Application for Prequalification of an

Active Pharmaceutical Ingredient (API)

Abridged Procedure

Please complete each section of this application form electronically. Please ensure an electronic and printed version of this application form accompanies your submission for API prequalification.

# 1. Application details

|  |  |
| --- | --- |
| 1. Application details Active pharmaceutical ingredient  *International Nonproprietary Name, including salts/counter ion, solvated state* |  |
| **API master file (APIMF) manufacturer’s internal API code (if applicable)** |  |
| **APIMF version number**  **Applicant’s part version number and date (yyyy-mm-dd)**  **Restricted part version number and date (yyyy-mm-dd)** | Open part:  Restricted part: |
| **APIMF holder company**  **Company name**  **Corporate address**  **Phone**  **Fax**  **Email** |  |
| **Agent's name (if applicable)[[1]](#footnote-1)** |  |
| **Contact person responsible for this application** | Title (*Ms, Mr Dr*):  First Name:  Family Name: |

|  |  |
| --- | --- |
| Contact person's position |  |
| **Contact person's postal address** | |
| **Unit** |  |
| **Building/PO Box Number** |  |
| **Road/Street** |  |
| **Plant/Zone** |  |
| **Village/Suburb** |  |
| **Town/City** |  |
| **District/Mandal** |  |
| **Province/State** |  |
| **Postal code** |  |
| **Country** |  |
| **Contact person's email address** |  |
| **Contact person's phone number** |  |
| **API manufacturing site(s) address**  **The steps undertaken at the site:**  ***Repeat section, as needed*** |  |
| **Manufacturer’s name** |  |
| **Unit** |  |
| **Building/PO Box Number** |  |
| **Road/Street** |  |
| **Plant/Zone** |  |
| **Village/suburb** |  |
| **Town/City** |  |
| **District/Mandal** |  |
| **Province/State** |  |
| **Postal code** |  |
| **Country** |  |
| **Phone** |  |
| **Fax** |  |
| **Email** |  |
| **GPS (WGS 84) of site (place to be specified if not main entrance) expressed to 1/10th of a second accuracy** |  |

|  |  |
| --- | --- |
| API intermediate manufacturing site(s) address  The steps undertaken at the site:  *Repeat, as needed* |  |
| **Manufacturer’s name** |  |
| **Unit** |  |
| **Building/PO Box number** |  |
| **Road/Street** |  |
| **Plant/Zone** |  |
| **Village/Suburb** |  |
| **Town/City** |  |
| **District/Mandal** |  |
| **Province/State** |  |
| **Postal code** |  |
| **Country** |  |
| **Phone** |  |
| **Fax** |  |
| **Email** |  |
| **GPS (WGS 84) of site (place to be specified if not main entrance) expressed to 1/10th of a second accuracy** |  |
| **Sterility status** | Sterile  Non-sterile |
| **Quality standard claimed for the API**  *e.g. pharmacopoeial (state which), or in-house* |  |
| **Elemental impurities approach based on ICHQ3D** | Option 1: No risk assessment summary is provided  Option 2. Risk assessment summary is provided |
| **Nitrosamines Risk- Assessment** | A nitrosamine Risk Assessment Report is provided. |
| **Other relevant information**  *e.g. polymorphic form, manufacturing route identifier (e.g. process I), grade (e.g. particle size)* |  |

# 2. Active Pharmaceutical Ingredient Master File (APIMF)

The submitted APIMF has been assigned the following API manufacturer's version number:

Open part: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Closed part: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

(Please select one option below only and delete the remaining options.)

**OPTION 1 - APIMF Assessed Previously Using APIMF Procedure**

No APIMF is included with this application. In support of this application reference should be made to APIMF\_\_\_\_\_\_\_\_\_ (*WHO APIMF number*), which is currently accepted by the PQTm.

The currently submitted APIMF meets the documentation requirements specified on the PQTm website.

**OPTION 2 - Abridged Assessment of an APIMF Previously Approved by an Authority applying stringent standards**

The APIMF included with this application has not previously been submitted to the WHO Prequalification Team: medicines (PQTm).

