COMMUNICATION TO APPLICANTS IN THE BACKLOG CLEARANCE PROGRAM

This document is intended to provide communication to applicants wishing to resubmit applications for new registrations as well as variations as part of the Backlog Clearance Program. This will be a "living document" and will be updated over the course of the Program. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications. This document should be read in conjunction with SAHPRA's revised guidelines and templates, available from SAHPRA's website.

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ABBREVIATIONS AND ACRONYMS

API	Active Pharmaceutical Ingredient (also known as Drug Substance)
BAU	Business As Usual
BTIF	Bioequivalence Trial Information Form
eCTD	Electronic Common Technical Document
eSubmission	Electronic Submission
EMA	European Medicines Agency
FAQ	Frequently Asked Questions
GMP	Good Manufacturing Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
INN	International non-proprietary name (INN)
IPRP	International Pharmaceutical Regulators Programme
MCC	Medicines Control Council
ME&R	Medicines Evaluations & Research
NCE	New Chemical Entity
OCR	Optical Character Recognition
P&A	Pharmaceutical & Analytical
PC	Portfolio Coordinator
PI	Professional Information
PIL	Patient Information Leaflet
PV	Pharmacovigilance
RRA	Recognised Regulatory Authority
RMP	Risk Management Plan
SAHPRA	South African Health Products Regulatory Authority
SCoRE	Summary of Critical Regulatory Elements
TA	Therapeutic Area

1 INTRODUCTION

1.1 The Backlog Clearance Program

The South African Health Products Regulatory Authority (SAHPRA) was launched as a Schedule 3A independent public entity in February 2018, replacing the Medicines Control Council (MCC). At its formation, SAHPRA inherited a backlog of approximately 16 000 Category A medicine applications for both new registrations and variations. The Backlog Clearance Program has been created to fulfil the Board's commitment to clear this backlog in two years, starting August 2019.

1.2 Purpose of this document

The purpose of this document is to inform applicants how to consolidate, update and resubmit applications (both new registrations and variations) to the Backlog Clearance Program, as well as what to expect from SAHPRA during the evaluation.

Applicants should start by reading through this document with reference to the General Information Guideline [2.01]. Thereafter applicants should familiarise themselves with the latest/revised guidelines and templates. Appendix A contains a list of the most relevant guidelines and templates.

Please note that the communication in this document applies only to the Backlog Clearance Program. While the latest guidelines and templates are applicable to all applications submitted to SAHPRA, there are processes in place which are unique to the Backlog Clearance Program.

This is a living document, and will be updated frequently as experience is gained through the processing of the Backlog Clearance Program. During the Backlog Clearance Program, before contacting Davis Mahlatji or a member of the Backlog Clearance Team, please refer to this document – notably the FAQ section – for information.

2 GENERAL INFORMATION

2.1 Communication

2.1.1 Portfolio Coordinators

A Portfolio Coordinator (PC) is an applicant's designated point of contact at SAHPRA throughout the application process. Each application will be assigned to a PC, who will facilitate all internal and external communication related to the application. The name and contact details of the PC will be communicated to the applicant via email once the application has been allocated. The applicant will not be permitted to communicate directly with any evaluator: all queries and concerns should be communicated through the assigned application PC.

2.1.2 Online tracker

Applicants will be able to track the status of their applications online through an online tracking sheet. The tracker will contain a list of backlog application numbers along with the associated application status for each of the relevant SAHPRA units. The tracker is intended to reduce the volume of process-related queries submitted to the PC. PCs will not respond to queries which are readily-answered by the online tracker.

2.1.3 Applicant points of contact

SAHPRA has a record of the primary and secondary points of contact for all applicants in the backlog. If applicants would like to update the primary or secondary point of contact, please email Davis Mahlatji (Head of the Backlog Clearance Program) at mabatane.mahlatji@sahpra.org.za and backlog@sahpra.org.za

2.2 Eligibility

There are strict criteria for applications to qualify to be evaluated in the Backlog Clearance Program:

New registrations

Applications must have been submitted by the applicant on or before 31 January 2018. To confirm the new registration backlog, applicants were required to submit Application Surveys to SAHPRA by 25 January 2019. In addition, application payment was required in full by 12:00 on 25 January 2019. Country CEOs or General Managers signed declarations stating that they understood and accepted the terms for an application to be included in the Backlog Clearance Program. After reviewing the submissions, SAHPRA published the new registration backlog database on 16 May 2019. All queries have been addressed by SAHPRA directly with the relevant applicants, and the database is now considered finalised. Only those applications which are recorded in this database will be evaluated as part of the Backlog Clearance Program.

Variations

Registered products are eligible if they contain at least one variation submitted on or before 31 January 2018. For eligible registered products, if a variation application was submitted after 1 February 2018, this variation will be evaluated as part of the Backlog Clearance Program.

Through the Variation Deep Dive Survey, SAHPRA is creating a complete list of products with outstanding variation applications that will be evaluated as part of the Backlog Clearance Program. The launch of the Variation Deep Dive Survey will be communicated with industry shortly.

2.3 Resubmission windows

In order for SAHPRA to segment and prioritise applications successfully, applicants will need to adhere to resubmission windows strictly. Every new registration and variation application will have a pre-defined window for submission based on its associated API and therapeutic area. The sequence, content and duration of all resubmission windows for new registrations was published by SAHPRA on 7 June 2019 (please refer to Appendix B). The resubmission windows for variations will be published by SAHPRA after the close of the Variation Deep Dive Survey.

A resubmission window is the only period of time where its associated applications will be accepted for evaluation as part of the Backlog Clearance Program. Applications submitted either late or in the incorrect window will be considered withdrawn from the Backlog Clearance Program and will not be evaluated.

