South African Health Products
Regulatory Authority
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GUIDELINE FOR THE API MASTER FILE (APIMF) PROCEDURE

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of medicines and variations. It represents the Authority's current thinking on the safety, efficacy and quality of medicines. It is not intended as an exclusive approach. SAHPRA reserves the right to request any additional information to establish the safety, efficacy and quality of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The Authority is committed to ensure that all registered medicines will be of the required safety, efficacy and quality. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available on the SAHPRA website: www.sahpra.org.za

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue and published for implementation	June 2020
2	Issued for implementation: – To amend the method of submission of the APIMFs and restricted parts to SAHPRA in section 3.3. – To include the use of a specific subject line to use for communication on the APIMF email address. – To include that the submission form should be sent to the APIMF email address to express interest in submitting the APIMF or restricted part. – To include the process of the submission of the APIMF or restricted part to SAHPRA's FTP portal. – To amend the submission form titled as **Annexure C** in this document. – To include further details on the submission form regarding the associated product. – To include further details to describe the characteristics of the API such as BCS class, stability and proposed storage conditions.	January 2021
3	– Content structured on the new SAHPRA Guideline Template – Old guideline number 2.59 changed to SAHPGL-PEM-02	September 2022

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Contents

Glossary

Abbreviation/ Term	Meaning
API	Active Pharmaceutical Ingredient
APIMF	Active Pharmaceutical Ingredient Master File
API manufacturer	A party involved in the manufacturing chain of the API.
APIMF holder	The holder of an Active Pharmaceutical Ingredient master file (APIMF)
APIMF number	A unique reference number allocated to the APIMF upon receipt of applications
APIMF record	SAHPRA's record of an approved API + manufacturer combination, evidenced by a unique APIMF reference number.
Applicant	The applicant can also be called the proposed holder of the certificate of registration.
Category A	Medicines which are intended for use in humans and which are, without manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine.
Category C	Medicines intended for veterinary use which are, without further manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine.
Category D	Complementary medicines intended for use in humans and animals, which are, without manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine.
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
Closed part of the APIMF	An applicant generally does not have access to this information, which is confidential intellectual property of the API manufacturer, including individual steps of the manufacturing method and manufacturing quality control procedures.
CTD	Common Technical Document
EDQM	European Directorate for the Quality of Medicines
EMA	European Medicines Agency
FPP	Finished Pharmaceutical Product
GPS	Global Positioning System
HCR	Holder of certificate of registration
Manufacturing chain	A clear flow chart or written text explaining the manufacturing and distribution route of the API from the first starting materials to the final API as

	delivered to the applicant/HCR.
Open part of the APIMF	The applicant must have access to this information, and it must be sufficient for the applicant to ensure the suitability of the API used in the finished pharmaceutical product.
QOS	Quality Overall Summary
Quality	The suitability of either an API or FPP for its intended use. This term includes such attributes as the identity, strength and purity.
RRA	Recognised regulatory authority
SAHPRA	South African Health Products Regulatory Authority
SCoRE	Summary of Critical Regulatory Elements
SMF	Site Master File

1. INTRODUCTION

An Active Pharmaceutical Ingredient Master File (APIMF) contains all the required information for the quality[1] evaluation of an API. The APIMF is comprised of two parts:

- The open part[2]: The applicant must have access to this information, and it must be sufficient for the applicant to ensure the suitability of the API used in the finished pharmaceutical product (FPP)

- The closed part[3]: The applicant does not have always access to this information, which is confidential intellectual property of the API holder, including a detailed description of the manufacturing process (with individual steps[4]), manufacturing quality control procedures, process validation etc.

Please see **Annexure A** of this document for a high-level overview from the European Medicines Agency (EMA) on content guidelines for the open part versus the closed part of the APIMF.

Generally, API holder shares only the open part of the APIMF with the applicants to whom they supply the API. Applicants therefore only submit the open part of the APIMF in a new registration application. However, SAHPRA requires both the open and closed part of the APIMF to evaluate an API's quality.

