# DIRECTORATE GENERAL OF DRUG ADMINSTRATION

## MINISTRY OF HEALTH & FAMILY WELFARE

# GUIDELINES[1] FOR THE SUBMISSION OF BANGLADESH COMMON TECHNICAL DOCUMENT: GENERAL GUIDELINES AND MODULE 1

This document provides instructions to applicants intending to submit applications for the registration of medicines. The guidelines are governed by the Directorate General of Drug Administration's (DGDA) current thinking on safety, quality, and efficacy of medicines. The DGDA reserves the right to request additional information to establish the safety, quality, and efficacy of a medicine in keeping with current knowledge at the time of the evaluation of a medicine. The DGDA is committed to ensuring that all registered medicines are of the required quality, safety, and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Version 1 released for pilot implementation and comments
June 2015

[1] Adapted from Australian Government Department of Health, *Therapeutic Goods Administration, CTD Module 1 – Version 2.1,* May 2013, and *South African Medicines Control Council CTD General & Module 1*, August 2012.

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## MESSAGE FROM THE DIRECTOR GENERAL, DIRECTORATE GENERAL OF DRUG ADMINISTRATION

The Directorate General of Drug Administration (DGDA) of Bangladesh is changing and improving its medicines registration system to ensure the safety and efficacy of medicines as well as to strengthen the potential for the exportation of medicines. The DGDA is therefore adopting the Common Technical Document (CTD) formats and guidelines for the preparation of registration dossiers for pharmaceuticals that are submitted with the application for registration.

The DGDA is also planning to implement PharmaDex to track registration applications and to enhance its capacity to successfully manage the registration process in a timely manner.

The Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Bangladesh office has been providing technical assistance to the DGDA under the terms of cooperative agreement number AID-OAA-A-11-00021 in this regard. The DGDA established a Taskforce Team to review the CTD modules and customize module 1 of these guidelines to the Bangladesh context. With support from SIAPS, the Team also reviewed modules 2 and 3 to gain a clear understanding of the process.

To adopt the CTD and implement PharmaDex, a series of workshops were conducted for DGDA officials as well as other stakeholders.

It is hoped that the CTD will be adopted on a pilot basis within six months. Thanks are offered to all members of the Taskforce Team and the SIAPS team for their continuous support for the implementation of the CTD.

Major Gen Md. Jahangir Hossain Mollik
Director General, Directorate General of Drug Administration &
Licensing Authority of Drugs

## ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| API | active pharmaceutical ingredient |
| CoA | certificate of analysis |
| CPP | certificate of a pharmaceutical product |
| CTD | Common Technical Document |
| DGDA | Directorate General of Drug Administration |
| EU | European Union |
| FPP | finished pharmaceutical product |
| FPRC | Finished Product Release Control |
| FPRR | Finished Product Release Responsibility |
| GCP | good clinical practice |
| GMP | Good Manufacturing Practice |
| ICH | International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use |
| IPI | inactive pharmaceutical ingredient |
| MHRA | Medicines and Healthcare Products Regulatory Agency |
| PI | package insert |
| PI | prescribing information |
| PIC/S | Pharmaceutical Inspection Cooperation Scheme |
| PIL | patient information leaflet |
| PMF | Plasma Master File |
| SIAPS | Systems for Improved Access to Pharmaceuticals and Services |
| SmPC | summary of product characteristics |
| TGA | Therapeutic Goods Administration |
| UK | United Kingdom |
| USFDA | US Food and Drug Administration |
| VAMF | Vaccine Antigen Master File |
| WHO | World Health Organization |

# INTRODUCTION

These guidelines provide instructions for applicants preparing a Common Technical Document (CTD) for the registration of medicines for submission to the Directorate General of Drug Administration (DGDA). The document describes how to organize applications based on the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines on the CTD. The CTD is currently applicable only to human, not veterinary, medicines.

According to the CTD format, each application is a collection of documents, grouped into five modules.

This document provides information on the contents of the Bangladesh CTD module 1: Administrative Information, as module 1 is specific to the region. General information for the applicant on preparing and organizing the dossier is also provided.

This is one in a series of guidelines that provide recommendations for applicants preparing the CTD for the registration of pharmaceuticals for human use. The document presents the agreed upon ICH common format for the preparation of a well-structured, harmonized application that will be submitted to regulatory authorities. The CTD format is intended to save time and resources and to facilitate regulatory review and communication. This document also draws on the World Health Organization (WHO) guidelines on submission of documentation for a multisource (generic) finished pharmaceutical products (FPP): preparation of product dossiers in CTD format, 2010; and the European Notice to Applicants: Medicinal products for human use. Volume 2B: Presentation and format of the dossier CTD (July 2003). The CTD does not provide information about the content of a dossier and does not indicate the studies and data that are required for a successful approval. Regional requirements may affect the content of the dossier submitted in each region; therefore the dossier will not necessarily be identical for all regions.

The CTD guidelines, together with other existing Bangladesh Regulatory Guidelines, provide detailed information about the contents of an application. These guidelines apply to applications to register medicines and all related variations. Applicants should not modify the overall organization of the CTD. If not contained in the bulk of the documentation, any additional data should be included as addenda to the relevant part, together with additional expert comment that may be provided as a supplement to, or incorporated into, the relevant summary, overall summary, or overview.

## Module 1 - Administrative Information and Prescribing Information

Relevant administrative documentation and the proposed label for use in Bangladesh should be submitted in module 1 of the CTD dossier. This module should be divided into the relevant sections, as described in Part B of this document.

## Module 2 - Summary of the Dossier

Module 2 of the CTD dossier contains the summaries and overviews for the quality, nonclinical, and clinical sections of the dossier (refer to ICH M4Q, M4S, and M4E). The module begins with a general introduction to the medicine, including its pharmacological class, mode of action, and proposed clinical use. The summary of quality information should be provided according to WHO's Quality Overall Summary–product dossier (QOS-PD) template.