2.4 Rejection of applications in the Backlog Clearance Program

As communicated during the CEO Roundtables in September 2018, clearing the backlog in 2 years requires unprecedented collaboration amongst all stakeholders in South Africa's health system. Part of this process involves rejecting poor quality applications. SAHPRA expects strict adherence to the guidelines and communication provided. The deviations that will put an application at risk of rejection are detailed in this document, a summary of which can be found in Appendix C.

3 NEW REGISTRATIONS

3.1 Creating a new registration application

3.1.1 Update and consolidation of resubmissions

All resubmitted backlog applications will need to be of a high standard in order to be evaluated by SAHPRA. New registration applications will need to be updated and resubmitted digitally according to the new guidelines. Please make sure that all required documents are included in the required sections. Appendix A contains a list of all relevant guidelines that should be used during the compilation of the resubmission. The remainder of this section provides further detail for the creation of new registration applications.

3.1.2 Application number

The application number allocated to the original application should be used for the backlog application. If new application numbers were required due to inaccurate or duplicated application numbers, these have been created and assigned.

If the application has multiple strengths, they should be combined into one dossier. Please consult the Multiple Submissions guideline [2.40] for further information regarding duplicates and clones.

3.1.3 Previous correspondence

When applications are resubmitted, there may be previous SAHPRA correspondence directly applicable to that application (e.g. recommendations). This correspondence should be included as an annex to the letter of application in Section 1.0.

3.1.4 Electronic resubmissions

All applications that are re-submitted to SAHPRA must be electronic. SAHPRA will only accept submissions for the Backlog Clearance Program in eCTD or eSubmission format. Both submission types should be structured in accordance with CTD specifications, the ICH granularity document, and the ICH file naming conventions. This extends to the submission of all responses to screening and evaluation queries. Please refer to the eCTD [2.23] or eSubmission [2.58] guidelines for more information.

New registrations submitted to the Backlog Clearance Program should always start with sequence 0000. This holds even if the new registration was previously submitted to SAHPRA/MCC in eCTD format.

3.1.5 Reliance models

SAHPRA will be implementing reliance models for qualifying applications. The General Information Guideline [2.01] contains the latest information regarding SAHPRA's evaluation pathways as well as SAHPRA's Recognised Regulatory Authorities (RRAs) and collaborative / work sharing procedures. The General Information Guideline is the primary reference for information on reliance, with additional information contained in the Clinical Guideline [2.09] and Quality and Bioequivalence Guideline [2.02].

3.1.6 GMP

All sites affecting applications within the backlog are required to be GMP compliant prior to the resubmission of the relevant application. A GMP certificate or equivalent manufacturing licence is required as evidence of GMP compliance. Please refer to 3.2 of the SA Guide to GMP [4.01] for additional information.

Local sites

A GMP survey was sent to applicants on 23 November 2018 to identify which local manufacturing sites need certification and affect applications in the backlog. Based on the survey results, SAHPRA designed an inspection schedule for local sites affecting applications in the backlog. Resubmitted applications without GMP approval for the relevant site(s) and which weren't captured by the GMP survey will be at risk of rejection at screening.

International sites

No international inspections will be conducted for the Backlog Clearance Program. Applicants are required to provide a valid GMP certificate / manufacturing license from a PIC/S member state or WHO PQ as proof of GMP compliance for all international sites involved in the production of backlog applications. A list of SAHPRA's recognised regulators for GMP compliance can be found in the GMP guideline [4.01].

3.1.7 SCoRE document

The Summary of Critical Regulatory Elements (SCoRE) document is designed to enable a top-down summary-driven approach to reviews, reducing evaluation time of all applications.

All new registration applications will require a completed SCoRE document [6.31] in 3.2.R.8.

3.1.8 Biostudy and biowaiver review forms

If a biostudy has been included in the application, please review and complete the Bioequivalence Trial Information Form (BTIF) template [6.32].

For circumstances where a biowaver is submitted (no biostudy or biostudy done on a different product strength), please review and complete the following:

- IPRP template (for a BCS-based biowaiver)
- WHO template (for an additional strength biowaiver)

For the biowaiver templates, as well as additional information, please refer to the Quality and Bioequivalence Guideline [2.02].The location of where these documents should be placed in the dossier is indicated in the validation templates [6.16] and [6.30].

3.1.9 Format change to PI and PIL

SAHPRA will adopt the EMA format for Professional Information and Patient Information Leaflets. This format is reflected in the updated SAHPRA guidelines [2.14] and [2.16].

The format change requires amendments to General Regulations 10 and 11 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965, as amended). The comment period for these amendments closes on 31 August 2019, with SAHPRA expecting the final changes to be published in the Government Gazette in September 2019.

Despite the regulation amendments not yet being finalised, the guidelines [2.14] and [2.16] must be used for the submission of applications.

SAHPRA expects the regulation amendments to be finalised and published by the time the first backlog applications (submitted in August 2019) are ready for certification, providing the required legal basis for registration.

3.1.10 Repository of PIs and PILs

SAHPRA has published a repository of PIs and PILs on its website for the benefit of health care providers and patients, as well as to enable streamlined Clinical evaluations of applications for generic medicines. Where available for a given molecule, applications for generic medicines are required to reference the latest published SAHPRA-approved innovator PI in the application. Clinical screening queries will be immediately flagged for applications referencing an outdated / illegible PI where the latest version has been published on SAHPRA's website.

Note that the published PIs on SAHPRA's website may also be applicable to selected variation applications (e.g., safety update of a generic medicine where the same change has already been approved for the reference local innovator medicine).

