# Guideline for quality assurance of locally sourced medical products for public health priority disease

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## About PQM+

The Promoting the Quality of Medicines Plus (PQM+) Program is a six-year cooperative agreement between USAID and USP to sustainably strengthen medical product quality assurance systems in low- and middle-income countries. The program works to improve medical product quality through cross-sectoral and systems-strengthening approaches and the application of international quality assurance standards across the pharmaceutical system. By sharing scientific expertise and providing technical support and leadership, PQM+ helps create resilient and robust local health systems that address diseases such as HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases, as well as improve maternal, newborn, and child health.

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# MESSAGE FROM THE DIRECTOR GENERAL

The *Guideline for quality assurance of locally sourced medical products for public health priority disease* is essential to mitigate anticipated risks associated with public health procurement. It is obvious that local sourcing promotes better access, but quality assurance of essential healthcare products with complex formulations throughout the supply chain is a challenging and tedious task. The Directorate General of Drug Administration (DGDA) is the sole responsible authority for quality assurance and regulation of medical products for public health protection.

Though Bangladesh is meeting about 98% of the domestic needs for medicines through local production but still public health priority programs are largely dependent on international partners to access quality-assured health products which is a significant barrier for the government to achieve its goal of universal health coverage through improving access to quality-assured essential health product in Bangladesh. WHO-Prequalification (WHO-PQ) of medical products is required/essential to ensure the quality, safety, efficacy, and reliability of expected therapeutic outcomes.

Bangladesh is graduating from Least Developed Country (LDC) to Developing Country (DC) status and in line with that, the donor's support is gradually decreasing for the supply of public health priority medical products Bangladesh needs to be self-sufficient and ensuring access to quality-assured medical products for the treatment of public health priority diseases. I am happy that the local manufacturers are coming forward to produce and supply medical products for public health priority diseases.

I hope this guideline will promote the regulation of locally sourced non-WHO-PQ medical products, mitigating potential risks associated with quality assurance and therapeutic efficacy. I am grateful to USAIDs PQM+ program for the high-level technical support in developing this guideline. I hope all the relevant stakeholders of the Government of Bangladesh will implement this guideline.

**Major General Quazi Md Rashid-Un-Nabi**
Director General,
Directorate General of Drug Administration

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## Acknowledgments

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## Contributors

The guidance document for approval and sourcing of locally manufactured public health priority medical products is a high-level document for promoting compliance to ensure the supply of quality-assured, safe, effective, and reliable medical products for the treatment of public health priority diseases.

The Directorate General of Drug Administration (DGDA) is the sole responsible authority for regulation to ensure quality, safety, efficacy, reliability, affordability, and availability of medical products and therefore is the custodian for the development and implementation of this guideline. The following technical and intellectual contributors to the development and/or review of this guidance document are acknowledged:

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## Abbreviations and acronyms

| | |
|---|---|
| API | active pharmaceutical ingredient |
| BP | British Pharmacopoeia |
| CAPA | corrective and preventive action |
| CEP | certificate of suitability to the monographs of the European Pharmacopoeia |
| CoA | certificate of analysis |
| CRO | contract research organization |
| DGDA | Directorate General Drug Administration |
| DGHS | Directorate General of Health Service |
| EP | European Pharmacopoeia |
| IP | International Pharmacopoeia |
| FPP | finished pharmaceutical product |
| Global Fund | Global Fund to Fight AIDS, Tuberculosis, and Malaria |
| GMP | good manufacturing practices |
| HIV | human immunodeficiency virus |
| MDR-TB | multidrug-resistant tuberculosis |
| NOC | No Objection Certificate |
| NF | National Formolary |
| PQM+ | Promoting the Quality of Medicines Plus |
| TB | tuberculosis |
| TRS | Technical Report Series |
| USAID | US Agency for International Development |
| USP | US Pharmacopeial Convention |
| WHO | World Health Organization |
| WHO PQ | World Health Organization prequalification |

## Definition of terms

**Active pharmaceutical ingredient (API):** A raw material, intermediate, or API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house.