The clinical overview section should include a statement regarding good clinical practice (GCP) compliance.

## Module 3 – Quality

Module 3 of the dossier contains the chemical, pharmaceutical, and biological data relevant to the application. This information should be structured as described in the Bangladesh CTD Module 2 (Quality Overall Summary) and 3 (Quality) guidelines. Also, refer to the ICH Guidelines M4Q (M4Q (R1): QUALITY Module 2: Quality Overall Summary (QOS) and Module 3: Quality.

## Module 4 - Nonclinical Study Reports

Module 4 of the dossier contains the nonclinical (pharmacotoxicological) data relevant to the application.

Exemptions apply to multisource (generic) products.

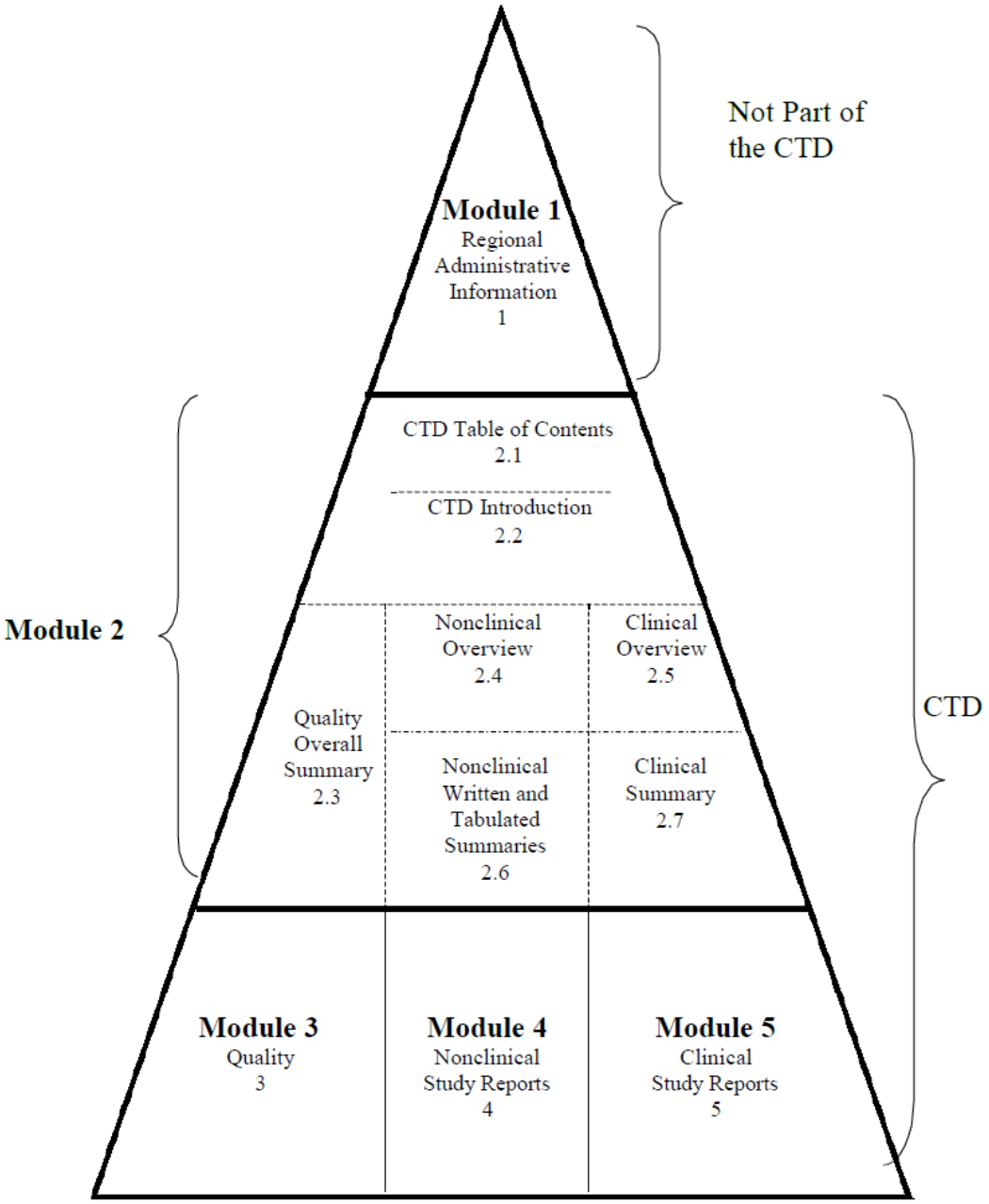
## Module 5 - Clinical Study Reports

Module 5 of the dossier contains the clinical data relevant to the application. In most circumstances, the clinical studies included in module 5 of the dossier will be international studies used to establish the pharmacodynamics, pharmacokinetics, safety, and efficacy of the medicine across an international patient population. However, where there is evidence to suggest that the pharmacokinetics or pharmacodynamics of the product may vary across the populations that will use the medicine in Bangladesh, the applicant should consider submitting studies relevant to those target populations. These reports should be presented in the order described in the Bangladesh CTD Module 2 (Clinical Overview), Guideline for Good

Clinical Practice (GCP) for Trials on Pharmaceutical Products, Bangladesh: Annexure 3, and CTD Module 5 (Bioequivalence Studies) guidelines. Also, refer to the ICH guideline M4E (M4E (R1): EFFICACY and Module 2: Clinical Overview and Clinical Summary Module 5 Clinical Study Reports.

In cases concerning well-known active pharmaceutical ingredients, the DGDA may grant exemption from the submission of clinical study reports, other than bioequivalence study reports, in module 5.

