each of the recommendations issued.

3.3.6 Upon successful implementation of the CAPA, a follow-up inspection may be conducted by the inspection team to ascertain the effectiveness of the implementation (where applicable).

3.3.7 A manufacturing facility shall only be licensed after an expert review team has duly reviewed the inspection report and CAPA (where applicable) and found it to be satisfactory.

3.4 Post license inspection

3.4.1 A licensed facility shall be subject to a post license inspection in accordance to provisions of the **Public Health Act, 2012, Act 851 of the Republic of Ghana**. Additionally, violations of international laws of which FDA Ghana subscribes to as well as violations that bear on the quality, safety and/efficacy of medicines manufactured by the facility may attract a post-license inspection of the facility.

3.5 Conditions for renewal of license

3.5.1 An application for renewal of license shall be made to the FDA three Months to expiry of the current licensed issued by the authority.

3.5.2 The application shall capture details of any variation (as stated in appendix 2) applied for within the period. Documents that have already been submitted in respect of the variation need not be submitted for the second time.

3.5.3 The approved fee shall be paid in respect of an application for renewal of a manufacturing license (see approved fee schedule via https://fdaghana.gov.gh/images/Quick%20links/FDA%20FEES%20SCHEDULE.pdf)

3.6 Acceptable Variations

3.6.1 The following classes of variations are allowable under a licensed pharmaceutical manufacturing facility. Note that the listed variations may not be exhausted enough to cover all possible variations as such clients are advised to contact the FDA for any guidance in this respect.

a. Major Variation
   i. Change of ownership
   ii. Additional production line
   iii. Transfer of location
   iv. Change of activity

b. Minor Variation-require prior approval
   i. expansion of establishment
   ii. change of business name
   iii. zonal change in address

c. Minor Variation-Notification
   i. change of pharmacist or qualified person for manufacturing
   ii. deletion of activity
   iii. transfer/ addition of storage facility

3.6.2 The manufacturing license holder shall inform the FDA Ghana of any changes listed above intended to be carried out in the facility.

3.6.3 Each information on any variation to the FDA Ghana shall be accompanied by the requisite documentations as indicated in appendix 2 of this guideline

3.6.4 Facilities intending to carry out minor variations (i.e. Categorized as Notifications) can continue to do business provided such variations have been filed with the FDA Ghana not more than twelve months after implementation.

3.7 How Variation Applications Are Handled

3.7.1 A variation application (including the filled variation application formGMP/GSP-GDP) shall be submitted along with a declaration letter undersigned by the Head of Regulatory Affairs that declares there is no other change except for the proposed variation.

3.7.2 NOTIFICATIONS (“Do and Tell”)

I. If the notifications fulfill the requirements (conditions and supporting documents as per guidelines) DID shall acknowledge receipt of a valid notification.

II. The DID shall respond to a notification within a period of 20 working days after receipt of the application.

3.7.3 MINOR VARIATION (PROIR APPROVAL)

I. If the application fulfills the requirements (conditions and supporting documents as per appendix 2) of a minor variation, DID shall issue approval in the form a written letter for the proposed change.

II. The DID shall issue the approval to the minor variation within a period of 30 working days after receipt of the application.

III. The manufacturer/marketing authorization holder shall implement/commence implementation of the variation within the next 30 days after receipt of approval from the FDA. This 30 days’ allowable period for commencement of implementation shall be indicated in the letter of approval.

3.7.4 MAJOR VARIATION

I. If the application fulfills the requirements (conditions and supporting documents as per appendix 2 of a major variation, DID shall issue approval in the form a written letter for the proposed change.

II. The DID shall issue the approval to the major variation within a period of 60 working days after receipt of the application. This timeline may be reviewed downwards to 40 working days based on the urgency of the variation, for example if it borders on safety. The timeline may also be adjusted upwards on the basis of scientifically justifiable evidence.

III. The manufacturer/marketing authorization holder shall implement/commence implementation of the variation within the next 30 days after receipt of approval from the FDA. The allowable period of implementation shall be indicated in the letter of approval.

IV. The FDA reserves the right to re-categorize the application type, where it's deemed appropriate.

V. Where a re-categorization of the variation is done by the FDA, it shall be communicated to the manufacture/marketing authorization holder only where additional conditions and documentations are required as per appendix 2. This shall be done within 15 working days after receipt of the application.