**Batch:** A defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it is expected to be homogeneous.

**Dosage form:** The physical form in which the manufacturer presents a pharmaceutical product (a form of presentation) and the form in which it is administered to the patients; examples include tablets, capsules, elixirs, injections, suppositories, and other forms.

**Finished pharmaceutical product (FPP):** A finished dosage form of a pharmaceutical product that has undergone all stages of manufacture, including the packaging in its final container and labeling.

**Labeling:** Information to the user is provided on the package label or in the patient information leaflet.

**Manufacturer:** Any person or legal entity engaged in the manufacture of a product subject to marketing authorization or licensing; may also refer to any person or legal entity that is an applicant or a holder of a marketing authorization or product license where the applicant assumes responsibility for compliance with the applicable product(s) and established standards.

**Marketing authorization:** A legal document issued by DGDA that authorizes the marketing or free distribution of a medical product in Bangladesh after evaluation of safety, efficacy, and quality; also referred to as product license or registration certificate.

**Pharmaceutical equivalence:** Products are pharmaceutical equivalents if they contain the same amount of the same active substance(s) in the same dosage form if they meet the same comparable standards, and if they are intended to be administered by the same route. However, pharmaceutical equivalence does not necessarily imply therapeutic equivalence, because differences in the excipients and/or the manufacturing process can lead to differences in product performance.

**Post-market control:** Activities applied by DGDA to the manufacturer and/or authorized distributor after the manufacturer placed the product on the market for patient use.

**Procurement:** The process of purchasing or otherwise acquiring any pharmaceutical product, vaccine, or nutraceuticals for human use. For the purpose of this document, ‘procurement’ means the release of the finished products by the manufacturers through a procedure of purchase order initiated by the procuring agency that is submitted to DGDA to ensure the product quality and continuous monitoring thereafter, meaning the purchase of the approved products from authorized

manufacturers. The procurement agency's preselection of the manufacturer is outside of this definition and the scope of this guideline.

**Procuring agency:** Public or private organization established as a not-for-profit organization, a nongovernmental organization, or a United Nations organization authorized for procurement, purchasing, storage, and distribution of pharmaceutical product(s) for human use.

**Quality control:** All measures designed to ensure the uniform output of batches of drugs that conform to established specifications, including identity, strength, purity, and other characteristics applicable to the dosage form.

**Shelf life:** The period of time during which a pharmaceutical product is expected to comply with the specification as determined by stability studies if it is stored as indicated on the label.

## Tables and annexes

## Executive summary

Bangladesh is a growing economy among the least-developed countries and is now in a transition phase of graduating to become a developing country by November 2026[1]. Several development organisations provide support to Bangladesh for supplying public health priority medical products, including anti-tuberculosis (TB), anti–human immunodeficiency virus (HIV), and antimalarial medicines. The Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund) provided seven grants with a total sum of up to US$169 million for 2021–2023 regarding diagnosis, detection, and treatment of HIV, TB, and malaria cases in Bangladesh. Two TB grants were allocated with a total sum of US$124 million for the year 2021–2023 to support the Government of Bangladesh. Diverse partners from the public, private, and community sectors intensify sustainable efforts for controlling the TB burden and the journey towards achieving Sustainable Development Goal 3, 'Good Health and Well-being,' which is linked to the World Health Organization's (WHO) End TB Strategy[2].

The Global Fund is providing support to Bangladesh for procuring anti-TB medicines to treat TB in the infected people of Bangladesh. Because Bangladesh is now graduating from a least-developed country to a developing country, the Global Fund support for anti-TB medicines started phasing out in 2022 by 20 per cent each year and will phase out completely in 2026. After 2026, the Government of Bangladesh needs to be self-sufficient with access to priority medical products for TB, HIV, and malaria. Currently, the Global Fund is providing the supply of anti-TB medicines from globally recognised WHO-prequalified sources. WHO-prequalified products are quality assured, which ensures interchangeability studies bioequivalence, comparative dissolution, and other essential quality attributes.