Previously, obtaining the closed part necessitated back-and-forth communication with the API holder through the applicant.

Going forward, SAHPRA will have an APIMF Procedure in place to avoid this, and to achieve other objectives.

1.1 Purpose

The objectives of the APIMF[5] Procedure are as follows:

- To ensure that the API holders proprietary information is managed confidentially end-to-end:

    - Communication on the closed part of the dossier is kept separate from that of the open part (i.e. the applicant will not receive queries on the closed part, which could contain sensitive information). The applicant will be notified that questions to the APIMF holder have been submitted.

    - A SAHPRA submission portal with strict access permissions for submission of the APIMF and restricted parts.

    - The APIMF will be stored electronically, with strict access permissions.

- To allow one evaluation of an API from a specific manufacturing site to be used across multiple finished pharmaceutical product (FPP) evaluations, reducing quality evaluation timelines.

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[1]Can be referred to as Chemistry, Manufacturing and Controls (CMC).
[2]Can be referred to as the Applicant's Part (AP).
[3]Can be referred to as the Restricted Part (RP).
[4]This can include starting materials, intermediates, reaction conditions, temperature, test methods, data of critical steps, in- process control procedures and process validation data.
[5]Can be referred to by different documents or regulators as the DMF (Drug Master File), DSMF (Drug Substance Master File) and ASMF (Active Substance Master File)

1.2 Scope

Until further communication is issued, the APIMF Procedure will apply exclusively to Category A medicines. This does not preclude a modified APIMF Procedure being applied to Category C or Category D medicines in the future.

The APIMF Procedure is not applicable to the following categories of medicines:

- Pre-evaluated APIs:
    - APIs with a certificate of suitability of monographs of the European Pharmacopoeia (CEP) from the European Directorate for the Quality of Medicines (EDQM)
    - APIs that are pre-qualified by the World Health Organisation (WHO)
- Biological active substances:
    - The concept of the APIMF is not applicable to biological active substances. In line with EMA's view (see Annex 5 of EMA's Guideline on Active Substance Master File Procedure), the characterisation and determination of a biological active substance's quality requires extensive knowledge of the manufacturing process and its controls, and the applicant therefore requires full and transparent access to all quality-related data.

The APIMF Procedure should always be associated with a new registration or variation application, i.e. SAHPRA will not create an APIMF record for an API that is not part of an FPP intended to be registered in South Africa. Please note that the APIMF Procedure may or may not be used when there is no confidentiality issue between the applicant / FPP manufacturer and the API manufacturer, i.e. when they are the same company. Should the company want to use the APIMF for future submissions then it is advised that they apply for the APIMF procedure.

2. LEGAL PROVISION

The legal provision for the registration of medicines, medical devices or IVDs is covered in the Medicines and Related Substances Act No. 101 of 1965, as amended and the gazetted General Regulations.

Section 15(1) - (10) of the Act states:

(1) Every application for the registration of a medicine, medical device or IVD shall be submitted to the Chief Executive Officer in the prescribed form and shall be accompanied by —

(a) the prescribed particulars;

(b) samples of the relevant medicines;

(c) where practicable, samples of medical devices or IVDs; and

(d) the prescribed registration fee.

(2) As soon as possible after receipt by the Chief Executive Officer of an application contemplated in subsection (1), he or she shall inform the applicant in writing that the application is being considered.

(3) (a) If after consideration of any such application and after any investigation or enquiry which it may consider necessary the Authority is satisfied that the medicine, medical device or IVD in question —

(i) is suitable for the purpose for which it is intended;

(ii) complies with the prescribed requirements; and

(iii) is safe, efficacious and of good quality and, in the case of a medical device and IVD, performs as intended.

the Authority shall issue the applicant with a certificate of registration to that effect.

(b) If the Authority is not satisfied as contemplated in paragraph (a), it shall cause the applicant to be notified in writing of the reasons why it is not so satisfied and cause the applicant to be informed that he or she may within a period of 30 days after the date of the notification furnish the Chief Executive Officer with his or her comments on the Authority's reasons for not being so satisfied.