3.2 Resubmitting an application

Applications should be delivered on a CD, DVD or USB with the supporting paper documents to the following address:

The Chief Executive Officer
South African Health Products Regulatory Authority
Building 38a
CSIR
Meiring Naude Road
Brummeria
Pretoria
South Africa

Upon submission, the receipt of the application will be logged and physical proof of receipt will be provided. Applications should be clearly labelled with the words "BACKLOG – NEW REGISTRATION" on the front page of the letter of application. SAHPRA will not take responsibility for resubmissions delivered to any other place or in any other manner. For further information on submission, applicants should refer to the General Information Guideline [2.01] as well as the eCTD [2.23] and eSubmission [2.58] guidelines.

Once received, SAHPRA will confirm that a given backlog application has been submitted in the correct resubmission window by comparing the application number and API against SAHPRA's finalised list of new registration backlog applications. As communicated in the resubmission window announcement on 5 July 2019, no application will be considered for evaluation if it is submitted in the incorrect window. It is thus imperative that the API(s) and application number of a given application appear on the letter of application, as per the template contained in the Backlog Clearance Program Starter Pack

Applications which are successfully confirmed as being part of the backlog will be allocated for screening.

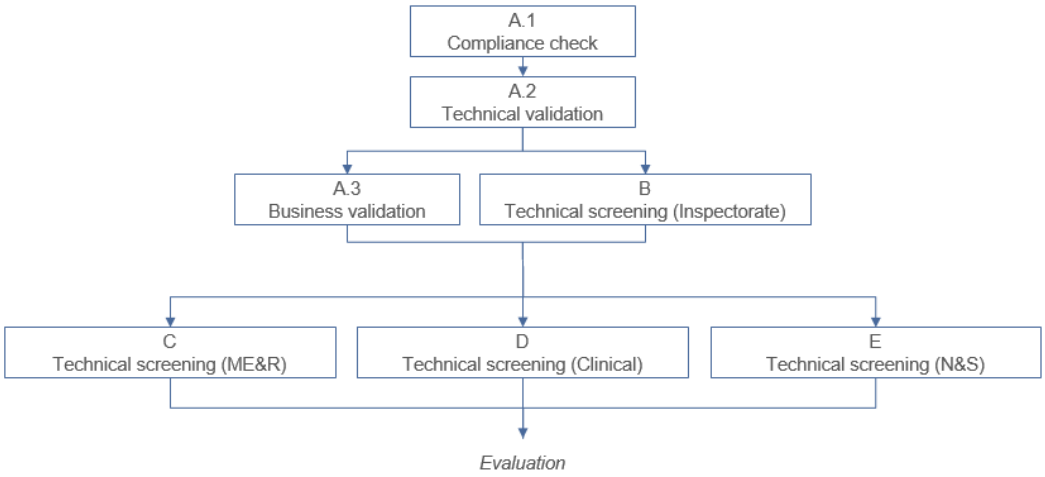
Registration samples for resubmission is not required.

3.3 Screening

Before an application is evaluated, it will go through a screening process. The screening process will confirm that all SAHPRA's requirements have been met, ensuring that only high-quality dossiers are allocated for evaluation. Applicants are required to complete and submit a validation template ([6.16] or

[6.30]) with all new registration applications. Any omitted data or deviations from the validation template must be accompanied by a motivation for the application to be accepted.

During screening, the following steps will be conducted (as detailed in the validation templates):



If an application fails a screening step, two outcomes are possible:

1. If the failure does not affect the next validation step, the application can proceed to the next screening step. When the next updated sequence is submitted, all previous queries will be consolidated and will need to be updated in a single sequence.
2. If the failure prevents the application from proceeding to the next validation step, a query round will be started and the applicant will need to submit an updated sequence.

In order to reduce the volume of query communications facilitated by the PC, the following screening queries will be consolidated and shared with the applicant together (where applicable):

1. A.3 and B
2. C, D and E

Applicants will be kept informed of their application's status via an online tracker, which will be updated when an application passes screening.

3.4 Evaluation

After passing screening, the application will be allocated to an evaluator from each relevant SAHPRA unit (e.g., Clinical, ME&R (quality and bioequivalence), Inspectorate and N&S for a new registration application). The primary evaluation from each unit will then be peer reviewed by a senior evaluator. Should there not be consensus on the final outcome or outstanding queries, then the application will be allocated to an Advisory Committee for input. This re-engineered process is intended to streamline evaluations, reserving the Advisory Committee for the evaluation of relatively complex evaluations and responses.

All evaluation queries will be centralised through the PC. Evaluation queries will not necessarily be consolidated, but typically shared via email by the associated unit.

If an application passes evaluation, the PC will consolidate all approved recommendations for final review and registration by SAHPRA. If an application is not approved by all relevant units after the allocated query rounds, it will be rejected.

As each evaluation is reviewed, the applicant will be updated on application status. Applications may be approved, queried, or rejected. If approved, the application will proceed to certification.

3.5 Responses to queries

Clearing the backlog in 2 years requires pragmatic and strict rules regarding the number and length of queries:

- Screening: 1 round of queries will be allowed for each stage of screening (i.e. 1 round for A1, 1 round for A2 etc.), and applicants need to respond to queries within 5 working days
- Evaluation: 2 rounds of queries will be allowed for each evaluation aspect (i.e. 2 rounds for ME&R, 2 rounds for Clinical etc.), and applicants need to respond to queries within 10 working days

If either the number of query rounds or the time to respond to queries is exceeded, the application will be at risk of rejection. Should a longer query response time be needed by an applicant, motivation should be provided to the PC via email. Extensions can be requested and they will be reviewed on a case by case basis.