Because the Global Fund support is phasing out, Bangladesh needs to budget for TB medicines. TB is a public health priority communicable disease, and therefore the treatment must be done with quality-assured medical products for global health security and to ensure public health protection. However, local private pharmaceutical manufacturers were not interested in manufacturing TB medicines, because private procurement and supply of TB medicines are restricted in Bangladesh.

With technical support from WHO and the US Agency for International Development (USAID), in 2018, the Directorate General of Drug Administration (DGDA) and the Bangladesh Association of Pharmaceutical Industries took the initiative to identify potential manufacturers for local production of first-line anti-TB drugs in country. Then, collaborating with the government, the USAID-funded Promoting the Quality of Medicines Plus (PQM+) Programme took the initiative to support the pharmaceutical industry for the development, manufacturing, and prequalification of ant-TB medicines, which will help to ensure a quality supply of prequalified priority medicines to

[1] Islam MT, Apurbo, SR. Revisiting the patent regime of Bangladesh: compatibility with TRIPS and international best practices. J Intellect Prop Law Pract. 2023 Jul;18(7):512–27.

[2] The Global Fund Bangladesh TB Profile. 2022, https://www.theglobalfund.org/media/12351/oig_gf-oig-22-015_report_en.pdf

Bangladesh, public health protection, and successful implementation of the global health security agenda.

DGDA is the sole responsible authority for the regulation of medicines, vaccines, biologics, medical devices, and in-vitro diagnostics in Bangladesh. In 1974, the Directorate of Drug Administration was established as a department under the Ministry of Health and Population Control, and on 10 January 2010, the Directorate of Drug Administration upgraded to DGDA as a separate division under the Ministry of Health and Family Welfare. DGDA plays a key role in licensing premises, regulatory inspection, registration and marketing authorization, laboratory testing, post-marketing surveillance, and pharmacovigilance of medical products. Through the all-regulatory functions, DGDA will put significant interventions in place for government procurement and supply of public health priority medical products to ensure quality, safety, and efficacy, in line with WHO prequalification (WHO PQ) standards.

WHO PQ is a long and time-consuming process, but in the meantime, DGDA can ensure the quality of the medical products for public health priority needs through good regulatory practices at WHO PQ standards. Local production, supply, and access to those medical products can be ensured with proven efficacy and by mitigating anticipated risks for public health protection.

## Background

The USAID-funded PQM+ Programme, led by the US Pharmacopeial Convention (USP), aims to strengthen the supply of quality-assured medicines in low- and middle-income countries. Towards this aim, the PQM+ program has been working with several implementing partners in Bangladesh, including the DGDA, the Bangladesh Association of Pharmaceutical Industries, and other stakeholders such as local manufacturers and contract research organizations (CROs), to increase the supply of quality-assured essential medicines.

Bangladesh is a highly populated nation within the low- and middle-income countries and is one of the 49 nations listed by WHO as a high TB burden country with multidrug-resistant tuberculosis (MDR-TB)[3]. Over the past several decades, multiple partners, including United Nations agencies, have engaged in the worldwide procurement and supply of essential medicines, such as anti-TB medicines, that are sourced primarily from WHO-prequalified manufacturers and suppliers. Recently, through government-financed public procurement, the Directorate General of Health Service (DGHS) is funding the procurement of TB medicines from local manufacturers. Currently, there are no WHO-prequalified anti-TB medicines produced by local manufacturers in Bangladesh, and DGDA is not involved in the approval of locally manufactured medicines. However, the government is responsible for funding the National TB Control Programme for procuring anti-TB medicines, is involved in approving the product, and is responsible for reviewing the medicines' quality, safety, efficacy, and compliance with regulatory standards.

TB is an opportunistic communicable disease that is borderless, and therefore the concern is increasing that the use of potentially ineffective medicines could pose various risks to TB patients, including the development of MDR-TB, increased MDR-TB transmission, and TB burden, wasting of scarce financial resources, treatment disruption and/or failure, adverse drug events, and antimicrobial resistance, among others. The supply of non-WHO-prequalified anti-TB medicines manufactured locally must be undertaken with extra precaution to safeguard public health from a proliferation of MDR-TB cases. DGHS is responsible for approving the supplier/vendor as part of the procurement of medical products for public health, and it is recommended that DGDA review the quality-related documents to ensure the quality of medical products through regulatory compliance. In response to this current situation, DGDA, collaborating with the PQM+ program, is undertaking initiatives to mitigate the potential risks that may arise from sourcing non-WHO-prequalified priority medicines. Accordingly, this guideline on risk-based approval of priority medicines is developed to strengthen the capacity of local manufacturers and to pave the way forward for approval of locally sourced priority medicines in Bangladesh.