The submitted APIMF is identical to the APIMF details currently accepted by either the European Directorate for the Quality of Medicines & HealthCare (EDQM) or The United States Food and Drug Administration (US FDA). WHO PQT is requested to assess this API on the basis of the assessment reports from the authority in indicated below.

European Directorate for the Quality of Medicines & HealthCare (EDQM)

The United States Food and Drug Administration (US FDA).

*Select one*

PLEASE ENSURE THE APPENDED HISTORY OF CHANGES DOCUMENT IS COMPLETED AND INCLUDED WITH THIS APPLCATION

# 3. Other information

In addition to the authority nominated above, if the APIMF document (current version) is lodged with other medicines regulatory agencies, please list each separately in the table below.

|  |  |  |
| --- | --- | --- |
| Agency |  |  |
| **Date of submission** |  |  |
| **Agency’s code for APIMF (if applicable)** |  |  |
| Is this active substance master file (ASMF)/drug master file (DMF) identical to the ASMF/DMF filed in the above mentioned country or jurisdiction? |  |  |
| If not, ensure that the differences are described in the ASMF/DMF. |  |  |

# 4. Site Master File

(Please select one option only and delete the remaining options.)

**Option 1**

1. The site master file (SMF) included with this application has not previously been submitted to PQTm.

2. The SMF has the assigned company version number:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

*(State the SMF version number.)*

**Option 2**

1. The SMF included with this application is an updated version of the SMF previously submitted to PQTm. The previously-submitted SMF has the version number \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.(*version number of previously submitted SMF*).

The SMF replaces the SMF currently held by PQTm.

2. The SMF has the assigned company version number:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

*(State the SMF version number.)*

**Option 3**

1. No SMF has been included with this application. Reference should be made to the SMF previously submitted to PQTm in correspondence dated \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (*date of previous submission*).

2. The previously submitted SMF has the assigned company version number:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

*(State the SMF version number.)*

# 5. Evidence of compliance with Good Manufacturing Practices (GMP)

## 5.1 Inspection declarations

(Please select one option only and delete the remaining options.)

**Option 1**

To establish that the indicated site(s) of API manufacture is/are operating in compliance with GMP, \_\_\_\_\_\_\_\_\_\_\_\_ (*company name*) requests that WHO arranges to inspect this/these facility(ies).

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Option 2**

To demonstrate that the indicated site(s) of API manufacture is/are operating in compliance with GMP, evidence of this compliance has been included with this application. Nonetheless, \_\_\_\_\_\_\_\_\_\_\_\_ (*company name*) acknowledges that WHO may need to inspect this/these facility(ies).

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_

## 5.2 A summary of the evidence of compliance with GMP submitted with application

(If supporting documentation has been provided, please summarize briefly below.)

|  |  |  |  |
| --- | --- | --- | --- |
| Type of document | Issuing authority | Date of issue | Remark |
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# 6. Declaration

I, the undersigned, on behalf of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (company name) declare that the information contained in this application form and in the submitted documents is accurate. I confirm that information in the application form and the submitted documents does not contain intentionally misleading information, nor has information been withheld that might affect the assessment of compliance with WHO requirements.

I confirm that the submitted APIMF meets the documentation requirements specified on PQTm’s website.

I confirm that the sites of manufacture specified in the submitted APIMF are operating in compliance with ICHQ7 GMP.[[2]](#footnote-2)

I confirm that the API manufacturer has undertaken review of their API intermediate suppliers to determine that they are operating in compliance with ICHQ7 GMP.2

I confirm that PQTm may undertake an on-site inspection at any time, either announced or unannounced, to confirm that the API manufacturing site, and or any associated intermediate, testing or contract manufacturing site, is manufacturing in compliance with WHO GMP standards.

I confirm that I understand the obligations and conditions of the API Prequalification procedure as outlined in Annex 4, WHO Technical Report Series, No. 953, 2009.

I confirm that a risk assessment for the presence of nitrosamines has been conducted for this API and that the risk assessment outcome has been integrated into the relevant CTD sections and the risk assessment report appended to the APIMF. In case a risk of presence of nitrosamines has been identified, I confirm confirmatory testing has been undertaken. In case the presence of nitrosamines has been confirmed, risk mitigation measures have been undertaken.