(c) If no such comments are submitted by the applicant within the said period, or if after consideration of any comments so submitted the Authority is still not satisfied as aforesaid, it shall reject the application.

(4) Every medicine, medical device or IVD shall be registered under such name as the Authority may approve.

(5) The Chief Executive Officer shall allocate to every medicine, medical device or IVD registered under this Act a registration number which shall be recorded in the register opposite the name of such medicine, medical device or IVD and which shall be stated in the certificate of registration issued in respect of such medicine, medical device or IVD.

(6) Any registration under this section —

(a) may be made subject to such conditions as may be determined by the Authority; and

(b) shall in the case of medicines, be valid for a period of five years.

(7) No condition shall be imposed under subsection (6) whereby the sale of the medicine in question by any person other than a pharmacist is prohibited or until after the applicant has in writing been notified by the Chief Executive Officer that the imposition of such condition is contemplated and invited to submit written representations to the Authority in regard to the matter.

(8) If no such representations are lodged by the applicant concerned within a period of 30 days after the receipt by him or her of any notification referred to in subsection (7), or if after consideration of any such representations the Authority is still of the opinion that the condition in question should be imposed, the Authority shall register the medicine, medical device or IVD concerned subject to the said condition.

(9) Notice of the rejection of an application for registration under this section in respect of a medicine, medical device or IVD referred to in subsection (3) of section 14 shall be given in the Gazette by the Chief Executive Officer.

(10) The Chief Executive Officer shall as soon as possible after the date of expiry of the appropriate period referred to in section 14 (3) publish in the Gazette the prescribed particulars in respect of all applications for registration received by him or her prior to such date.

Section 16(1) - (10) of the General Regulations states:

(1) Any person residing in the Republic may make an application for the registration of a medicine on an application form obtainable from the office of the Chief Executive Officer.

(2) The application referred to subregulation (1) must include the particulars of the person with appropriate knowledge of all aspects of the medicine who shall be responsible for communication with the Authority.

(3) The application contemplated in subregulation (1) shall be accompanied by-

(a) a screening form which is obtainable from the Chief Executive Officer which has

been completed by the applicant;

(b) a proposed label for use on the medicine;

(c) where applicable, a copy of the manufacturing licence together with the current Good Manufacturing Practice certificate from the regulatory authority of the country where the medicine is manufactured;

(d) in the case of specified Schedule 5, Schedule 6, Schedule 7 and Schedule 8 substances, a certified copy of a permit to manufacture such substances;

(e) all available data on the safety, efficacy and quality of the medicine, as may be determined by the Authority;

(f) proof of the existence of a manufacturing site, which may include a Site Master File;

(g) any other information as may be required by the Authority; and

(h) the applicable application fee.

(4) The information referred to in subregulation (3) shall be submitted in English.

(5) The application Form referred to in subregulation (1) shall contain at least the following information:

(a) particulars of the applicant and the prospective holder of certificate of registration, including:-

(i) name;

(ii) business address;

(iii) postal address;

(iv) telephone number;

(v) fax number, if applicable;

(vi) e-mail address, if applicable; and

(vii) contact details of the person referred to in subregulation (2) in the case of a juristic person; and

(b) particulars of a medicine, including -

(i) proposed proprietary name;

(ii) dosage form;

(iii) strength per dosage unit;

(iv) route of administration;

(v) the country where the medicine is manufactured;

(vi) registration status outside the Republic;

(vii) category, class and a statement identifying the discipline if falling under Category D;

(viii) the name of the manufacturer(s);

(ix) the name of any site where any bioequivalence data was generated; and

(x) approved name of each active pharmaceutical ingredient.

(6) A medicine, in respect of which an application for registration is made, must comply with the technical requirements as determined by the Authority.

(7) An application shall be made in respect of each individual dosage form and strength of a medicine.