**Schematic of the Organization of the ICH CTD**



## PART A. GENERAL INFORMATION FOR APPLICATIONS

### 1 Preparing and Organizing the Common Technical Document

To facilitate the review of the basic data and to help the evaluator become oriented with the application's contents, the presentation of information should be unambiguous and transparent throughout the CTD.

If additional or supplementary data are submitted, the appropriate module(s) should be identified and numbering of each section should follow from the original documentation.

The applicant should not submit modules that are not used, i.e., it is unnecessary to include "not applicable" pages for any unused CTD headings.

For new applications, detailed statements justifying the absence of data or specific CTD sections should be provided in the relevant quality overall summary and/or nonclinical/clinical overviews (modules 2.3, 2.4, 2.5). If relevant, justification for blank sections of module 1 should be provided in the cover letter. Acronyms and abbreviations should be defined the first time they are used in each module.

### 2 Documentation

#### *2.1 Submissions*

**Set 1 – Full dossier. The dossier should also be submitted on a CD along with the paper copy (if desired).**

**Ensure that:**

- **Modules 1 and 3 are in MS Word format.**
- **Module 2 is in both MS Word and PDF format.**
- **PDF documents are text searchable (produced from an electronic source document).**

One complete application for registration dossier should include the following items:

- Proof of payment in accordance with DGDA approved fees (proof of payment should be included in section 1.2.2.1 of module 1).
- Sample and a copy of the sample's active pharmaceutical ingredient(s) (API) and final product release certificates of analysis.
- Copy of the sample's API certificates of analysis (if applicable).
- Copy of the final product release certificates of analysis.

On completion of the administrative screening the following should be included:

- Original letter of application for final submission should be included in section 1.0 of module 1. (This date becomes the date of the application and should be amended in section 1.2.1. by the applicant.)
- All administrative screening outcome correspondence (if applicable) (module 1.10).
- Application fee or proof of payment according to DGDA approved fees (proof of payment should be included in section 1.2.2.1 of module 1).
- The number of copies of dossier sets requested by the DGDA (for paper submission).

### *2.1.1 Composition of Copy Sets*

Only the information indicated should be included in each set. If sub-modules are not specifically singled out, a module implies all the sub-modules included under that section.

For example, “module 1.7” implies modules 1.7.1 to 1.7.11.

The sets should be compiled in the chronological order of the CTD.

## 3 Organizing Documents

Documents may be combined in volumes so long as they are separated by appropriately named tab identifiers. For example, the package insert should be separated from the other documents by a tab identifier. In general, documents from different CTD modules should not be included in the same volume. Documents from different modules may be combined in the same volume for amendments consisting of a small number of short documents.

Administrative documents (e.g., application letter) are included in module 1. The organization of such documents should be consistent with the structure described in these guidelines. Since the administrative documents are limited in number, they should be placed in the same volume, separated by tab identifiers.

## 4 Volume Identification

Volumes should be numbered by module, resulting in a separate set of numbers for each module. The labeling of each volume should include:

- Name of applicant
- Name of medicine

Module and volume number: The volumes for each module should be numbered separately and sequentially using the format: *x of y volumes,* where x is the number of the specific volume and y is the total number of volumes submitted for the respective module, e.g., module 3, Vol.1 of 6.

- Copy number: The copies of modules 1, 2 and 3 should be numbered as copies *x of y.*
- Contents. Each volume should also be labeled according to the section(s) it contains, e.g., section 3.2.P.4 means:

3. – Module 3 – Quality
2. – Body of data
P. – Product
4. – Control of excipients

## 5 Pagination

A document is a set of pages, numbered sequentially and divided from other documents by a tab.

Page numbering should be at the document level and not at the volume or module level. (The entire submission should never be numbered consecutively by page.) In general, all documents should have page numbers. Since the page numbering is at the document level, there should only be one set of page numbers for each document.

Cross-referencing to documents should be made by referring to the CTD module, volume, tab identifier, and page number (for example: "*see Module 3, Vol. 6, P.4.3 Method validation, p. 23"*).

Documents should be printed on both sides of the page. Legibility should not be impaired and margin space should be sufficient on both the left and right side so that information is not obscured when the page is placed in a binder. However, module 1.3 Bangladesh Labeling and Packaging (1.3.1, 1.3.2, 1.3.3) and patient information leaflet amendments/updates should be copied single-sided. Copying of each document should start on a new page and should be separated from the next document by a tab.

## 6 Paper Size

Standard A4 paper should be used for all submissions. Text and tables should be prepared using margins that allow the document to be printed on A4 paper. The left-hand margin should be sufficiently large that information is not obscured by binding.

## 7 Fonts

Font sizes for text and tables should be of a style and size that are large enough to be easily legible, even after photocopying or when provided electronically. Arial 12 point font is preferred for narrative text, but printing in a font size with a legibility equivalent to at least Arial 10 point black on white may be used. The copies, including figures, tables, and photos should be clearly legible. Shading and/or colored filling/background and/or print, e.g., in tables and headers, or across pages, is unacceptable and should be avoided.