[3] World Health Organization [Internet]. Geneva: The Organization; High TB burden country profiles. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022/high-tb-burden-country-profiles

# Introduction

This guideline provides instructions on fulfilling the requirements for each batch consignment approval prior to their distribution for public use. The DGDA enforces the basic registration of medicines for the purpose of marketing authorization in Bangladesh. DGDA issues marketing authorization for locally manufactured products as per the requirements stated in form 1/88 (a requirement for marketing authorization for compendial medical products) or form 2/88 (a requirement for non-compendial medical products).

DGDA is responsible for making regulatory decisions and for the product's quality assurance, including the risk-based approval of priority medicines based on marketing authorization requirements and the mandates vested in it to ensure regulatory compliance. However, DGDA is not responsible for the manufacturer's selection process for procurement purposes. A risk-based evaluation is essential for public health priority medicines before placing the product on the market. DGDA is also mandated to conduct post-marketing surveillance and pharmacovigilance of all registered and marketed medical products. Currently, DGDA does not approve locally sourced batches of products except for the one-time licensing and marketing authorization of the product. However, DGDA issues a No Objection Certificate (NOC) for each consignment (lot/batch) of products imported from abroad. Regardless of the product source (imported or produced locally), all applicants should seek and obtain the NOC from DGDA.

DGDA continues to support local manufacturing and encourages procurement agencies to source products from the list of DGDA-accepted manufacturers because locally sourced products are the most cost-effective and sustainable market solutions to the public health needs of the citizens of Bangladesh. The supply of medicines from local manufacturers is a paradigm shift to the market dynamic compared to import, which brings benefits for the local manufacturers as well as increasing access to affordable medicines in the country.

This guideline is intended for locally manufactured priority medicines, such as anti-TB medicines, and lays out the requirements the local manufacturer must fulfill before shipping the product to local procuring agencies in Bangladesh. In this guideline, 'approval for distribution' means consignment approval as part of pre-shipment before the release of each batch for distribution and for patient use. All priority medicines procured under projects funded by the Government of Bangladesh are required to comply with DGDA's quality assurance and marketing authorization requirements. In addition, documents submitted in support of risk-based approval of locally manufactured priority medicines will be evaluated in line with the common technical document components of multisource generic products as outlined in Annex 4 of the WHO Technical Report Series (TRS) 970[4].

[4] World Health Organization Expert Committee on Specifications for Pharmaceutical Preparations. Annex 4 Guidelines on submission of documentation for a multisource (generic) finished Pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part. In: WHO Expert Committee. Forty-sixth report: WHO TRS No. 970: 2012. Geneva: The Organization.

## Submission requirements for vendor selection to procure medicines

The following criteria are prerequisites that must be fulfilled to apply for the risk-based approval of locally manufactured priority medicines:

- The product manufacturer has submitted a marketing authorization application for the product to DGDA **or** the WHO PQ team **or** stringent regulatory authority **and** accepted for review or obtained approval for pre-marketing authorization, **and**
- The product is manufactured at a site with a valid DGDA-issued manufacturing license, Drug Administration Registration (DAR) certificate, Marketing Authorization (MA) certificate, and the company complies with all standards of good manufacturing practices (GMP) as verified after inspection by DGDA **or** the WHO PQ team **or** stringent regulatory authority (SRA).

## Submission of documents for vendor selection to procure medicines

Applicant(s) who fulfill the above tender submission requirements of locally manufactured priority medicines should provide all the supporting documentation for a full evaluation for vendor selection.

### Cover letter

A cover letter written on company letterhead should be submitted, expressing interest in the supply of public health priority medicines.