(8) In the case where a medicine in respect of which an application for registration is made, is or was registered with any regulatory body outside the Republic, the following information in respect of such medicine shall accompany the application:

(a) a copy of the certificate of registration;

(b) professional information relating to the medicine;

(c) conditions of such registration; and

(d) any other information as may be required by Authority.

(9) The provisions of this regulation shall, with the necessary changes, apply to the application for the registration of veterinary medicines.

(10) An application referred to in subregulation (1) shall be accompanied by one sample of such medicine subject to the provisions of regulation 6(2).

3. NEW REGISTRATIONS

3.1 Submission requirements

Prior to submitting a new registration application, the applicant must obtain the following from the API manufacturer:

- A copy of the latest version of the open part of the APIMF
- A copy of the QOS of the latest version of the open part of the APIMF
- Letter of access (**Annexure B** of this document)
- APIMF number, if allocated by SAHPRA

3.1.1 Existing APIMF record

The applicant must include the letter of access and reference to the APIMF number in their new registration application to SAHPRA:

- The letter of access should be included in module 1.2.2.6.
- The APIMF number should be referenced in the application letter, as well as in the relevant parts of the Summary of Critical Regulatory Elements (SCoRE) document.
- SAHPRA's other submission requirements must be adhered to, and the full dossier must be submitted, including the open part of the APIMF.

3.1.2 No existing APIMF record

If the API manufacturer has not been allocated an APIMF number for that specific API, this means that an APIMF record has not been created by SAHPRA for the specific API + manufacturer combination.

In this case, the applicant should still include the letter of access in their new registration application. In addition, the applicant must request the API manufacturer to submit the following directly to SAHPRA:

- Submission form (**Annexure C** of this document)
- If applicable, reliance documentation (detailed in **Annexure C** of this document)
- The APIMF (both open and closed parts)

The Common Technical Document (CTD) structure applies to the APIMF. The granularity and placement of documents should follow SAHPRA's existing guidelines. For the submission of an initial APIMF, the relevant modules are as follows:

- Module 1.0: Submission letter (in place of application letter) as per **Annexure C**
- Module 1.4.1: Information about the experts
- Module 2.3.S: Quality Overall Summary (relevant section)
- Module 1.10: Reliance documentation (if applicable)
- Module 3.2.S: Quality information (relevant section)

The APIMF submission may be submitted in eSubmission format, as stipulated in SAHPRA's guidelines, but documents should be clearly labelled as closed part (CP) or open part (OP)[6].

Reliance can be used for the APIMF. If the same APIMF is on record with one of SAHPRA's recognised regulatory authorities[7] (RRAs), the API manufacturer can submit relevant documentation (approval letters, unredacted assessment reports) for the APIMF in Module 1.10 to expedite the evaluation process.

A situation may arise where multiple applicants submit applications for the same new API + manufacturer combination (i.e. where there is no existing APIMF record) at a similar time. If an API manufacturer has submitted the submission form and APIMF, but has not yet received an APIMF reference number, the date of submission can be referenced in the letter of access for subsequent applicants until the APIMF reference number is created.

[6]Documents can also be labelled applicant's part (AP) and restricted part (RP)
[7]Please see section 5.2 of SAHPRA's Quality and Bioequivalence Guideline for the list of RRAs.

It is the API manufacturer's responsibility to notify the applicants and SAHPRA about any changes to the open and/or closed part of the APIMF, so that applicants can update all affected dossiers accordingly.

The API holder can submit the submission form to SAHPRA via the following method:

- The submission form should be shared with SAHPRA via the dedicated email, APIMF@sahpra.org.za. The subject line of the email should clearly reference the associated FPP application as follows, Application number of FPP_Applicant name_API name (e.g. 123456_XYZ Pharmaceuticals_Dolutegravir Sodium)

- The APIMF documents will then be submitted to SAHPRA via a secure SAHPRA submission portal. Information on access to this portal will be shared with the APIMF holder once the Submission form has been received or by contacting, APIMF@sahpra.org.za.