**Table 1: Presentation of Information in the CTD Format**

| Module Number | Title and Main Section Headings | Cross-reference to modules | Binder/label color | Number of paper copies (if applicable) |
|---|---|---|---|---|
| 1 | **Administrative and Prescribing Information** | | | |
| 1.0 | Letter of application | | | |
| 1.1 | Comprehensive table of content (module 1) | | | |
| 1.2 | Application | | | |
| 1.3 | Bangladesh labeling and packaging | | | |
| 1.4 | Information about the experts | | | |
| 1.5 | Specific requirements for amendment application of registered products | | | |
| 1.6 | Environmental risk assessment | 2, 3, 4, & 5 | Red | 1* |
| 1.7 | Good manufacturing practice | | | |
| 1.8 | Foreign regulatory status | | | |
| 1.9 | Pharmacovigilance plan | | | |
| 1.10 | Details of compliance with screening outcomes | | | |
| 1.11 | Bioequivalence trial information | | | |
| 1.12 | Information on price | | | |
| 1.13 | Pediatric development program | | | |
| 1.14 | Risk management plan | | | |
| 2 | **CTD Summaries** | | | |
| 2.1 | Table of contents (modules 2 to 5) | 2 to 5 | | |
| 2.2 | Background | 2 to 5 | | |
| 2.3 | Quality overall summary | 2 to 3 | | |
| 2.4 | Nonclinical overview | 2 and 4 | Yellow | 1* |
| 2.5 | Clinical overview | 2 and 5 | | |
| 2.6 | Nonclinical written and tabulated summaries | 2 and 4 | | |
| 2.7 | Clinical summary | 5 | | |
| 3 | **Quality** | | | |
| 3.1 | Table of contents of module 3 | | | |
| 3.2 | Body of data | | Green | 1* |
| 3.3 | Literature references | | | |
| 4 | **Nonclinical study reports** | | | |
| 4.1 | Table of contents of module 4 | | | |
| 4.2 | Study reports | | Blue | 1* |
| 4.3 | Literature references | | | |
| 5 | **Clinical study reports** | | | |
| 5.1 | Table of contents of module 5 | | | |
| 5.2 | Tabular listings of all clinical studies | | Black | 1* |
| 5.3 | Clinical study reports | | | |
| 5.4 | Literature references | | | |

*For combination products that require a joint review, an additional copy of modules 1, 2, and 3 is required.

## PART B. BANGLADESH MODULE 1 – ADMINISTRATIVE AND PRESCRIBING INFORMATION

Module 1 should contain all administrative documents (e.g., application forms and certifications), labeling, general correspondence, and annexes. Generally, all of the documents in module 1, other than the annexes, can be provided in a single volume. The annexes to the module should be submitted in separate volumes.

### Module 1.0 Letter of Application

| Documentation | | |
|---|---|---|
| 1. | 1.0 | Letter of Application |

Applicants should include a *Letter of Application* with all applications. A copy of the letter should be placed at the beginning of module 1.

The letter of application should address the following information, at a minimum:

- If the application is being submitted simultaneously with one or more additional applications for the identical product, this should be stated. It should also be confirmed that the submissions are identical except for the proprietary name.
- The brand name(s), generic name, active ingredient name(s), dosage forms, and strengths of the medicine(s).
- Clarification if the proprietary name in the original dossier (e.g., where a product has been licensed) differs from the proposed brand name included in the application.
- Justification for any empty sections in module 1 should be provided in the cover letter, as relevant.

For further submissions during the registration process or post-registration amendments, the cover letter should be included in this section of the dossier.

If replying to a letter from the DGDA, a copy of this letter should be included here.

### Module 1.1 Comprehensive Table of Contents

| Documentation | | |
|---|---|---|
| 1. | 1.1 | Comprehensive table of contents |

Module 1 should include a comprehensive table of contents for the entire application. The comprehensive table of contents should include a complete list of all documents provided in the application, by module.

In the table of contents, the location of each document should be identified by referring to the volume number that contains the document and any tab identifier. In general, the name for the tab identifier should be the name of the document (section heading according to the CTD format, e.g., 3.2.P.4.2). If the full name of the document is too long for the tab identifier, an alternative name that adequately identifies the document should be given.

Page numbers should not be used in the table of contents to refer to documents; rather, tab identifiers as described above should be used. Page numbers, in addition to the tab identifier, should be used to facilitate location within documents, where relevant.

## Module 1.2 Application

| Documentation | | |
|---|---|---|
| 1. | 1.2.1 | Application form |
| 2. | 1.2.2 | Annexes to the application form |

### *1.2.1 Application Form*

An application to register a prescription medicine for human use in Bangladesh must be accompanied by a completed application form.[2] The application form is available from the automated medicine registration system (PharmaDex) on the DGDA's website.[3]

The application form should also be submitted with every response to a DGDA recommendation and/or an application for amendment of the dossier.

### *1.2.2 Annexes to the Application Form*

| | | |
|---|---|---|
| 1.2.2 | 1.2.2.1 | Proof of payment |
| | 1.2.2.2 | Letter of authorization for communication on behalf of the applicant |
| | 1.2.2.3 | Summary of the dossier product batch information (details are presented in module 3) |
| | 1.2.2.4 | Electronic copy declaration (applicable to paper submission) |
| | 1.2.2.5 | Curriculum vitae of the qualified person for pharmacovigilance |
| | 1.2.2.6 | Copy of written confirmation from the manufacturer of the API to inform the applicant in case of modification of the manufacturing process or specifications (API change) |
| | 1.2.2.7 | Certificate for a Vaccine Antigen Master File (VAMF), if applicable |
| | 1.2.2.8 | Certificate for a Plasma Master File (PMF), if applicable |

#### *1.2.2.1 Proof of Payment*

Include the original copy of the receipt from the Bangladesh Central Bank. For the

[2] Printout of the completed and signed application form on PharmaDex.
[3] www.dgda.gov/bd.

various fees, refer to information about medicine registration fees available on the DGDA website.[3]

### *1.2.2.2 Letter of Authorization for Communication on Behalf of the Applicant*

The application should be signed by the pharmacist/person responsible for the compilation of the application. There should be an original signature; a scanned signature is not acceptable. An individualized, person-specific letter of authorization for the signatory should be attached, issued by the person responsible for the overall management and control of the business (i.e., the chief executive officer).