It is recommended that applicants use the status updates on the online tracker to plan to have resources available to answer queries within the timelines (e.g. when an application enters the evaluation phase, a resource should be on standby to answer queries)

All responses to evaluation queries / recommendations should be submitted to the SAHPRA reception via CD/DVD/USB with an incremental sequence number. Submission of the response should be accompanied by a notification to the associated PC via email.

3.6 Certification

Once a new registration application is approved, the PC will contact the applicant requesting the pre-filling of the new registration certificate template.

Certificates will be released once a month on a defined day to be determined. The PC will communicate the pick-up time and place to applicants.

4 VARIATIONS

Please note
The Digital Variations Portal is still in development. Information in this section represents the preliminary thinking for variations in the Backlog Clearance Program and will be updated in time.

4.1 EU variation classification

SAHPRA has adopted the EU variation classification guideline, with the full details (including the associated exceptions) published in the Variations Addendum for Human and Veterinary Medicines [2.08]. This includes information on the treatment of Type IA, Type IA_{IN} and Type IB applications submitted prior to the implementation date of the addendum.

Note that SAHPRA has withdrawn the SR-PIN guideline [2.17]. SAHPRA requests all applicants to include a summary history of all implemented SR-PINs as part of the resubmission for updating records. This should be submitted as part of the amendment history under module 1.2.1.

4.2 Application entry through the Digital Variations Portal

The starting point for all variation applications in the Backlog Clearance Program is the Digital Variations Portal. The purpose of the Digital Variations Portal is twofold:

- Facilitate the submission and processing of variation applications, particularly the immediately implementable Type IA variations
- Provide an electronic database of implemented variations for use by Port Health, reducing the need for industry to wait for updated paper certificates

Only variation applications captured by the Variations Deep Dive Survey will be eligible for the Backlog Clearance Program, and these variation applications will be submitted through the Digital Variations Portal.

4.2.1 Creating a user profile

Before creating a variation application on the Digital Variations Portal, applicants will need to register a user account on the Portal. Details regarding the registration for a user account will be provided to applicant points of contact in due course.

4.2.2 Submitting a variation

Only products captured by the Variations Deep Dive Survey will be eligible for a variation application via the Digital Variations Portal. Applicants will be required to select the product requiring a variation application from a drop-down list which will be populated from the Variations Deep Dive Survey. Applicants will subsequently select the EU variation codes relevant to the selected product.
Upon submission through the Portal, variation applications will be dealt with in 1 of 3 ways:

1. Type I with lapsed evaluation period[1]: Applicant can implement immediately
2. Type I in evaluation period[1]: Applicant can implement after evaluation period has lapsed
3. Type II: Variation application will require evaluation before applicant can implement

[1] The evaluation periods for SAHPRA's units are defined in the Variations Addendum for Human and Veterinary Medicines [2.08]

Applicants are advised to consolidate all Type I variations for a single registered product in a single application, and all Type II variations for a single registered product in a separate application. If Type I and Type II variations are consolidated in a single application, the applicant cannot implement the Type I variation/s until the Type II variation/s have been approved.

Applicants are required to submit the supporting documentation (i.e. the variation application dossier) as required by the EU variations classification guideline and SAHPRA's Variations Addendum for Human and Veterinary Medicines [2.08][2] within 10 days of submitting the variation application via the Digital Variations Portal. The supporting documentation must be in eCTD or eSubmission format as per the eCTD [2.23] and eSubmission [2.58] guidelines.

4.3 Variations requiring evaluation

Type II backlog variations will require evaluation by SAHPRA. After creating the variation on the Digital Variations Portal, applicants will need to send through supporting documentation in line with the variations resubmission windows to SAHPRA in either eCTD or eSubmission format (see guidelines [2.23] and [2.58]).

Type II variations and Type IA_{IN} and Type IB applications of which SAHPRA's evaluation period as per the Variations Addendum for Human and Veterinary Medicines [2.08] has not lapsed require evaluation by SAHPRA (if the evaluation period lapses and no communication is received from SAHPRA, the variation can be implemented). The evaluation process of variations will closely follow that of new registrations (please see Section 3).

4.4 Certification

In light of the new Digital Variations Portal and associated database, only selected variation applications require the issuing of a revised registration certificate:

1. Changes in the proprietary name of a product (A.2.a & A.2.b in the EU Variation Classification Guideline)
2. Transfer of the Holder of Certificate of Registration (A.0.1 in the Variations addendum)

Should an approved application not require a revised registration certificate, the applicant will be provided with a variation summary, which effectively serves as an addendum to the registration certificate. The updated variation summary will be provided to the applicant on the Digital Variations Portal within 48 hours of approval of the variation application. A read-only database of all approved variation applications will be made available to Port Health to act as a primary source of approved variations with the variation summary providing a secondary source of approval. Further details pertaining to the approved variation applications requiring a revised registration certificate will be provided in due course.

[2] Note that any new data requirements (as per the newly-adopted EU guidelines) will only become binding and effective 6 months from the implementation date of the Variations Addendum [2.08].