### Manufacturing and GMP

The manufacturer should comply with GMP requirements at the time of submission and during the procurement period or during the application evaluation. The validity of the GMP status and the types of documents submitted should be stated in the application form (see Annex I).

### Active pharmaceutical ingredients source validation

The active pharmaceutical ingredient (API) supplier should preferably be WHO-prequalified and/or a holder of a certificate of suitability to the monographs of the European Pharmacopoeia (CEP) or a US FDA-submitted drug master file holder. The applicant may submit an application for an API sourced from a new supplier. However, using such a supplier carries a risk that may make sourcing the final product objectionable for procurement.

### Components and formulation

The finished product's components, including the formulation and the molar amount of the API and excipient's quantitative and qualitative composition, should be such that products manufactured locally are pharmaceutical equivalent to their comparators. The relative number of excipients

present in two solid oral finished pharmaceutical products (FPPs) is considered quantitatively similar if the differences in amount fall within the limits as described in WHO TRS 10003 Annex 6, Table A6.1[5].

### Certificate of Analysis (COA)

The product's test certificate is essential for quality evaluation. The manufacturer or marketing authorization holder or supplier should submit the certificate of analysis (COA) of the same batch intended to be supplied for public health procurement. The COA should be issued in the standard certification form provided in Annex II of this guideline.

For further quality evaluation, if needed and requested by the DGHS, the DGDA may evaluate the manufacturing process validation, Analytical Methods Validation, Cleaning Validation, etc.

### Product specification and methods of analysis

Applicants should submit official signed and dated specifications along with compendial references if available. For in-house specification, analysis method validation is essential for the quality evaluation. The DGDA may ask for further evidence documents like analysis methods validation and method of analysis to evaluate product specification.

### Stability data and storage condition

To support the proposed shelf life, applicants should present a long-term stability study on at least three commercial batch sizes. The study should be conducted in the proposed container closure for marketing so support storage conditions (temperature, relative humidity). The stability study should cover the product's full shelf life, and testing should be conducted on a product with the same formula and API source as the product that will be supplied and that was manufactured on the same site and packed in the same packaging material. In addition, the product's remaining shelf life should be at least 75 percent of its total shelf life before shipping the product from the manufacturer's warehouse.

### Bioequivalence (BE) and interchangeability data

To demonstrate therapeutic equivalence, applicants should submit a bioequivalence study a biowaiver study, or both. The DGDA will evaluate the Bioequivalence (BE) and interchangeability data during product registration, but if missing during product registration, the DGDA may ask for submission before evaluation of source for the procurement of public health priority medicines.

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[5] World Health Organization Expert Committee on Specifications for Pharmaceutical Preparations. Annex 6 Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. In: WHO Expert Committee. Fifty-first report: WHO TRS No. 1003: 2017, 188. Geneva: The Organization.

### Surveillance and post-marketing commitments

To ensure the fulfillment of marketing conditions, DGDA will use surveillance to monitor the quality and safety of commercially marketed products, including sampling and testing products, inspecting facilities, and analyzing complaints and adverse drug reaction reporting submitted by health professionals. To conform to these requirements, the applicant should submit the letter of commitment as outlined in Annex IV.

## Evaluation and risk-based categorization

For all priority products manufactured locally, DGDA will apply risk-based categorization based on the evaluation of submitted documents. The decision outcome will be categorized as follows:

- **Risk category 1:** DGDA has no objection to sourcing; voluntary post-market control is recommended.
- **Risk category 2:** DGDA has no objection to sourcing; mandatory post-market control is recommended.
- **Risk category 3:** DGDA has objection to sourcing; allowed only if there are no alternatives; mandatory post-market control is recommended.
- **Risk category 4:** DGDA has an objection to sourcing the product(s).

DGDA will review the application and the supporting evidence to determine the dossier's extent of completeness and its impact on product quality, safety, and efficacy based on the product's key attributes, including the API sourcing, components and formulation, quality control, stability, bioequivalence, and monitoring after batch release. Based on the supporting data evidence, the product will be categorised into one of the four risk categories based on the extent and perceived impact of observed dossier deficiencies. DGDA will issue a NOC only if it classifies the product as risk category 1 or 2 but will not issue a NOC for a product in category 3 or 4. However, the product may be sourced under a special agreement between the manufacturer and the procuring agency if there is a risk-benefit. Products in category 4 should not be sourced, and the manufacturer is recommended to provide additional documentation to improve the risk category.