Name:

Signature: Date:

Position within company:

# 6. Application Checklist

To ensure a complete application, please use this checklist to verify that all required information has been prepared for submission on a single CD or DVD.

|  |  |
| --- | --- |
| Item | *Submitted*  *(Yes / Not applicable)* |
| 1. A cover letter (paper copy) |  |
| 1. A **single** clearly labelled CD or DVD containing: |  |
| * the cover letter (Word or text-selectable PDF) |  |
| * the API prequalification application form (Word)   AND   * the signed API prequalification application form (PDF) |  |
| * the APIMF correctly formatted (Module 3, see documentation requirements section) |  |
| * the Module 2 Quality Overall Summary |  |
| * the [site master file (SMF)](http://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesDraftingSiteMasterFileTRS961Annex14.pdf?ua=1) for each manufacturing site (Word or text-selectable PDF) |  |
| * evidence of compliance with GMP, or a request for inspection by WHO for each manufacturing site (Word or text-selectable PDF) |  |
| * a copy of the letter to EDQM or US FDA authorizing sharing of the APIMF assessment report with WHO |  |
| * a copy of the History of Changes document if reliance upon another authority’s assessment reports is proposed. |  |

The cover letter and CD/DVD should be sent to:

World Health Organization  
WHO Prequalification Team: medicines  
MHP/RPQ/PQT Room 613  
20 Avenue Appia  
1211 Geneva 27  
Switzerland

Or

Via a secure link to an online document repository.  The link should be sent in an email  to the following email address: [APIassessment@who.int](mailto:APIassessment@who.int)  The Subject line of the emails should clearly indicate the application and the specific medicine procedure referred to. The date of receipt will be the date the file is successfully downloaded. If you have any questions regarding this please contact Dr Matthias Stahl, [stahlm@who.int](mailto:stahlm@who.int)

# 7. APPENDIX 1 – History of Changes

|  |  |
| --- | --- |
| WHO application number |  |
| Date |  |
| Manufacturer |  |
| API |  |
| Version number of AP master file (APIMF) submitted to WHO: |  |

|  |  |
| --- | --- |
| History of original submission to recognized authority | |
| Name of authority |  |
| Date of original submission to authority |  |
| Date of responses to authority |  |
| Date of approval |  |

|  |  |
| --- | --- |
| Document versions | |
| Identifying document version number of APIMF originally submitted to authority |  |
| Identifying document version number of APIMF finally accepted by authority. |  |
| Identifying document version number of APIMF current held by authority |  |

IMPORTANT NOTE:

*When completing this form please keep in mind that the primary purpose of requesting this information is that the reference authoritiesassessment report will often mention APIMF details that are no longer stated in the current APIMF. This form should allow the assessor to quickly determine what has changed, when this change occurred, for what reason and by what mechanism.*

*The assessor must reconcile those details assessed originally by the* authority *and those details currently proposed. It is important therefore to:*

1. identify the differences between the details mentioned in the assessment report and those stated in the APIMF submitted to WHO
2. explain why these details are different, i.e. were they changed at the request of the authority during assessment, changed by post-approval variation, or changed for the purposes of submission to the WHO.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| History of Changes table | | | | | | | |
| Common Technical Document (CTD) section | APIMF Details originally submitted to the authority | APIMF details accepted by the authority at time of initial approval | APIMF details currently accepted by the authority for this APIMF | | | | APIMF details being proposed to WHO |
| **Current details accepted by authority** | **Reason for change** | **Notification type** | **Date of notification to authority** |
|  |  |  |  |  |  |  |  |
| *For example* |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| *3.2.S.4.1* | *Original API specifications*  *V001 – Aug-11* | *Updated specifications to include a test for residual solvents*  *V003 – Nov-11* | *V004 – Feb-12* | *Tightening of solvent limit* | *Type IA* | *24th January 2012* | *V004 – Feb-12* |
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1. If an agent is making this application on behalf of the manufacturer then a relevant letter of authorization from the API manufacturer should be attached to this application form. [↑](#footnote-ref-1)
2. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. See: [www.ich.org/](http://www.ich.org/). [↑](#footnote-ref-2)