APPENDIX A: RELEVANT DOCUMENTS

New / revised guidelines

[2.01]	Jul 2019	General information guideline
[2.02]	Jul 2019	Quality and Bioequivalence Guideline
[2.08]	Jul 2019	Variations addendum for Human and Veterinary Medicines
[2.09]	Jul 2019	Clinical guideline
[2.14]	Jul 2019	Guideline for Patient Information Leaflet for Human Medicines
[2.16]	Jul 2019	Guideline for Professional Information for Human Medicines
[2.23]	Jul 2019	Submission in eCTD format
[2.58]	Jul 2019	Submission in eSubmission format
[4.01]	Jul 2019	SA Guide to Good Manufacturing Practice

Templates

[6.16]	Jul 2019	New registration validation template for eCTD
[6.30]	Jul 2019	New registration validation template for eSubmission
[6.31]	Jul 2019	Summary of Critical Regulatory Elements
[6.32]	Jul 2019	Bioequivalence Trial Information Form (BTIF) template
[6.33]	Jul 2019	Abridged review template (P&A)
[6.34]	Jul 2019	Verified review template (P&A)

APPENDIX B: RESUBMISSION WINDOWS

1 Resubmission windows for NCE[3] applications

Resubmission window	Therapeutic area / type of medicine	Opening date	Closing date
1	HIV	01 Aug 2019	30 Sep 2019
	TB		
	Hepatitis		
	Vaccines		
	Oncology		
	Mental and behavioural disorders		
	Infectious / parasitic diseases		
	Maternal and newborn health		
	Diabetes		
	Malaria		
2	Priority APIs	01 Oct 2019	31 Oct 2019
	Respiratory system diseases		
	Cardiovascular disease		
	Haematological / immunological diseases		
	Analgesics & NSAIDs[4]		
	Genitourinary system diseases		
	Nervous system diseases		
3	Endocrine, nutritional and metabolic diseases	01 Nov 2019	29 Nov 2019
	Digestive system diseases		
	Musculoskeletal system and connective tissue diseases		
	Skin and subcutaneous tissue diseases		
	Eye and adnexa diseases		
	Ear and mastoid diseases		
	Other		

[3] Includes innovator biological applications

[4] Non-steroidal anti-inflammatory drugs

2 Resubmission windows for generic[5] applications

Resubmission window	Therapeutic area / type of medicine	Opening date	Closing date
1	HIV	01 Aug 2019	30 Sep 2019
	TB		
	Hepatitis		
	Vaccines		
2	Oncology	01 Oct 2019	31 Oct 2019
3	Mental and behavioural disorders	01 Nov 2019	29 Nov 2019
4	Infectious / parasitic diseases	03 Feb 2020	28 Feb 2020
5	Maternal and newborn health	02 Mar 2020	31 Mar 2020
	Diabetes		
	Malaria		
	Priority APIs		
6	Respiratory system diseases	01 Apr 2020	30 Apr 2020
7	Cardiovascular disease	04 May 2020	29 May 2020
8	Haematological / immunological diseases	01 Jun 2020	30 Jun 2020
	Analgesics & NSAIDs[6]		
9	Genitourinary system diseases	01 Jul 2020	31 Jul 2020
	Nervous system diseases		
10	Endocrine, nutritional and metabolic diseases	03 Aug 2020	31 Aug 2020
	Digestive system diseases		
11	Musculoskeletal system and connective tissue diseases	01 Sep 2020	30 Sep 2020
	Skin and subcutaneous tissue diseases		
12	Eye and adnexa diseases	01 Oct 2020	30 Oct 2020
	Ear and mastoid diseases		
13	Other	02 Nov 2020	30 Nov 2020

[5] Includes biosimilar applications

[6] Non-steroidal anti-inflammatory drugs

APPENDIX C: SUMMARY OF REJECTION POINTS

Clearing the backlog in 2 years requires unprecedented collaboration amongst all stakeholders in South Africa's health system. Part of this involves rejecting poor quality applications. SAHPRA expects strict adherence to the guidelines and communication provided.

The tables below summarise the possible rejection points in the Backlog Clearance Program.

1 Submitting an application

1.1	If an application does not qualify as a backlog application, it will be rejected (e.g., a new registration application which is not contained in SAHPRA's database of backlog applications)
1.2	If an application is submitted outside of the assigned resubmission window, the application will be rejected

2 Screening

2.1	If an application requires more than 1 screening round per screening step, the application will be at risk of rejection
2.2	If the response time for a screening query exceeds 5 working days, the application will be at risk of rejection

3 Evaluation

3.1	If an application requires more than 2 screening rounds per evaluation aspect (e.g. ME&R, Clinical), the application will be at risk of rejection
3.2	If the response time for an evaluation query exceeds 10 working days, the application will be at risk of rejection

APPENDIX D: FREQUENTLY ASKED QUESTIONS

1 New registrations

1.1 Questions about submission process

1.1.1	Q: How should the eCTD identifier for clones/duplicates be handled if they have not been submitted at the same time as the master application?
	A: All applications in the Backlog Clearance Program that did not have application numbers were assigned a new 6 digit application number. The eCTD identifier should be the application number/s of the master application. The name/s and application number/s of the clone/s or duplicate/s should be included in the envelope under Multiple/Duplicate Applications.
1.1.2	Q: What happens if my application was part of Project Starburst, but it has not been registered before 1 August 2019?
	A: For an application originally submitted to Project Starburst, unless communication has been sent to the applicant prior to 1 August 2019 that the application has been finalised and registered, the application did not meet the requirements for Project Starburst and should be resubmitted in the appropriate window. All responses to recommendations made during Project Starburst should be included in the resubmitted application.
1.1.3	Q: Since the original submission of the application, we have received recommendations from SAHPRA's various units. The applicable parts of the dossier were updated based on these recommendations. Should we resubmit the original dossier, or the updated dossier (i.e. including the recommendations)?
	A: Please submit the most updated / recent dossier, based on previous recommendations received. Resubmission is an opportunity to consolidate recommendations and outstanding variation applications. The dossier does not need to be the same as the original one submitted to SAHPRA.
1.1.4	Q: Will previous recommendations and approvals from SAHPRA for an application be considered?
	A: Yes; please include all previous relevant communication with SAHPRA in your resubmitted application as attachments to the letter of application in module 1.0. Previous recommendations and approvals will be considered, to hasten evaluation time.
1.1.5	Q: Do applications in advanced stages of evaluation (i.e. only awaiting approval from one unit) need to be resubmitted?
	A: Yes; all applications for new registration applications that were submitted prior to 1 February 2018 and remain unregistered need to be resubmitted, regardless of the stage of evaluation. Please update your application by including any changes to the dossier upfront, as part of the new registration resubmission. Please include all recommendations, approvals and other relevant communication in the resubmission, to reduce duplicated effort in evaluation. If updates have been made to the dossier after approval was received, please complete Appendix 3 of the Quality and Bioequivalence Guideline. SAHPRA will consider all recommendations, approvals and other relevant communications included in the resubmission, to speed up evaluation time.
1.1.6	Q: Do applications for registration for biological medicines need to be resubmitted as part of the Backlog Clearance Program?
	A: Yes. They have been included in the resubmission windows.