### *1.2.2.3 Dossier Product Batch Information*

The table below should be completed to clarify the pharmaceutical development of the dosage form, from which data furnished in the modules mentioned below were derived:

| | 3.2.P.3 | 3.2.P.5 | 3.2.P.8 | 3.2.R.1 | |
|---|---|---|---|---|---|
| | Manufacture | Control of final pharmaceutical product | Stability | Bioequivalence | Dissolution |
| Types of batches* | | | | | |
| Batch/lot number(s) | | | | | |
| Batch/lot size(s) | | | | | |
| Date(s) of manufacture | | | | | |
| Composition and manufacturing process | | | | | |
| Site of API** | | | | | |

*Experimental, pilot, or production

**Add as many rows as necessary for API manufacturing sites

### *1.2.2.4 Electronic Copy Declaration (applicable paper submission)*

When paper dossiers are submitted, the applicant should submit an affidavit in which it confirms that the data on the paper application are identical to the checked documents in PharmaDex for the online medicine registration application.

### *1.2.2.5 Curriculum Vitae of the Qualified Person Responsible for Pharmacovigilance*

Provide a copy of the curriculum vitae of the qualified person responsible for pharmacovigilance.

### *1.2.2.6 API Change Control*

A formal agreement (letter of commitment) exists between the applicant for medicine registration and each manufacturer of the API(s), which ensures that information will

be communicated between them and to the DGDA before any significant change is made to the site of manufacture, manufacturing procedure, or quality control specifications of the API. Except as permitted by any DGDA amendment to guidelines relating to changes to medicines, changes will not be made to the API(s) to be used in the manufacture of medicines destined to be distributed in Bangladesh before written approval is granted by the DGDA. Both parties understand that the consequences of failure to obtain approval for changes, where approval is necessary, may include de-registration and recall of batches of medicines containing the material in Bangladesh.

#### *1.2.2.7 Certificate for a Vaccine Antigen Master File, if applicable*

Insert a copy of the certificate for a VAMF, if applicable. This is based on the countries as required by the Government of Bangladesh by the notification released in the official Gazette.

The VAMF is a medicine application dossier for a vaccine. It contains all relevant information of a biological, pharmaceutical, and chemical nature for a given vaccine antigen, which is common to several vaccines from the same applicants.

#### *1.2.2.8 Certificate for a Plasma Master File, if applicable*

Insert a copy of the certificate for a PMF, if applicable. This is based on the countries as required by the Government of Bangladesh by the notification released in the official Gazette.

PMF is a medicine dossier for applicants that provides all relevant detailed information on the characteristics of the entire human plasma used as a starting material and/or a raw material for the manufacture of sub/intermediate fractions, constituents of the excipient, and active substance (s), which are part of medicinal products incorporating stable derivatives of human blood or human plasma.

## Module 1.3 Bangladesh Labeling and Packaging

| Documentation | |
|---|---|
| 1.3 | Bangladesh labeling and packaging |
| 1.3.1 | Package insert (PI) |
| 1.3.2 | Patient information leaflet (PIL) |
| 1.3.3 | Labels (outer and inner) |

Applicants should include the proposed or approved texts of the package insert (PI) (module 1.3.1) and the patient information leaflet (PIL) (module 1.3.2). Bangladesh-specific labels should be submitted in module 1.3.3 (drafts, specimens, or text). For more information, refer to the DGDA's Guidelines on Product Information on packaging materials available on its website.[3]

### *1.3.1 Bangladesh Package Insert*

Module 1.3.1 should include a copy of the Bangladesh PI, either the proposed PI in the case of a new application, or the currently approved PI in the case of amendments. A PI guideline and any class labeling requirements may be issued by the DGDA from time to time.

PI requirements:

1. Product name
2. Name and strength of active ingredient(s)
3. Product description
4. Pharmacokinetics / pharmacodynamics
5. Indication(s)
6. Recommended dose
7. Mode of administration
8. Contraindication(s)
9. Warnings and precautions
10. Interactions with other medications
11. Pregnancy and lactation
12. Undesirable effects
13. Overdose and treatment
14. Storage conditions
15. Dosage forms and packaging available
16. Name and address of manufacturer/marketing authorization holder
17. Date of revision of PI

### *1.3.2 Bangladesh Patient Information Leaflet*

Module 1.3.2 should contain a copy of the proposed or approved Bangladesh consumer medicine information, also known as the *PIL*.

PIL requirements:

1. Name of product
2. Description of product
3. What is the medicine?
4. Strength of the medicine
5. What is the medicine used for?
6. How much and how often should you use this medicine?
7. When should you not take this medicine?
8. Undesirable effects
9. What other medicine(s) or food(s) should be avoided when taking this medicine?

10. What should you do if you miss a dose?
11. How should you keep this medicine?
12. Signs and symptoms of overdose
13. What to do when you have taken more than the recommended dosage?
14. Name/logo of manufacturer/importer /marketing authorization holder
15. Care that should be taken when taking the medicine? (drug interactions)
16. When should you consult your doctor?
17. Date of the revision of the PIL

### *1.3.3 Labels*

If the applicant has a specimen or drafts of the sales presentation of the medicine available at the time of the initial application, it should be included in module 1.3.3.

A mock-up is a copy of the flat design (artwork) in full color that provides a replica of both the outer and immediate packaging, and a two-dimensional presentation of the packaging/labeling of the medicine. It is also referred to as a paper copy or computer-generated version.

A specimen is a sample of the actual printed outer and inner packaging materials and package leaflet.

If there are multiple strengths and/or pack sizes, one representative specimen or mock-up will be sufficient. If batch number and expiry date are to be printed on the label during packaging, a statement to this effect should accompany the labels. If mock-ups or specimens are not available at the time of the initial application, a text version may be submitted.

