SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

MULTIPLE SUBMISSIONS OF THE SAME APPLICATION FOR REGISTRATION WITH DIFFERENT PROPRIETARY NAMES

This guideline is intended to provide recommendations to applicants wishing to submit multiple applications for the registration of medicines. It represents the South African Health Products Regulatory Authority's (SAHPRA) current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy 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. SAHPRA is committed to ensure that all registered medicines will be 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.

Guidelines and application forms are available from the office of the CEO and the website.

Version 1 published for comment	June 2013
Deadline for comment	30 September 2013
Version 2 published for comment	Aug 2015
Deadline for comment	16 Sept 2015
Version 3 published for implementation	December 2015
Version 4 published for implementation	May 2019

TABLE OF CONTENTS

This document describes the process for the submission and handling of multiple submissions of the same application for registration of a medicine which are identical but have different proprietary names.

1 Definitions

1.1 **Duplicate** or **multiple** applications are defined as two or more applications submitted simultaneously by the same applicant, which are identical in every aspect except for the proposed proprietary name(s) and include duplicate or multiple applications of innovator and generic products.

1.2 A **clone** is defined as an application submitted by the HCR of the innovator or generic product as a copy of its own product under a different proprietary name at any stage during the product life cycle (of the registered product).

2 Background

Applicants often submit multiple applications for the same product under different proprietary names. Generally, in practice the first application is compiled by the applicant and then additional applications for the additional product names are prepared by replacing the proprietary name of the first, or master application, with each of the additional proprietary names.

These types of submissions are generally referred to as ‘duplicates’ / ‘refer to’ or in Europe as ‘clones’ and should not be confused with the applications for the same molecule from different Applicants, final product (FP) and active pharmaceutical ingredient (API) manufacturers.

Sometimes the additional applications are not submitted together with the first or master application but even many years later.

3 Principles

3.1 A **duplicate** application may be for an innovator or a generic product.

3.2 A duplicate application must be submitted at the same time as the master application. If, for example, an application is submitted days, months or years after the master, it is regarded as **not** being linked to a master and would follow the normal evaluation process.

3.3 An application for a **clone** is submitted after the registration of the original product.

4 Process for duplicate applications

4.1 A single “master” dossier for an application for registration is required with a module 1.2.1 for each proprietary name. The application must be accompanied by a *single* sample of the product and a *single* package insert and patient information leaflet where the product name is indicated as [PRODUCT NAME]. A list of all the proposed proprietary names must be included in module 1.5.3. The application must be accompanied by the applicable screening and application fees for each application.

4.2 The applicant must indicate which proprietary name should be regarded as the “master”; if not indicated the invented name will usually be regarded as the master.

4.3 Additional product applications (same API and source, same indications, same FP manufacturer) not linked to the master will not be handled as a duplicate application. In this case, each application will stand on its own, and be evaluated on its own, and a committee recommendation on one product may not be applied and responded to for the other applications.

4.4 An application number is allocated to the master dossier, and a linking application number to the master for the additional proprietary names, e.g. 500010 for the master and the additional proprietary names 500013.10, 5090016.10 – the ".10" indicates the link to the master application.

Example of application numbers for three copies of an application with three strengths:

	Master	Duplicate 1	Duplicate 2	Duplicate 3
5 mg	500010	500013.10	500016.10	500019.10
10 mg	500011	500014.11	500017.11	500020.11
20 mg	500012	500015.12	500018.12	500021.12

4.5 The single master dossier is fully evaluated by all the relevant Committees and all the proposed proprietary names are reviewed by the Names and Scheduling Committee.

4.6 When approved by all Committees the master product and all the duplicates are registered.

4.7 A registration certificate is issued for each approved proprietary name linked to the master dossier (reflecting the application number indicating the link e.g. 50/2.5/0013.10).

4.8 Pre- and Post-registration changes (refer to the Amendments guideline) are effected to and reviewed only for the single master dossier.

4.8.1 The declaration provided with submission of amendments must include a clause in which the Responsible Pharmacist confirms that the change will be made for all the linked dossiers.

4.8.2 If an application is made for an amendment which is *not intended* to be implemented across all the linked dossiers, the affected dossier will be automatically delinked and will be considered to be a stand-alone dossier. Such an application requires submission of a complete dossier and the relevant amendment fee(s) to amend the registration certificate because of the amendment(s) to the entry in the register in terms of section 15A and/or 15B of Act 101 of 1965.
A certified copy of the original registration certificate may be submitted on submission of the amendment, in which case the amended certificate will only be issued on approval of the amendment and submission of the original certificate.

4.8.3 If the master dossier has not been updated within the past five years, a full update must be submitted with the amendment applied for. If the dossier is up-to-date, a full update must be submitted within one year of the delinking.

4.8.4 Upon approval of a stand-alone dossier the linking number is removed (e.g. 500013.10 becomes 500013) and this application then stands on its own.

5 Applications already in the system

These applications will be handled as follows

5.1 Applications currently in the process of evaluation: When responding to recommendations, clearly indicate the duplicates. The applications will then be finalised together. Following registration, conversion to eCTD will be required for any amendments submitted. Refer to the guideline 2.23 Submission in eCTD format regarding the requirements for baseline submissions.

5.2 Post-registration of multiple applications.
Applications that are still registered by the same applicant that meet the criteria of a multiple application and where the status of the master dossier will be applicable to all duplicates post-registration: Conversion to eCTD will be required. Refer to the guideline 2.23 Submission in eCTD format regarding the requirements for baseline submissions.

6 Process for Clones

6.1 Where the original registration is still in paper format, a submission in eCTD format will be required as for a baseline submission, as sequence 0000. The application for the clone will then be sequence 0001.

Refer to guideline 2.23 Submission in eCTD format,

Include copies of the latest Authority letters of

- approval of any amendments to the registered product, including the PI and PIL,
- the allocation of the shelf-life of the product, and
- the allocation of the retest period of the API/s

as bookmarked annexes to the letter of application in section 1.0

At this stage different strengths should be combined into one dossier, with the first application number being used as the eCTD identifier.

The application for a clone should not be submitted until all amendments applied for have been approved for the registered product.

6.2 For an existing eCTD of a registered product, the clone should be submitted similar to a duplicate application.

The letter of application, M1.2.1, 1.2.2.1, 1.2.2.4, labelling (1.3.1.1, 1.3.2, 1.3.3) reflecting the proposed proprietary name as [PRODUCT NAME] and 1.5.3 reflecting all proprietary names should be submitted. This is apart from the MD5 checksum and validation report required as hard copies.

6.3 The name/s and application number/s of the clone/s should be included in the envelope under Multiple/Duplicate Applications.

7 Fees payable

The application fee for multiple applications will be as follows:

7.1 The fee for the master application will remain as published.

7.2 The fee for the duplicates will be the same as for the master.

7.3 The fee for the clone will be the same as for the registered product, according to the current fees.

8 Update History

Date	Reason for update	Version & publication
July 2013	Published for comment	Version 1 June 2013
30 September 2013	Deadline for comment	
	Published for comment	Version 2 Aug 2015
16 Sept 2015	Deadline for comment	
Dec 2015	Published for implementation	Version 3 Dec 2015
	Date of implementation	
With immediate effect	New applications	
TBA	Applications in the system - Phase I, II, III, IV	
May 2019	Change from MCC to SAHPRA Changes to section 1.2, 5 (old 6) and 7 (old 5) Section 5 moved to 7 New section 6	Version 4 May 2019
With immediate effect	Date of implementation	