The applicant must ensure that SAHPRA receives the submission form and the APIMF to arrive at approximately the same time as the registration application, i.e. not more than one month before and not later than one week after the application is received. If the aforementioned documents are not received within this timeframe, the application could be rejected. Note that SAHPRA will no longer receive any hard copies or couriered mail of the restricted part and complete APIMF.

3.2 Evaluation process

3.2.1 Existing APIMF record

The full dossier (including the open and closed parts of the APIMF) will undergo screening to ensure that all the required documents listed under 3.2. Existing APIMF record have been submitted.

Upon evaluation of the API, SAHPRA will reference the APIMF number in evaluating Module 3.2.S. The APIMF approval letter will be sufficient proof that the API + manufacturer combination has been previously evaluated and thorough quality evaluation of the API (Module 3.2.S) can be bypassed.

3.2.2 No existing APIMF record

The dossier will undergo screening to ensure that all the required documents listed under 3.3. No existing APIMF record have been submitted. SAHPRA will communicate directly with the API holder regarding screening queries on the closed part of the APIMF.

SAHPRA will evaluate the API (Module 3.2.S) in a separate report to the rest of the dossier. Evaluation queries for the closed part of the APIMF will be sent directly to the API holder. Evaluation queries for the open part of the APIMF will be sent to the applicant and the APIMF holder.

Once the API + manufacturer combination has been evaluated, SAHPRA will send an outcome letter to the API manufacturer, with a unique APIMF number for the specific API. The API manufacturer will be responsible for sharing this APIMF number (in the letter of access) with other applicants whose products use the API in question.

4. VARIATIONS

The APIMF holder, is responsible for keeping the content of their APIMF updated with respect to the actual synthesis / manufacturing process and controls. The quality control methods should be kept in line with the current regulatory and scientific requirements.

The applicant, on the advice of the APIMF holder, will submit a variation to SAHPRA. If the variation is contained in the closed part of the APIMF, the applicant must send the variation and advise the APIMF holder to submit the detailed closed part directly to SAHPRA.

The APIMF holder shall not make any changes to the content of the APIMF that may affect the quality or performance of the FPP without informing each relevant applicant and/or HCR, as well as SAHPRA. The notification to SAHPRA should be done through email to APIMF@sahpra.org.za, referencing the APIMF number, if allocated.

4.1 Submission requirements

4.1.1 Existing APIMF record

All variations to a product with an existing APIMF record must include a reference to the APIMF number. Apart from the APIMF number reference, the variation application submission follows the exact requirements of the latest relevant guidelines:

- Variations Addendum For Human And Veterinary Medicines [2.08] https://www.sahpra.org.za/document/variations-addendum-for-human-and-veterinary-medicines/
- Quality and Bioequivalence Guideline [2.02] https://www.sahpra.org.za/document/quality-and-bioequivalence/

The application should clearly indicate the change being proposed in the Tabulated Schedule of Amendments in Module 1.5.2.1.

Note: No variation application for a registered product with an APIMF number will be considered for evaluation without direct reference to the APIMF number in the application.

4.1.2 No existing APIMF record

If a registered product does not have an associated APIMF number, the variation application submission follows the exact requirements as outlined in 3.3. above and the latest relevant guidelines:

- Variations Addendum For Human And Veterinary Medicines [2.08] https://www.sahpra.org.za/document/variations-addendum-for-human-and-veterinary-medicines/

- Quality and Bioequivalence Guideline [2.02] https://www.sahpra.org.za/document/quality-and-bioequivalence/

The application should clearly indicate the change being proposed in the Tabulated Schedule of Amendments in Module 1.5.2.1.

Note: SAHPRA may request a full APIMF (Open and Restricted part) for variations affecting the restricted part of the APIMF of a registered product.

4.2 Evaluation process

4.2.1 Existing APIMF record

The evaluation of a proposed change to the APIMF will be done for the first variation application. If more than one HCR submits the same variation application, it will not be re-evaluated in full. SAHPRA will verify the sameness of the variation applications, looking at the content and APIMF reference number, and reject or approve the subsequent applications based on the initial evaluation.