1.1.7	Q: Will applicants be allowed to apply for new duplicates or line extensions of an existing backlog application as part of the backlog resubmission instead of applying for a new registration as part of BAU?
	A: No. Applicants will not be allowed to do so, as the applications in the backlog are finalised, and no new / different applications can be considered. This would need to go through BAU.
1.1.8	Q: Will there be a process for applicants to motivate for late submissions in extenuating circumstances?
	A: No. If an applicant cannot meet the deadline for resubmission, they should resubmit through business as usual, i.e. not as part of the Backlog Clearance Program. Due to batch processing and capacity work planning, late submissions cannot be accommodated.
1.1.9	Q: What software product should be used to prepare the eCTD dossiers?
	A: SAHPRA does not mandate or recommend any particular software product for eCTD preparation. There are a number of options and vendors that can provide eCTD preparation software (e.g. installed software, software as a service, service providers). Applicants are encouraged to use an eCTD validation tool that supports checking of the SAHPRA eCTD validation criteria.
1.1.10	Q: If a dosage form has changed, can we resubmit the old dosage form as well as the new dosage form?
	A: A new dosage form requires a new application number. All application numbers for the Backlog Clearance Program have already been allocated. Any new application numbers will therefore need to be submitted in Business As Usual (BAU)
1.1.11	Q: Should clones be resubmitted in the NCE or generic resubmission window?
	A: As per SAHPRA's multiple submissions guideline[7], a clone is defined as an application submitted by the innovator as a copy of its own product under a different proprietary name at any stage during the product lifecycle. For an NCE, if a clone application is submitted with the master application for an unregistered NCE, the clone application should be resubmitted in the NCE window. If the clone is submitted after the innovator product has been registered, the clone application should be resubmitted in the generic window.
1.1.12	Q: Should innovator line extensions be submitted in the NCE or generic resubmission window?
	A: A line extension for a registered innovator product should always be submitted in the generic resubmission window. A line extension submitted with an unregistered NCE application (i.e. at the same time) should always be submitted in the NCE resubmission window.
1.1.13	Q: Will the Backlog Clearance Program continue running over December 2019/January 2020?
	A: No applications will be resubmitted during this time, however evaluations will continue, and applicants should have resources ready to answer queries. Evaluation query periods will take into account office closures from 17 December – 1 January.
1.1.14	Q: If our application has been partially evaluated for BAU when it is submitted for the Backlog, will the BAU work stop?
	A: Yes. The application will only be evaluated through the Backlog Clearance Program once it has been resubmitted.

7. 2.40_Multiple submissions of the same application for registration with different proprietary names

1.1.15	Q: Will SAHPRA be prioritising products which have previously received "fast track" approval?
	A: No, "fast track" status no longer exists at SAHPRA. Public health priority has been incorporated into the design of the resubmission windows in consultation with the National Department of Health.
1.1.16	Q: Do applicants need to respond to new recommendations received for a backlog product prior to the associated resubmission window? (E.g., recommendations received from SAHPRA today, where the resubmission of the product is due in 6 months' time)
	A: No, the evaluation of backlog products should be handled entirely by the backlog clearance team via the associated resubmission windows. No backlog product will be rejected as a result of a lack of response to new recommendations received outside of the product's resubmission window.
1.1.17	Q: Will backlog products require payment of the updated registration / screening fee (R1760)?
	A: No. If the applicant has already paid the registration / screening fee, no further payment is required as a result of newly-published fee increases.
1.1.18	Q: What is the process for withdrawing applications from the Backlog Clearance Program?
	A: Applicants must provide SAHPRA with a declaration on company letterhead indicating the applications that are to be withdrawn from the backlog. The declaration must be signed by the Chief Executive Officer and / or the General Manager of the company and emailed to backlog@sahpra.org.za. SAHPRA appreciates applicants informing the regulator of withdrawals, as this facilitates improved workplanning. Note that no refunds will be issued through this process.
1.1.19	Q: Certain principals and manufacturers are only willing to share unredacted assessment reports and / or site inspection reports directly with SAHPRA – how can this be facilitated?
	A: These documents can be shared directly with the portfolio coordinator via email, including the following at the start of subject line: [Reliance documentation] Master application number – Applicant. Note that SAHPRA still has a clear preference for receiving unredacted assessment reports directly from the applicant within the dossier where possible.
1.1.20	Q: Where can one access the "SAHPRA Registered Medicines Database" referenced in section E of the validation template?
	A: This currently refers to the registration notifications published under "publications" on the SAHPRA website. SAHPRA is in the process of creating a consolidated, searchable database of this information.
1.1.21	Q: Where should applicants direct queries regarding any potential APIs which are missing from the resubmission windows?
	A: Queries should be directed to backlog@sahpra.org.za and include [Resubmission window queries] in the subject line of the email. Note that SAHPRA will not be responding to queries where the API is clearly listed for a given resubmission window. SAHPRA will also not be confirming the mapping of products to resubmission windows for individual applicants.
1.1.22	Q: How long before a given resubmission window opens will the reference PI and PILs be published on the SAHPRA website?
	A: SAHPRA is working to publish PI and PILs as soon as possible. At a minimum, SAHPRA endeavours to publish the latest-approved PI and PILs in their current (old MCC) format one month before the opening of a given resubmission window.
1.1.23	Q: Where in the dossier must the Bioequivalence Trial Information Form (BTIF) be submitted?
	A: The BTIF must be submitted in Word format (**not** PDF) in the working documents folder.