Labeling parameters required for unit carton and inner label:

1. Product name
2. Dosage form
3. Name of active ingredient(s)
4. Strength of active ingredient(s)
5. Batch number
6. Manufacturing date
7. Expiration date
8. Route of administration
9. Storage conditions
10. Registration number
11. Name and address of marketing authorization holder or product owner
12. Name and address of manufacturer
13. Special labeling (if applicable), e.g., sterile, external use, cytotoxic, alcohol content

14. Warning (if applicable)
15. Pack sizes (unit/volume)

Labeling parameters required for blisters/strips:

1. Product name
2. Name of active ingredient
3. Strength of active ingredient
4. Batch number
5. Expiration date
6. Name/logo of manufacturer/product owner/marketing authorization holder
7. Country's registration number

## Module 1.4 Information about the Experts

| Documentation | |
|---|---|
| 1.4.1 | Particulars of quality control manager |
| 1.4.2 | Name and qualifications of production manager |
| 1.4.3 | Name and qualifications of clinical manager (when applicable) |

Experts must provide detailed reports of the documents and particulars, which constitute modules 3, 4, and 5. The requirement for these signed expert reports may be met by providing:

- The Quality Overall Summary, Nonclinical Overview/Summary, and Clinical Overview/Summary in module 2.
- A declaration signed by the experts in module 1.4.
- Brief information on the educational background, training, and occupational experience of the experts in module 1.4.

References must be provided for any additional claims not supported by the dossier.

## Module 1.5 Specific Requirements for Amendment Application of Registered Products

| Documentation | | |
|---|---|---|
| 1. | 1.5.1 | Literature-based submissions |
| 2. | 1.5.2 | Amendments/variations<br>• Tabulated schedule of amendments<br>• DGDA registration details (include the original or copy of the registration certificate)<br>• Affidavit by responsible person |
| 3. | 1.5.3 | Proprietary name applications and changes |
| 4. | 1.5.4 | PI and PIL amendments/updates |

### *1.5.1 Literature-Based Submissions*

If clinical evidence in support of efficacy is not submitted, studies and data to demonstrate the pharmaceutical and/or biological availability of the product should be included. If in the opinion of the applicant no data are required to substantiate efficacy (e.g., parenteral solutions), the rationale for accepting safety and efficacy, including reference to standard reference books, should be clearly stated.

For package insert amendments, refer to the Package Insert Guideline.[3]

### *1.5.2 Amendments /Variations*

Amendments to the registered products or registration dossier are necessary to maintain the safety, quality, and efficacy of a medicine and to ensure compliance with current technical requirements. It also assures adherence to administrative aspects of the dossier, keeps the DGDA abreast of scientific progress, and reflects new therapeutic indications/warnings or other safety matters. It is therefore the objective of the DGDA to process, as quickly as possible, amendment applications made by the applicants.

*1.5.2.1 Tabulated schedule of amendments (refer to Amendments Guideline)[3]*
*1.5.2.2 DGDA registration details*
*1.5.2.3 Affidavit by responsible person (refer to Amendments Guideline)[3]*

### *1.5.3 Trade Name Applications and Changes*

Submit a letter with details on the current and proposed names and the reason for the change in module 1.0. Include any information in support of a proposed name or alternative proposed names in this section 1.5.3.

Changing the trade name during the evaluation and registration phase will only be permitted if the regulatory authority has not accepted the name originally proposed by the applicant.

The policy on trade name and detailed requirements may be found in the Amendments Guideline and proof of payment must be filed.

### *1.5.4 Package Insert and Patient Information Leaflet Amendments/Updates*

Include the annotated PI/PIL for any proposed amendments to an approved PI/ PIL.

When updating or amending clinical aspects of the PI/PIL, the storage instructions should be updated to reflect the currently accepted wording. Refer to the Amendments Guideline for additional information.

## Module 1.6 Environmental Risk Assessment

Environmental risk assessment of medicinal products for human use is the process through which the regulatory authority ensures that the potential effects of pharmaceuticals on the environment are studied and adequate precautions are taken in case specific risks are identified. It is performed to evaluate and limit the potential effects of medicines on the environment.

The applicant should perform and submit the environmental risk assessment of their medicinal products during their development.

## Module 1.7 Good Manufacturing Practice

| Documents required by the DGDA | | |
|---|---|---|
| 1. | 1.7.1 | Date of last inspection of each site |
| 2. | 1.7.2 | Inspection reports or equivalent documents |
| 3. | 1.7.3 | Latest Good Manufacturing Practice (GMP) certificate or copy of the appropriate license |
| 4. | 1.7.4 | Batch release procedures |
| | 1.7.4.1 | Active pharmaceutical ingredients |
| | 1.7.4.2 | Inactive pharmaceutical ingredients |
| | 1.7.4.3 | Finished Product Release Control (FPRC) tests (for imported products) |
| | 1.7.4.4 | Finished Product Release Responsibility (FPRR) criteria (for imported products) |
| 5. | 1.7.5 | Confirmation of contract |
| 6. | 1.7.6 | Certificate of a pharmaceutical product (CPP); WHO certification scheme, if applicable |
| 7. | 1.7.7 | Proof of current registration of the responsible pharmacist |
| 8. | 1.7.8 | Sample and documents |
| | 1.7.8.1 | Confirmation of submission of the sample |
| | 1.7.8.2 | Batch manufacturing record of the sample |
| | 1.7.8.3 | Certificate of analysis (CoA) of the sample |
| 9. | 1.7.9 | Certified copy of permit to manufacture |
| 10. | 1.7.10 | Inspection flow diagram (self-inspection) |
| 11. | 1.7.11 | Organogram |

For all medicines, irrespective of the country of origin, it is expected that key manufacturing and/or processing steps in the production of active ingredients and finished pharmaceutical products are performed in plants of acceptable standards (see WHO Guide to Good Manufacturing Practices).