If there are specific evaluation queries on the closed part, these will be sent directly to the API holder. The APIMF report kept on record will be updated with the latest information (approved variations) for future reference.

4.2.2 No existing APIMF record

If a registered product does not have an associated APIMF number, evaluation of the variation application follows the exact requirements as outlined in 3.4.2. above and the latest relevant guidelines:

- Variations Addendum For Human And Veterinary Medicines [2.08] https://www.sahpra.org.za/document/variations-addendum-for-human-and-veterinary-medicines/

- Quality and Bioequivalence Guideline [2.02] https://www.sahpra.org.za/document/quality-and-bioequivalence/

5. REFERENCES

The following related documents are referenced:

5.1 Medicines And Related Substances Act, 1965 (Act No. 101 Of 1965) As Amended

5.2 Medicines And Related Substances Act, 1965 (Act No. 101 Of 1965) As Amended: General Regulations

6. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the previous guideline for The API Master File (APIMF), old document number 2.59. It will be reviewed on this timeframe or as and when required.

7. ANNEXURES

7.1 Annexure A: Overview of APIMF content

Module	Content	Open part	Closed part
3.2. S.1	**General information**	x	
3.2. S.1.1	Nomenclature	x	
3.2. S.1.2	Structure	x	
3.2. S.1.3	General properties	x	
3.2. S.2	**Manufacture**	x	x
3.2. S.2.1	Manufacturer(s)[8]	x	
3.2. S.2.2	Description of manufacturing process and process controls	a)	b)
3.2. S.2.3	Control of Materials		x
3.2. S.2.4	Control of critical steps and intermediates	c)	d)
3.2. S.2.5	Process validation and/or evaluation		x
3.2. S.2.6	Manufacturing process development		x
3.2. S.3	**Characterisation**	x	
3.2. S.3.1	Elucidation of structure and other characteristics	x	
3.2. S.3.2	Impurities	x	e)
3.2. S.4	**Control of drug substance**	x	
3.2. S.4.1	Specification	x	
3.2. S.2.2	Analytical procedures	x	
3.2. S.4.3	Validation of analytical procedures	x	
3.2. S.4.4	Batch analysis	x	
3.2. S.5.5	Justification of specification	x	f)
3.2. S.5	**Reference standards or materials**	x	
3.2. S.6	**Container closure system**	x	
3.2. S.7	**Stability**	x	
3.2. S.7.1	Stability summary and conclusion	x	
3.2. S.7.2	Post-approval stability protocol and stability commitment	x	
3.2.S.7.3	Stability data	x	

[8]Including all companies involved in the manufacture of the active substance, including control/in process testing sites, intermediate manufacturers, milling and sterilisation sites.

a) Flow chart and short description is regarded as sufficient if detailed information is presented in the closed part. However, full validation data on the sterilisation process may be requested in the open part (in cases where there is no further sterilisation of the final product).
b) Detailed information
c) As far as the information is also relevant for the applicant.
d) As far as information is related to the detailed description of the manufacturing process and as far as information is not relevant for the applicant.
e) In so far as the information is related to the detailed description of the manufacturing process and in so far as the APIMF holder sufficiently justifies that there is no need to control these impurities in the final API.
f) As far as information is related to the detailed description of the manufacturing process, control of materials and process validation.

7.2 **Annexure B:** Example of a Letter of Access template (GLF-PEM-02B)

From APIMF holder on headed paper

The Chief Executive Officer

South African Health Products Regulatory Authority

[Include address as per SAHPRA website, https://www.sahpra.org.za/head-office/]

Letter of access for SAHPRA, in reference to APIMF record [APIMF number, if allocated]

Name of API: [Fill in here]

APIMF holder: [Fill in here]

The aforementioned APIMF holder hereby authorises the South African Health Products Regulatory Authority (SAHPRA) to refer to and review the aforementioned APIMF record in support of the following new registration application(s) or variation(s) submitted by [Name of applicant] on [planned date of submission]:

Name of product: [Fill in here]

Application number: [Fill in here]

The aforementioned APIMF holder commits to ensure batch-to-batch consistency and to inform [Name of applicant] and SAHPRA of any change in the APIMF.