1.2 Questions about submission content

1.2.1	Q: Does SAHPRA make use of the term “hybrid” medicine as per EMA?
	A: No. SAHPRA uses the term “generics with clinical data” instead.
1.2.2	Q: What are the requirements for the submission of an RMP for new registration applications?
	A: SAHPRA’s PV directorate will publish separate guidance on the exact nature of these requirements. A number of SAHPRA’s new / updated guidelines have simply made reference to the requirement of an RMP to minimise further updates shortly after publication. No application submitted **before** the implementation of this guidance will be at risk of rejection as a result of the new RMP requirements. In the interim current guidelines and practices will apply (note that the RMP should be submitted in M1.13 and any PSURs in 5.3.6).
1.2.3	Q: For a new registration application, do both the completed SCoRE document and WHO Quality Overall Survey (QOS) templates need to be completed and submitted?
	A: No. Only the SCoRE document needs to be completed and submitted. SAHPRA has removed its requirement for the WHO QOS because of duplication of information across the templates.
1.2.4	Q: Which procedures of medicines’ registration in the European Union (EU) are recognised by SAHPRA for reliance?
	A: Only the European Medicines Agency (EMA) Centralised Procedure and Decentralised Procedure will be recognised for reliance. The National Authorisation Procedure and the Mutual Recognition Procedure will not be considered for reliance. The only exception to this is the UK MHRA, which is recognised as a stand-alone RRA.
1.2.5	Q: Are master / blank production documents required for submission?
	A: Yes. SAHPRA requires the submission of the master / blank production documents for validation of information included in the dossier (i.e. Module 3.2.P.3). In line with the European Medicines Agency’s (EMA’s) requirements, master / blank production documents can be bracketed for different strengths, batch sizes and pack sizes. However, master / blank production documents must cover all proposed sites. If the production process has not been scaled up to commercial batch size, master / blank production documents for a pilot scale batch (minimum 10% of commercial batch) are sufficient.
1.2.6	Q: Do master / blank production documents need to be submitted to SAHPRA each time there is a change? In SCoRE, would the reference number and/or version need to be updated?
	A: The SCoRE document needs to be updated every time the reference or version number changes, unless the change is purely administrative. The SCoRE document needs to reflect the current information in the dossier. If the change justifies a variation application, updated master / blank production documents would need to be submitted and the reference number and/or version would need to be updated. The reference number and/or version do not need to be updated unless the changes have an impact on registration.

1.2.7	Q: If I previously received approval from the Names and Scheduling Unit for the proprietary name for an unregistered product in the backlog, may I change the approved name of the product in my resubmission?
	A: According to section 7.4 of the Proprietary Names Guideline: "Changes to proprietary names approved by SAHPRA in respect of applications for new medicine registrations which are still in progress can only be considered once the process for the registration of the new medicine has been completed." As a result of the extensive time period of the backlog, changing an already-approved proprietary name will be permitted in exceptional circumstances. Sufficient motivation must be provided for the name change; this motivation, and the proposed new name, will be evaluated by SAHPRA. Please note that changing an already-approved name may lengthen evaluation time.
1.2.8	Q: A number of SAHPRA guidelines make reference to an 'applicant declaration letter.' Will SAHPRA provide a template, and if so, when?
	A: SAHPRA is in the process of drafting a template for the applicant declaration letter. The intention of this template is to a) standardise and b) consolidate a number of declarations in a single place. Until such time as this document is finalised, applicants may provide declarations in their existing / current module locations. If it is unclear where a declaration should be placed, applicants may append them to the end of the validation template in M1.8. SAHPRA will issue separate communication when the declaration letter is ready for publication.
1.2.9	Q: Can the Risk Management Plan (RMP) and Module 1 content be the same as what was registered for other regulators?
	A: No. The RMP and Module 1 content needs to be localised to South Africa.
1.2.10	Q: If a product has tentative approval through the FDA, can this be used for reliance?
	A: Yes, as long as the approval is pending only due to a marketing / patent issue and not a technical issue.3
1.2.11	Q: Does the declaration of sameness cover all aspects of the dossier?
	A: The declaration of sameness covers only the technical information of the product. It does not cover Module 1, Module 3.2.R and minor administrative differences and other regional requirements.
1.2.12	Q: If a unit has already received approval (e.g. P&A approval received), do we need to submit a SCoRE document?
	A: Yes, all new registration applications require a SCoRE document.
1.2.13	The completed abridged review template [6.33] or verified review template [6.34] must be included in Word format in the working documents folder, but there is also a requirement to include hyperlinks to the location of information in the dossier. It will not be possible to do both – which requirement should be adhered to?
	Please submit the completed template in Word format in the working documents folder. SAHPRA will publish revised versions of the templates on the website in the next week, excluding the requirement of hyperlinking. Applicants who have not yet prepared their submissions should use the latest published versions of these templates going forward.