*Table 1: Risk categorisation for sourcing of medical products*

| Attributes | Risk category | | | |
|---|---|---|---|---|
| | Category 1 | Category 2 | Category 3 | Category 4 |
| API source | API is sourced from a supplier that is WHO-prequalified and/or holds a CEP. Letter of access is available indicating the name of supplier and FPP | API is sourced from a supplier that is WHO-prequalified and/or holds a CEP. Letter of access is available indicating the name of supplier and FPP manufacturer. No | API is claimed to be sourced from a supplier that is WHO-prequalified and/or holds a CEP. However, no letter of access supports the claim, | API is not sourced from a supplier that is WHO-prequalified and/or holds a CEP, and the API manufacturing site |

| | | | | |
|---|---|---|---|---|
| | manufacturer. API manufacturing site is GMP compliant. | evidence exists to determine the GMP compliance status of the API manufacturing site. | and no supporting document exists to determine the GMP compliance status of the API manufacturing site. | is not GMP compliant. |
| API specification and control | The API specification is based on monograph and supplier specifications. The manufacturer has adequate quality control in place, including validated analytical methods. | The API specification is based on monograph and supplier specifications. The manufacturer has adequate quality control in place, including validated analytical methods. | The API specification is based on monograph and supplier specifications. However, one or more critical quality attributes of the analytical parameter are not validated. | The API specification is not based on monograph and supplier specifications. No evidence exists that the FPP manufacturer applied a validated analytical method. |
| FPP manufacturer | The FPP manufacturer facility is GMP compliant.<br>No pending corrective and preventive actions (CAPAs) are of concern. | The FPP manufacturer facility is GMP compliant. No pending CAPAs are of concern. | The FPP manufacturer facility is not GMP compliant, but no pending CAPAs are of concern. | The FPP manufacturer facility is not GMP compliant, or one or more pending CAPAs are of concern. |
| Manufacturing and formulation | The manufacturing process is validated, and the formulation has a similar qualitative and quantitative composition as with the comparator product. | The manufacturing process is validated, and the formulation has a similar qualitative and quantitative composition as with the comparator product. | The manufacturing process is validated, but the formulation has a significant qualitative and quantitative composition difference against the comparator product. | The manufacturing process is validated, but the formulation has significant qualitative and quantitative composition differences against the comparator product. |
| FPP specification and control | The FPP specification is based on a monograph. Supporting evidence exists that the manufacturer | The FPP specification is based on a monograph. Supporting evidence exists that the manufacturer has adequate quality | The FPP specification is based on a monograph. However, there is supporting evidence for | The FPP specification is not based on a monograph. No evidence exists that a validated |

| | | | | |
|---|---|---|---|---|
| | has adequate quality control methods in place, including a validated analytical method. | control methods in place, without a validated analytical method. | analytical methods and analytical method validation. | analytical method was applied. |
| Bioequivalence and interchangeability | A bioequivalence study report or dissolution profile study report to support biowaiver for biowaiver-eligible products is available, and related issues such as the source of a comparator and the CROs used for the bioequivalence study are acceptable. | A bioequivalence study report or dissolution profile study report to support biowaiver for biowaiver-eligible products is available, and related issues such as the source of the comparator but the CROs used for the bioequivalence study are not acceptable. | A bioequivalence study report or dissolution profile study report to support biowaiver for biowaiver-eligible products is available. However, issues exist with the source of the comparator, and the CROs used for the bioequivalence study are not acceptable. | A bioequivalence study report or dissolution profile study report to support biowaiver for biowaiver-eligible products is not available. |
| Stability and shelf life | The stability data support the claimed shelf life and storage conditions along with the study protocol. | The stability data support the claimed shelf life and storage condition but without an established protocol. | Stability data are available but incomplete to support the claimed shelf life and storage condition. | Stability data are not available to support the claimed shelf life and storage condition. |

*Note:* category 1: DGDA has no objection to sourcing; voluntary post-market control is recommended; Category 2: DGDA has no objection to sourcing; mandatory post-market control is recommended; Category 3: DGDA has objection to sourcing; allowed only if there are no alternatives; mandatory post-market control is recommended; category 4: DGDA has an objection to sourcing the product(s).