The aforementioned APIMF holder is hereby informed of and accepts that SAHPRA may share the evaluation reports of the aforementioned APIMF record within the regulator.

_____

Signature for the APIMF holder (above)

7.3 **Annexure C:** Example of a Submission Form template (GLF-PEM-02A)

From APIMF holder[9] on headed paper

Attention: South African Health Products Regulatory Authority

[Include address as per SAHPRA website, https://www.sahpra.org.za/head-office/]

[Date]

Submission of documents relating to an APIMF for [Name of API] [SAHPRA APIMF number, if allocated]

The APIMF (open and closed parts) is submitted in relation to the following new registration application submitted by [Name of applicant] on [planned date of submission]

Required information:

[Final product Manufacturer]	
Name of Product	
Final Product Application number	
Name of FPP manufacturer	
Final Product applicant	
Application from Backlog pre-reg/ BAU pre-reg/ Backlog post-reg/ Backlog post-reg[10] (please tick)	☐Backlog pre-reg ☐BAU pre-reg ☐Backlog post-reg ☐BAU post-reg
Type off application	☐New application ☐Response to queries

APIMF holder	
APIMF holder name	[Fill in here]
Full APIMF holder administrative address	[Fill in here]
Site master file number (for API manufacturing site(s) located in South Africa)	[Fill in here]

[9]API manufacturer

[10]Pre-reg: Pre registration unit, post-reg: Post registration unit, BAU: Business as usual application

APIMF holders APIMF number, version and	
Contact person	[Fill in here]
Telephone number	[Fill in here]
E-mail address	[Fill in here]

API manufacturing site(s)	
API manufacturer name	[Fill in here]
Manufacturing site name	[Fill in here]
Manufacturing site SMF (site master file) number (for API manufacturing site(s) located in South Africa)	[Fill in here]
Manufacturing site role[11]	[Fill in here]
Manufacturing site physical address (including block / unit / number)	[Fill in here]
GPS coordinates[12] of manufacturing site	[Fill in here]
Manufacturing site contact person	[Fill in here]
Manufacturing site telephone number	[Fill in here]
Manufacturing site e-mail address	[Fill in here]
It is hereby confirmed that copies of the latest GMP certificate for manufacturer(s) and/or a copy of the appropriate manufacturing license(s) have been included	☐

BCS classification of API	
Polymorphic form	
Packaging	
Proposed retest period	
Proposed storage conditions	

Please replicate this table for additional manufacturing sites. Manufacturing sites are all sites involved in the manufacture of the active substance, from the introduction of starting material(s), including quality control / in process testing sites, intermediate manufacturers, milling, micronisation and sterilisation. Each manufacturing site should be listed in a separate table and its role should be specified.

If the APIMF has been approved by one of SAHPRA's recognised regulatory authorities (RRAs), please complete the table below.

[Please check the tick-box for Yes, and leave it blank for No. Please duplicate the table for additional RRAs as required.]

[11]Please see text below the table for examples of manufacturing site roles.

[12]Latitude (S or N) and Longitude (E or W) expressed in Degrees Minutes Seconds to 1 decimal place, alternatively Degrees to at least 5 decimal places, or Degrees Minutes to at least 3 decimal places.

Name of RRA	{Insert name of RRA}
Date of submission	DD/MM/YYYY
Is this APIMF identical to the APIMF on file in the above mentioned RRA?	☐ [If no, please provide an explanation of changes below.]
Are approval letters from the RRA for the APIMF included in this submission? (Module 1.10)	☐
Are assessment reports for the APIMF included in this submission? (Module 1.10)	☐

The undersigned hereby declares that all the information herein, and in the Annexes and Modules hereto, are correct and true and are relevant to this particular API, and that all existing data which are relevant to the quality, safety and efficacy of the API have been supplied in the dossier, as appropriate.

_____

Signature for the APIMF holder (above)

Name and function: [Fill in here]