1.2.14	Q: Point 5.3 of the Quality and Bioequivalence Guideline [2.02] states that all approved variations for the RRA's registered product should be incorporated in the application submitted for registration by SAHPRA, but not pending variation applications for the foreign registered product. Please clarify why pending variations should not be included in the application, as this will lead to immediate post-registration variation applications.
	A: The principal of reliance is that the product registered with the RR should be the same product as the application submitted to SAHPRA. The less similar the two are, the less reliance can be used to minimise evaluation time. However, to avoid immediate post-registration variations, **all** variations for the foreign registered product (approved and pending) that are relevant for the application made to SAHPRA should be included in the new registration application. The full, unredacted assessment reports will be used whenever possible; in cases where a variation pending with the RRA has been included in the application made to SAHPRA, full review of these sections will need to be done. The letter of application should detail which aspects of the dossier fall under the scope of unredacted assessment reports, and which aspects reflect new variations requiring full review by SAHPRA.
1.2.15	Q: When compiling the resubmission for a biological product, what guidelines should we follow?
	A: Many of the updated guidelines did not include biological products in their scope. Therefore, when resubmitting an application for a biological product, please follow the existing guidelines. The submission format should be either eCTD or eSubmission to meet the digital only requirements of the Backlog Clearance Program.

1.3 Questions about registration process

1.3.1	Q: Will registration times differ for different applications of the same API?
	A: Yes, registration times may differ for similar products due to a variety of reasons (applications can have partial approval, different reliance pathways, varying query times etc.). All finalised certificates will be released once per month, on a day communicated by your Portfolio Coordinator. It is thus in the best interests of SAHPRA's industry partners to obtain unredacted assessment reports for abridged and verified reviews, and to respond to queries timeously.

2 Variations

2.1 Questions about submission process

2.1.1	Q: Will SAHPRA's variations resubmission windows take into account products which are currently stocked out, or are expected to be stocked out in the near future, due to an outstanding variation application?
	A: Yes. While the resubmission windows will be broadly structured by therapeutic area and API, SAHPRA will prioritise products which are unable to be marketed due to outstanding variations. The exact nature of this prioritisation will be communicated as part of the variations resubmission windows.
2.1.2	Q: Will SAHPRA provide evaluation timelines for Type II variation applications for all directorates?
	A: SAHPRA aspires to provide target evaluation timelines in the future, but is not in a position to do so currently. SAHPRA will be closely tracking evaluation timelines under its new processes in order to set realistic expectations for its industry partners.
2.1.3	Q: Do manufacturer, packer and FPRC changes get an updated certificate?
	A: No, they will be reflected in the variation summary.

2.1.4	Q: Do changes in the name/address of the Holder of Certificate of Registration (A.1 in the EU Variation Classification Guideline) result in an updated certificate?
	A: No, they will be reflected in the variation summary. Only those name changes which result from a Transfer of the HCR will require an amended registration certificate.
2.1.5	Q: Will there be different resubmission windows for Type I and Type II variations?
	A: No, only Type II variations will have resubmission windows. These will be broadly structured according to the same therapeutic areas and prioritisation as for new registrations.
2.1.6	Q: Should all related sequences (i.e., baseline plus first variation) be submitted on the same CD / DVD / USB?
	A: Yes, a single storage device should be used.
2.1.7	Q: Should the tabulated schedule of amendments still be submitted under module 1.5.2.1?
	A: Yes, this should be submitted in 1.5.2.1 and not part of the letter of application. SAHPRA will rectify this formatting in the next iteration of the Variations Addendum [2.08].

2.2 Questions about submission content

2.2.1	Q: Will applicants be required to conform to new data requirements (as per the EU variations classifications guidelines) for resubmitted backlog variation applications?
	A: No. Any new data requirements will only become effective / binding for new variation applications 6 months from the implementation date of the Variations Addendum for Human and Orthodox Medicines [2.08].
2.2.2	Q: How does SAHPRA intend to handle variations which were formerly under the scope of the SR-PIN guideline?
	A: SAHPRA's Variations Addendum for Human and Veterinary Medicines [2.08] contains codes C.I.0.3 and C.I.2 which facilitate Type IB safety updates of innovator and generic medicines respectively. These two codes are intended to cover variations formerly classified as SR-PINs, requiring limited evaluation by SAHPRA.
2.2.3	Q: Will reliance apply to variation applications?
	A: Yes. Applicants are encouraged to make reference to relevant variations which have already been approved by an RRA. For example, where a safety update has already been approved by the UK MHRA, applicants should make reference to the associated SmPC as part of the variation application to SAHPRA.
2.2.4	Q: Does the Variations Addendum for Human and Veterinary Medicines [2.08] replace the existing USRN communication [9.13]?
	A: Yes. Information pertaining to the USRN procedure is now contained in the Clinical section of the Variations Addendum for Human and Veterinary Medicines [2.08].
2.2.5	Q: Will a SCoRE document need to be submitted with variation applications?
	A: For registered products where no SCoRE document was submitted with the initial new registration application, a SCoRE will not be required for subsequent variation applications. If a new registration application is submitted with a SCoRE document, variations for that product will require a SCoRE document.

2.2.6	Q: What does SAHPRA mean by the term “importer” in section 4.3.4 of the Variations Addendum [2.08]?
	A: Applicants should interpret the term as Marketing Authorisation Holder (MAH) / Holder of the Certificate of Registration (HCR)
2.2.7	Q: What code should be used for safety updates of innovator medicines are yet to be approved by a RRA?
	A: Applicants should make use of code C.I.4. Where the safety update / restriction is deemed urgent, code C.I.3 should take preference and the USRN procedure followed.