## Annex I: Application form

This application form is intended to be completed by the applicant(s)/manufacturer(s) who would like to distribute the product to the market in the next six months. Please complete this application in two (2) copies and return to DGDA with supporting documents as outlined in this guideline.

| | | |
|---|---|---|
| 1. | **General information** | |
| | Name of manufacturer | |
| | Address | |
| | **Contact information** | Email: |
| | | Telephone: |
| 2. | Distributor/procuring agency name | |
| 3. | **Product information** | |
| | Product name | |
| | Strength and dosage form | |
| | Packaging description and packaging material of construction | |
| | Does the product have a marketing authorisation issued by the Directorate General of Drug Administration (DGDA)? | Yes ☐ No ☐ |
| | Marketing authorisation number and validity | |
| | **Shelf life and storage condition** | |
| | Is the shelf life and storage condition based on stability data reviewed and approved by DGDA? | Yes ☐ No ☐ |
| | Is there any variation to the approved marketing authorisation condition listed above? | Yes ☐ No ☐ |
| 4. | **Manufacturing site good manufacturing practices (GMP) and inspection status** | |
| | Manufacturing licence | |
| | Validity date of the GMP certificate | |
| | Date of last DGDA inspection | |
| | Are B-lactam products or cytotoxic or hormonal products manufactured at this | Yes ☐ No ☐ |

| | | |
|---|---|---|
| | facility with the product listed under item 2 above? | |
| | Is there a major pending corrective and preventive action (CAPA) not yet addressed? | Yes ☐ No ☐ |
| | Are there pending GMP-related CAPA that are not addressed? | Yes ☐ No ☐ |
| | Other international certification(s) | Yes ☐ No ☐ |
| | Names of all other regulatory authorities that have inspected the company | Provide copies of GMP and other certifications |
| 5. | **API source, specification, and control** | |
| | Is the API sourced from a supplier prequalified with World Health Organization and/or in possession of a certificate of suitability to the monographs of the European Pharmacopoeia? | Yes ☐ No ☐ |
| | Is the specification based on drug master file and monograph? | Yes ☐ No ☐ |
| | Does the specification and control support with validated analytical method? | Yes ☐ No ☐<br>Provide API specification and validated analytical method |
| 6. | **Finished pharmaceutical product (FPP) specifications and control** | |
| | The FPP is in line with the monograph as indicated in the: | BP ☐ EP ☐ USP ☐ International Pharmacopoeia ☐<br>Validated in-house ☐ Other ☐ Specify_____<br>Provide FPP specification and validated analytical method as an attachment |
| 7. | **Manufacturing process** | |
| | Is the manufacturing process validated for commercial batch-sizes using three prospective validation runs? | Yes ☐ No ☐ |
| 8. | **Stability study and storage condition of finished product** | |
| | Is the stability study available to cover the claimed shelf life and storage condition? | Yes ☐ No ☐<br>Provide stability study data as an attachment |

| | | |
|---|---|---|
| | Is the stability study conducted in the packaging materials of the product to be marketed? | Yes ☐ No ☐<br>Provide process validation documents as an attachment |
| 9. | **Equivalence and interchangeability** | |
| | Bioequivalence study is available and conducted using acceptable comparator at acceptable contract research organisations | Yes ☐ No ☐<br>Provide bioequivalence study report and supporting documents |
| | Product is eligible for biowaiver, and dissolution study profile using an acceptable comparator is available | Yes ☐ No ☐<br>Provide biowaiver supporting documents, including API solubility study and dissolution profile study report |
| 10 | **Commitment** | |
| | All the commitment letters are signed and submitted with the standard language recommended | Yes ☐ No ☐ |