3.8 Timelines for licensing activities
Refer to appendix 3 **3.9 Sanctions: Revocation/Cancellation/Suspension of license**

The Authority shall cancel, suspend or withdraw a licensure of a facility if;

3.8.1 The facility contravenes GMP requirements

3.8.2 Any of the conditions under which the license was issued no longer exist

3.8.3 The information on which the approval was given is later found to be false

3.8.4 The circumstances under which the approval was given no longer exist

3.8.5 Where the licensure is suspended, withdrawn or cancelled, the Authority shall issue a notice to the management of the facility.

3.7.6 The Authority shall take steps to ensure that the manufacturing facility is stopped from manufacturing until otherwise decided by the Authority.

3.7.7 Measures towards enforcing section 3.7 may include the publication of the FDA's action on its website and other relevant media.

3.10 Penalties

3.8.1 The Authority shall impose an administrative fine in accordance with the approved fees and charges Act applicable to the FDA.

3.8.2 Other penalties as provided for in section 129 of the Public Health Act, 2012, Act 851, related to contraventions to the provisions of this guideline may be imposed.

APPENDIX 1

LIST OF DOCUMENTARY REQUIREMENTS FOR LICENSING OF A PHARMCEUTICAL MANUFACTURING FACILITY

Initial Application

1. Application letter
2. Application form
3. Proof of Business name registered
4. Credentials of pharmacist
5. Site mater file
6. Location plan
7. Proof of payment

Renewal of application

1. Application letter
2. Application form
3. Copy of initial certificate issued
4. Proof of payment

Reissuance of Lost Certificate or Destroyed Certificate

1. Letter of request
2. Affidavit of loss or destruction
3. Proof of payment

Voluntary cancellation of license

1. Letter of request
2. Original license

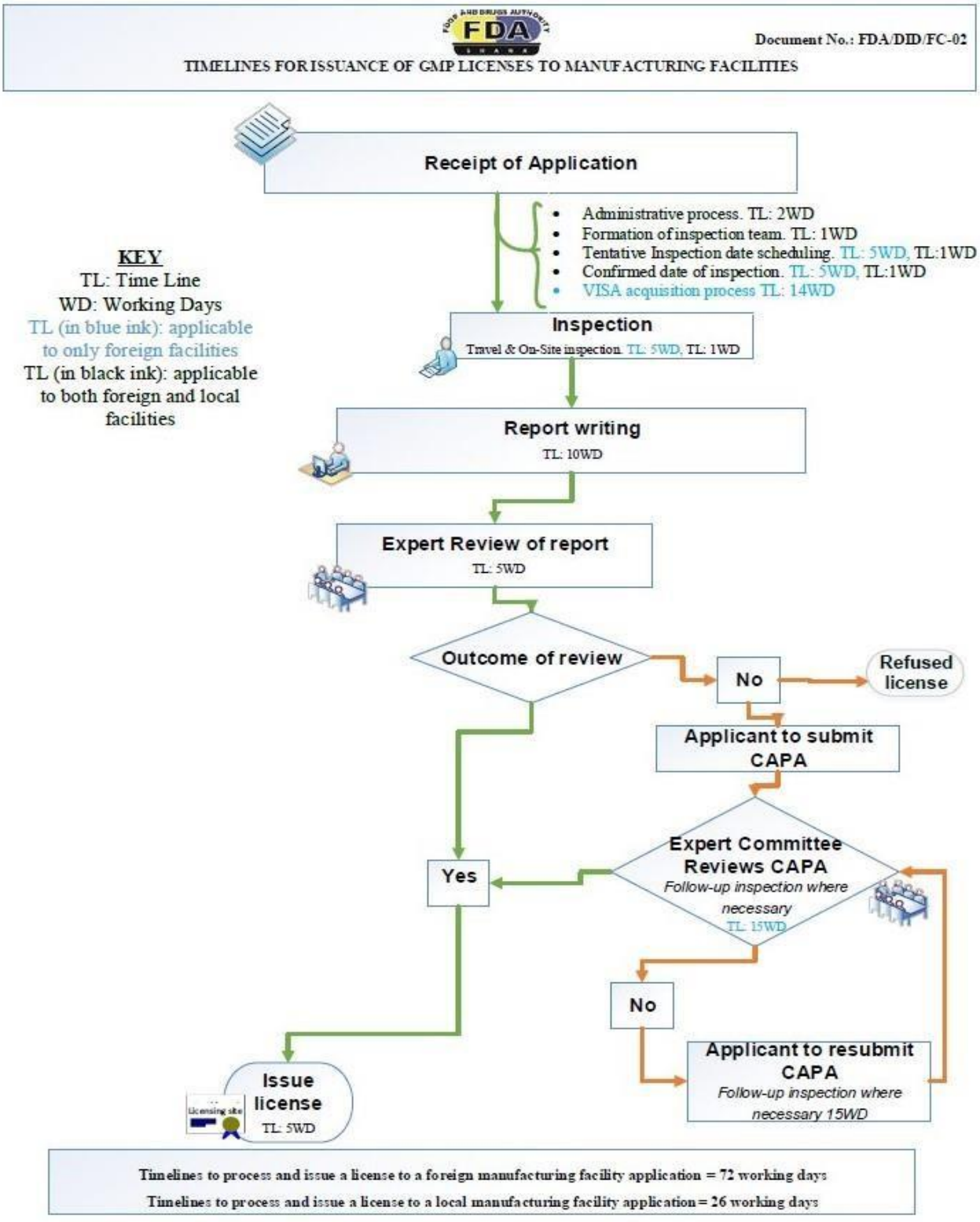
APPENDIX 2

LIST OF REQUIRMENTS FOR APPLICATION FOR VARIATION TO PHARMACEUTICAL MANUAFTURING FACILITY (refer to guidelines for handling variations-NUMBER)

MAJOR VARIATION		
VARIATION	**CONDITION**	**DOCUMENTS REQUIRED**
Change of ownership	If there is change of ownership of the pharmaceutical manufacturing facility licensed	1. Application letter 2. Proof of business name registration reflecting the name of new owner 3. Deed of sale or transfer of 4. Proof of payment
Transfer of location	If the location of the facility has been physically transferred with changes in previously approved address	1. Application letter 2. Proof of business name registration reflecting the new address 3. New location address 4. Proof of payment
MINOR VARIATIONS		
VARIATION	**CONDITION**	**DOCUMENTS REQUIRED**

Change of activity	If the entity engages in additional activities such as distribution, import or export. It also refers to a change in the initial license activity	1. Application letter 2. Contract agreement to proof activity 3. Proof of payment
Expansion of establishments	Expansion adjacent to existing licensed facility. Includes additional floors as well.	1. Application letter 2. Proof of payment
Change of business name	Change of business name without change in location of business owner	1. Application letter 2. Proof of business name registration reflecting the new name of the drug establishment 3. Proof of payment
Zonal change in address	Refers to change in the name/number of the street/building without physical transfer of the facility	1. Application letter 2. Document issued by the local authority as proof of zonal change 3. Proof of payment
MINOR VARIATIONS- NOTIFICATIONS		
VARIATION	**CONDITION**	**DOCUMENTS REQUIRED**
Deletion of activity	Deletion of any approved/added distributor activity	1. Application letter 2. Termination of contract or conformance letter 3. Proof of payment
Transfer/addition of warehouse	Refers to the physical transfer of warehouse. Also refers to the addition of warehouse the existing or previously inspected warehouse.	1. Application letter 2. New location plan 3. Proof of payment

APPENDIX 3: Timelines for licensing activities


FDA
Document No.: FDA/DID/FC-02
TIMELINES FOR ISSUANCE OF GMP LICENSES TO MANUFACTURING FACILITIES
Receipt of Application
Administrative process. TL: 2WD
Formation of inspection team. TL: 1WD
Tentative Inspection date scheduling. TL: 5WD, TL:1WD
Confirmed date of inspection. TL: 5WD, TL:1WD
VISA acquisition process TL: 14WD
KEY
TL: Time Line
WD: Working Days
TL (in blue ink): applicable to only foreign facilities
TL (in black ink): applicable to both foreign and local facilities
Inspection
Travel & On-Site inspection. TL: 5WD, TL: 1WD
Report writing
TL: 10WD
Expert Review of report
TL: 5WD
Outcome of review
No
Refused license
Applicant to submit CAPA
Expert Committee Reviews CAPA
Follow-up inspection where necessary
TL: 15WD
Yes
No
Applicant to resubmit CAPA
Follow-up inspection where necessary 15WD
Issue license
TL: 5WD
Timelines to process and issue a license to a foreign manufacturing facility application = 72 working days
Timelines to process and issue a license to a local manufacturing facility application = 26 working days

APPENDIX 4:
Change History

SN.	Date	Ver No.	Description of Change (section)
1.	15/03/2019	01	Initial Issue
2.	26/07/2019	02	Inclusion of sections 3.7, 3.8, & 3.9