### *1.7.1 Date of Last Inspection of Each Site*

The applicant should provide a list of the manufacturers', packers', and FPRCs' names and license numbers, with a list of the dates of inspection by the regulatory authorities of either the DGDA, US Food and Drug Administration (USFDA), Medicines and Healthcare Products Regulatory Agency (MHRA), Therapeutic Goods Administration (TGA), European Union (EU), or Pharmaceutical Inspection Cooperation Scheme (PIC/S) country at each site.

### *1.7.2 Inspection Reports or Equivalent Documents*

The applicant should provide copies of inspection reports or equivalent documents, not older than two years, from the regulatory authorities of either the DGDA, USFDA, MHRA, TGA, EU, Canada, or PIC/S country, at each site.

### *1.7.3 Latest GMP Certificate or a Copy of the Appropriate License*

Include the latest GMP certificate, not older than two years, for the manufacturer(s), packer(s), and FPRCs, or a copy of the appropriate license.

### *1.7.4 Batch Release*

#### *1.7.4.1 Active Pharmaceutical Ingredients (API)*

The following minimum requirement should be confirmed and the name and physical address of the laboratory (ies) performing the tests provided:

a) Identification and assay of the API will be performed by the product manufacturer irrespective of the possession of a CoA from the API manufacturer.
b) Any tests included in the specifications and not included in a valid CoA will be performed.

#### *1.7.4.2 Inactive Pharmaceutical Ingredient (IPI)*

1) The following minimum requirement should be confirmed and the name and physical address of the laboratory(ies) performing the tests provided:

    a) Identification of the IPI will be performed irrespective of the possession of a CoA from the supplier.
    b) Any tests included in the specifications and not included in a valid CoA will be performed.

2) For IPIs for which a conclusive identification test is not described, all parameters that are specific to the identification of such ingredients should be listed and the tests performed irrespective of the possession of a CoA from the supplier.

#### *1.7.4.3 Finished Product Release Control Tests*

For imported products, at least the identification and assay of the API content should be performed by an approved laboratory (FPRC) after importation. This is to verify that the product has not been adversely affected during transport.

*1.7.4.4 Finished Product Release Responsibility Criteria*

The final non-analytical release criteria should include the verification of the appearance of the dosage form, the container, the package insert, the label, the batch number, the expiry date of the product, the CoA (including re-analysis for imported products), and the batch release documents (batch manufacturing record compliance).

### *1.7.5 Confirmation of Contract*

The applicant should include a signed declaration that contracts with all third party manufacturer(s) and/or packer(s), and FPRC(s) are in place. These contracts should be available for inspection purposes.

### *1.7.6 CPP (WHO Certification Scheme) (if applicable)*

WHO certification scheme on the quality of pharmaceutical products is an administrative instrument which states that registration of a medicine in the country of origin is a prerequisite for exporting to other countries. If the exporting country has authorized the product to be placed on its own market, the WHO-type certificate, in addition to certifying the manufacturing standard at the site in question, implies that the country issuing the certificate accepts that the product is of adequate quality, safety, and efficacy to remain on its own market. For details, refer to WHO Technical Report Series, No. 863, 1996 (Annex 10): Guidelines for implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

The CPP is required by the DGDA, if applicable.

### *1.7.7 Bangladesh Pharmacist Registration*

*1.7.7.1 Proof of Current Registration of the Responsible Pharmacist by the Bangladesh Pharmacy Council*

Submit a copy of the Bangladesh Pharmacy Council Registration certificate of the responsible pharmacist and also proof of current registration (annual registration card).

*1.7.7.2 Proof of Current Registration by the Bangladesh Pharmacy Council of the Pharmacist Signing the Dossier*

Submit a copy of the Bangladesh Pharmacy Council Registration certificate of the pharmacist signing the dossier and also proof of current registration (annual registration card), if different.

### *1.7.8 Sample and Documents*

*1.7.8.1 Confirmation of Submission of a Sample*

All medicine applications for registration must include a sample. It should be submitted to the National Control Laboratory, Drug Testing Laboratory.

*1.7.8.2 Batch Manufacturing Record of the Sample*

a) Included in module 3.2.R or
b) Available for inspection

*1.7.8.3 CoA of the Sample*

Include the CoA of the FPP and of the API used in the sample. Ensure that the batch number on the CoA corresponds with the batch number on the sample.

### *1.7.9 Certified Copy of a Permit to Manufacture*

Include a duly certified license to manufacture.

### *1.7.10 Inspection Flow Diagram*

Submit the inspection flow diagram, also of FPP intermediates, clearly indicating the sites and processes, including a clear distinction between primary and secondary packers.

### *1.7.11 Organogram*

Include the current company organogram, reflecting the responsible pharmacist and other key positions.

## Module 1.8 Foreign Regulatory Status (Importers Only)

| Documentation | | |
|---|---|---|
| 1. | 1.8.1 | List of countries to which an application for the same product has been submitted |
| 2. | 1.8.2 | Information and signature of manufacturer's authorized agent |
| 3. | 1.8.3 | Number of manufacturer(s)/importer(s) already manufacturing/importing to Bangladesh |
| 4. | 1.8.4 | Estimated market for this product/product group in Bangladesh |
| 5. | 1.8.5 | Registration certificates or marketing authorization |
| 6. | 1.8.6 | Foreign prescribing and patient information |
| 7. | 1.8.7 | Data set of similarities |

### *1.8.1 List of Countries to which an Application for the Same Product has Been Submitted*

The applicant should provide a list of countries to which an application for the same product has been submitted and the dates of submission (if available). This list should include details about approvals (with indications).

### *1.8.2 Information about the Manufacturer's Authorized Agent*

The name, address, and signature of manufacturer's authorized agent in Bangladesh should be provided.

### *1.8.3 Number of Manufacturer(s)/Importer(s) Already Manufacturing/Importing in Bangladesh*

Provide the total number of companies already manufacturing/importing the same product in Bangladesh.

### *1.8.4 Estimated Market for this Product/Product Group in Bangladesh*

The proposed prices for the product/product group should be provided for DGDA review.

### *1.8.5 Registration Certificates or Marketing Authorization*

In the case of registration in the country of origin, or where a marketing authorization has been granted by the regulatory authority of a country with which the DGDA aligns, copies of the registration certificates or marketing authorization should be provided.

### *1.8.6 Foreign Prescribing and Patient Information*

In the case of marketing authorizations in the country of origin, or where marketing authorizations have been granted by the regulatory authority of a country with which the DGDA aligns, copies of relevant prescribing and patient information should be provided, e.g., the Canadian product monograph, the summary of product characteristics (SmPC) in the EU, and US prescribing information (PI). If the overseas SmPC, monograph, or PI has not been approved at the time the application is made in Bangladesh, a draft document may be included. The approved overseas SmPC, monograph, or PI should be supplied to the DGDA when it becomes available.

### *1.8.7 Data Set Similarities*

Module 1.8.7 should contain a summary of the similarities/differences in the data packages submitted in other countries.

## Module 1.9 Pharmacovigilance Plan

This should include proof that the applicant has the services of a qualified person responsible for pharmacovigilance and the necessary means for the notification of any adverse reaction occurring either in Bangladesh or in a third country. The description of the marketing authorization holder's pharmacovigilance system should follow the requirements and format given in the DGDA's adverse drug events guidelines that are available on its website.

## Module 1.10 Details of Compliance with Screening Outcomes

| Documentation | |
|---|---|
| 1. | Details of compliance with screening outcomes |
| 2. | Details of any additional data submitted |

Address the screening comments, and where documentation is involved, provide only an overview of the relevant documentation submitted. Applicants should not modify the overall organization of the CTD; amended modules should be filed under the appropriate CTD section.

A copy of the completed screening template should be included in module 1.10, with the original completed form submitted separately with the application.

## Module 1.11 Bioequivalence Trial Information

| Documentation | | |
|---|---|---|
| 1. | 1.11.1 | Study title(s) (or brief description giving the design, duration, dose, and subject population of each study) |
| | 1.11.2 | Protocol and study numbers |
| | 1.11.3 | • Investigational products (test and reference) details, including:<br>o Active ingredient<br>o Strength<br>o Dosage form<br>o Manufacturer<br>o Batch number<br>o Expiry or retest date<br>o Country in which procured |
| | 1.11.4 | Confirmation that the test product formulation and manufacturing process are what is being applied for |
| | 1.11.5 | Proof of procurement of the biostudy reference product |
| | 1.11.6 | Name and address of the contract research organization (CRO) where the bioequivalence studies were conducted |
| | 1.11.7 | Sponsor and responsible sponsor representative: name and address, contact details |
| | 1.11.8 | Duration of clinical phase: dates of dosing and last clinical procedure |
| | 1.11.9 | Date of final report |

Bangladesh's requirements for biopharmaceutical studies are described in the Guideline for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products, Bangladesh, Annexure 3 and Bioequivalence Guidelines.[3]

The Bioequivalence Guideline is largely based on the ICH M4E(R1) Efficacy module 5 and relevant WHO guidelines. It also takes into account relevant USFDA guidelines.

In relation to the content of biopharmaceutical study reports, this guideline states that: The report of a bioavailability or bioequivalence study should give the complete documentation of its protocol, conduct, and evaluation complying with GCP rules.

The DGDA considers it essential that the principal investigator(s) sign the study reports after their completion, either in an unqualified fashion or clearly taking responsibility for all aspects of the conduct of the study for which they might reasonably be held responsible. If the signature of the principal investigator is absent from the report of a bioavailability or bioequivalence study, it will be requested by the DGDA during the evaluation process.

## Module 1.12 Information on Price

| Documentation | |
|---|---|
| 1.12.1 | Proposed maximum retail price/indicative price |
| 1.12.2 | Estimated price per dose, per day treatment, and cost of the recommended course of treatment |

***1.12.1 The manufacturer should provide the proposed maximum retail price for the product.***

***1.12.2 The estimated price/dose/day treatment and cost of the recommended course of treatment for the medicine should be provided by the manufacturer.***

## Module 1.13 Pediatric Development Program (For Future Implementation by DGDA)

| Documentation | |
|---|---|
| 1. | References to pediatric development program |

There is a recognized global problem with the availability of pediatric-specific formulations and a lack of information from proper investigations of the use of medicines in children. This problem leads to medicines being used outside of their approved indications, and at times, being reformulated by pharmacists to make them more suitable for use by children. However, the basic precept that children should

not be discriminated against by being supplied poorly investigated medicines has been accepted internationally.

The CTD guidelines require that the safety and efficacy in the pediatric population should be routinely analyzed in applications for a proposed indication that occurs in children.

Please state whether there is a pediatric development program for this medicine and if so, refer to the relevant sections of the dossier.

## Module 1.14 Risk Management Plan

The applicant should include a risk management plan for biological products and for a generic medicine, where a safety concern with the reference product requires additional risk minimization activities.

Unless the DGDA has agreed that it is not required, include a risk management plan for applications involving:

- A significant new registration (for example, new dosage form, new route of administration, significant change in indications).

- A significant variation in a registration (for example, new manufacturing process of a biotechnologically-derived product).

In some circumstances, products, such as fixed-dosed combination applications, may require a risk management plan.