## Annex II: Standard batch release certification

For each consignment, the product must be accompanied by the certificate of analysis (CoA) and the standard batch release certificate issued in the format provided below. The standard batch release certificate conforms to the format recommended by the World Health Organization (general instructions and explanatory notes attached)[6], and it must be issued by the manufacturer's authorised person with the company letterhead, signed, and dated.

| | |
|---|---|
| 1. Certificate number: | |
| 2. Name of distributing/procuring agency | |
| 3. Name of the product | |
| 3.1. Dosage form | |
| 3.2. Active ingredient and amount per unit dose | |
| 3.3. Is the composition of the product identical to that approved by Directorate General of Drug Administration? | Yes ☐ No ☐ |
| If no, please attach formula (including excipients) of both products, and provide justification for the difference in formulation composition. | |
| 4. Name and address of manufacturer (licence holder) | |
| 4.1. Marketing authorisation number | |
| 4.2. Date issued | |
| 5. Production reference number (batch manufacturing record) | |
| 5.1. Batch number | |
| 5.2. Batch size | |
| 5.3. Date of manufacture | |
| 5.4. Shelf life (months) | |
| 5.5. Package size | |
| 5.6. Primary container material | |
| 5.7. Secondary container material | |
| 5.8. Storage conditions | |
| 6. Certificate of analysis number (provide the certificate as an attachment) | |
| 6.1. The specification complies with: | BP ☐ EP ☐ USP ☐ International Phar ☐<br>Validated in-house ☐ Other ☐<br>Specify_____ |

[6] WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce (Revision 5); https://iris.who.int/handle/10665/63547

| | |
|---|---|
| | Provide finished pharmaceutical product specifications and validated analytical method as an attachment |
| 6.2. Does the batch comply with all parameters tested? | Yes ☐ No ☐ |
| Name and address of authorised person: stamp and date: | |
| Telephone number: | |
| Signature of authorised person: | |
| Stamp | |
| Date | |

## Annex III: Purchase order request form

Once the product is reviewed and listed in the approved risk-based evaluated list by DGDA, the primary recipient or procuring agency or third-party distributor on behalf of the principal recipient and/or the manufacturer of the product should complete this purchase order. Complete three (3) copies using the company letterhead and submit the completed form for approval of each consignment before shipping the product from the manufacturer to the distributor warehouse. The PO should always be accompanied by the manufacturer's proforma invoice and batch release certification form.

| Product name | Dosage form | Strength | Pack size | Quantity | Remaining shelf life |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

| Billing information | | | |
|---|---|---|---|
| Manufacturer name | | Reference number | |
| Contact person name | | | |
| Email | | | |
| Telephone | | | |
| Designation/title | | | |
| Recipient information | | | |
| Company name | | | |
| Contact person name | | | |
| Email | | | |
| Telephone | | | |
| Designation/title | | | |
| **To be completed by DGDA** | | | |
| Approved by | | Approval number | |

| | | |
|---|---|---|
| Email | | |
| Telephone | | |
| Designation/title | | |
| Signature | Date | |

## Annex IV: Post-marketing commitments

I, the undersigned, [name, position in the company], acting as a responsible person for [name of the company], certify that the information provided in this document is correct and true.

☐ I certify that the product to be supplied will meet the required standard in all aspects of manufacturing, including formulation, process, method, and site of manufacture. The sources of active and excipient starting materials, quality control of the product and starting material, packaging, shelf life, and product information are consistent with the marketing authorisation requirements and the standards issued by DGDA.

☐ I certify that if any changes occur to the information after the submission of this product application, the manufacturer/supplier commits to provide the relevant update to DGDA as soon as possible.

☐ I certify that a sample of product from at least one batch of the product is subjected to ongoing stability monitoring. Any out-of-specification or significant changes or atypical trends will be investigated and reported to DGDA.

☐ I commit and confirm that we have a round complaint-handling system to monitor post-marketing activities of our product related to safety, quality, and effectiveness. All complaints will be investigated, and any complaints that have an impact on product quality and are warranted for product recall will be reported to DGDA.

Signature:

**Stamp and/or official seal:**

Name:

Designation:

Organisation

Date: