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BACKLOG CLEARANCE PROGRAM IN SOUTH AFRICA

Pharmacy

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ABSTRACT

Backlog Clearance Program has been one of the most important priorities by SAHPRA as during its inheritance it had a massive backlog of 16 000 medicinal regulatory applications from MCC.
This included applications for "new registrations, variations, duplicates, clones and multiple doses and different dosage forms". While 50% of backlogged applications were submitted in the past five years, the backlogged applications date all the way back to 1992 and include applications for high priority public health products, including medicines for HIV, tuberculosis, cancer and diabetes. SAHPRA has set a target to clear the regulatory backlog in two years – but notes that, at current capacity with no new applications, clearing the backlog will take up to eight years. SAHPRA's annual performance plan clarifies that the regulator has developed a costed strategy to clear the backlog and has secured ring-fenced funding for the backlog clearance strategy from the government, development partners and donors[1].
SAHPRA's strategy to reduce the backlog involves three key elements, including reducing the number of backlogged applications to remove applications that are no longer relevant, prioritising the remaining applications for review according to public health needs and risk, and implementing new regulatory pathways to reduce regulatory decision times

KEYWORDS

Backlog Clearance , SAHPRA, Applications

INTRODUCTION

It has been one of the critical priorities of South African Products Regulatory Authority (SAHPRA), since its launch in February 2018, has been the clearance of its medicinal products backlog. At its formation, SAHPRA inherited a backlog of ~16 000 applications – over 8 000 new registration applications and just under 8 000 variation applications. SAHPRA's Board has committed to a very ambitious timeline to clear the backlog within two (2) years.

The Backlog Clearance Program[1] will evaluate registered products if they contain at least one variation submitted on or before 31 January 2018. This means that if a product has at least one backlog variation application, all the variation applications for that product will be evaluated through the Backlog Clearance Program. Through the Variation Deep Dive Survey[2], SAHPRA has created a complete list of products with outstanding variation applications from applicants' survey submissions that will be evaluated as part of the Backlog Clearance Program. All other variations are considered BAU variations and will be evaluated by Business as usual (BAU) evaluators.

Hence the variations which were previously Type C amendments which are re classified as Type IA, IA_{IN} and IB will be in the scope of soft launch and amendments which are re classified as Type II will be under the scope of Full Launch.

So the features of Soft Launch and Full Launch are as follows:

SOFT LAUNCH SCOPE CAPTURE AND IMPLEMENT ALL EXISTING TYPE I VARIATIONS

Soft launch scope

Previously submitted Type C Amendments reclassified as Type 1 (Type IA, Type IAIN and Type IB variations are in scope for the soft launch.

The portal will initially be opened for a brief window to allow industry to notify the Authority of all unfinalised, former Type C applications, that have been re-classified Type I variation applications previously submitted to SAHPRA, for both BAU (i.e., a product with no outstanding variations submitted on 31 January 2018 or before) and backlog products (products with at least one outstanding variation submitted before 1 February 2018). Only resubmissions of unfinalised applications submitted prior to the "soft launch" date will be accepted in the soft launch.

Process to submit variations in the soft launch

During the soft launch, applicants are required to explain the full details of the variation in free- text fields. Defined fields based on the variation code will be added for the full launch.

Applicants can save variation applications that are in progress before submitting if the user does not complete the full application in one sitting. Upon submission through the soft launch of the portal, variation applications will be dealt with in 1 of 3 ways:

1. Type I with lapsed evaluation period1: Applicant can implement immediately
2. Type I in evaluation period1: Applicant can only implement after evaluation period has lapsed (calculated automatically by the portal, based on original submission date) and if no additional information or clarification is requested by SAHPRA
3. Type IB evaluation period exception codes (B.II.b.1.e and B.II.b.1.f): Requires additional supporting document to be submitted via the portal (see section 4.4); the evaluation date commences upon online submission to SAHPRA

Following notification via the portal, variations that are part of the soft launch will be deemed implementable where the evaluation period has lapsed. An automatic notification will be sent with the status change to the applicant 24 hours after portal submission. For Type I variations where the evaluation period has not yet lapsed, the applicant will have to wait the appropriate number of calendar days prior to implementation (e.g., a re-classified Type IB submitted to SAHPRA only 5 days prior to the "soft launch" date). If the applicant does not hear from SAHPRA by the end of the remaining evaluation period, the applicant may implement the Type I variation. Note that former Type A and Type B variations are already deemed implementable where the evaluation / waiting period has lapsed, and will not require re-notification to SAHPRA via the portal Please note, if a Type I variation with a lapsed evaluation period is submitted together (i.e. as one application submission on the portal) with a Type I variation which is still within its evaluation period, both variations will only be deemed implementable once the evaluation period of the latter has lapsed (if no rejection or query response is received from SAHPRA during that period).

Documents required for submission of soft launch

- SAHPRA requires submission of several documents outlined below for soft launch variation applications, but will not require previously submitted dossiers.
- All documentation for Type I resubmissions in the soft launch should be submitted through the Digital Variations Portal on the last step of the online submission process. The following documents are required:

1. A PDF copy of the applicant's proof of original variation application submission (only the SAHPRA/MCC stamped page is necessary). Original submission date indicated on the online resubmission should match the stamped proof of submission
2. A PDF copy of the product's latest registration certificate if the

variation(s) change(s) the information included on the registration certificate (not required in other cases) Reminder: SAHPRA will not reissue certificates for any Type I variations

3. For variation codes B.II.b.1.e and B.II.b.1.f, please see section 4.4 for additional document submission requirements
4. PI/PIL documentation, if a resubmission of a variation during the soft launch impacts the PI/PIL (EMA format updates are not required in the soft launch of the portal):

a. Annotated PI and PIL (showing what was changed in MS Word format)
b. Clean PI and PIL (in MS Word format); and
c. Reference used (e.g. innovator PI/SmPC in PDF format)

Exceptions

There are two codes of variation which are exceptional under the soft launch portal i.e.

"Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product"

- B.II.b.1.e
- B.II.b.1.f

Resubmission of these reclassified type IB requires three more documents in additional with respect to the above mentioned documents

1. Application Form – Module 1 – 1.2.1
2. Tabulated schedule of amendments 1.5.2.1
3. GMP Certificates- Any PIC/S Members, WHO, and Zazibona (Zambia, Zimbabwe, Botswana and Namibia) certified documents are accepted. Resolution letters of SAHPRA and MCC are also acceptable

Professional Information (PI) and Patient Information Leaflets (PIL) Variations

Applicants should submit PI/PIL documentation if a resubmission of a variation during the soft launch impacts the PI/PIL. Format changes to align PI/PILs with EMA are not required during the soft launch of the Digital Variations Portal.

Please note, the date of revision on PI and PILs within the soft launch should be the date of original notification to SAHPRA if the applicant has already implemented the change (i.e., former Type A and Type B variations already deemed implementable where the evaluation / waiting period has lapsed and do not require re-notification to SAHPRA via the portal). For applicant resubmissions of reclassified Type C variations where the evaluation waiting period has not yet lapsed, the revision date on the PI and PIL should be the day after the waiting period is over. For reclassified Type C variation resubmissions where the evaluation period has lapsed, the revision date should be the date of notification/resubmission through the Digital Variations Portal.

FULL LAUNCH -RE-OPEN THE PORTAL FOR ALL OTHER VARIATION APPLICATIONS

SAHPRA will reopen for all variation applications which were not submitted during the soft launch and are projected to SAHPRA will re-open the portal for all other variation applications during the full portal launch (projected to be between February and March, 2020). This includes all new applications which are yet to be submitted to SAHPRA, as well as the resubmission of Type II variations, even if the applicant has received SAHPRA responses from evaluation. Full resubmission is required even if progress has been made on evaluations of variations.

In order for SAHPRA to divide and prioritise the applications, in the full launch operation the applicants will need to stick on to resubmission windows stringently for backlog Type II resubmissions Every backlog 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 variations will be published by SAHPRA.

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. All applications that are deemed ineligible for evaluation through the Backlog Clearance Program will be evaluated by BAU.

Process to submit variations in the full launch

Applicants will first enter information identifying the product for which variation applications are being submitted. Based on input received from the Type II Variations Deep Dive Survey[2], the system will automatically distinguish the product as one requiring evaluation by either the Backlog Clearance Team or BAU team. Applicants will subsequently select the EU variation codes relevant to the selected product. Note that certain variation codes will require the applicant to provide additional information (e.g., for a proprietary name change, the applicant will be required to include the proposed proprietary name as part of the portal submission). Type II Variation applications will require evaluation before the applicant can implement.

In general, the implementation of variation applications grouped as a single submission will move at the pace of the most restrictive / slowest individual variation type. Applicants are thus 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.

Document submission requirements for full launch

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][3] within 10 working 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][4] and eSubmission [2.58][5] guidelines. For variations submitted in eCTD format for the first time, applicants will be required to include a baseline as part of the dossier. For variations submitted in eSubmission format, applicants may opt to include a baseline where relevant and practical.

For new variation applications and Type II resubmissions, a SCoRE document will be required when the variation impacts the information contained within the SCoRE. A SCoRE document in most cases can be updated from its previous version; if there was no original SCoRE document, the applicant must draft the SCoRE document reflecting the proposed variation(s) with their application. If the variation has no impact on the SCoRE document, it is not required with the application regardless of whether there is an existing SCoRE document or not.

Format change to PI and PIL

SAHPRA will adopt the EMA format for PI and PILs. This format is reflected in the updated SAHPRA guidelines [2.14][6] and [2.16][7].

The format change requires amendments to General Regulation 11 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965, as amended)[8] . The comment period for these amendments closed on 31 August 2019, with SAHPRA expecting the final changes to be published in the Government Gazette.

After final changes are reflected in the Government Gazette, applicants will be required to submit format updates. Submissions of format updates will be handled in the full launch of the Digital Variations Portal according to resubmission windows for backlog products. Please use the guidelines [2.14] and [2.16] for the submission of applications.

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 out dated / 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)

Exceptions: unforeseen changes (z-codes)

Applicants can submit "z" code variations for unforeseen changes not

accounted for in the EMA guidelines to SAHPRA under the same classification codes as evaluated under EMA, but only during the full launch of the portal. Any codes that have not been detailed in the SAHPRA variations addendum should be considered Type II.

Deep Dive Survey

This survey is concerned with outstanding / un-finalised Type II variations which still require evaluation by SAHPRA. Former Type As, Bs and Cs which have been reclassified as either Type IA, Type IAIN or Type IB variations are considered approved and implementable where the mandated waiting period has lapsed. Former Safety-related Package Insert Notifications (SR-PINs) are also outside of the scope of this survey and should not be included.

For example, an application for an additional manufacturer which was historically considered as a Type C 26 may now have been reclassified as a Type IB variation. This application is NOT to be included in the Type II survey, and will be deemed implementable where the 30-day waiting period has lapsed

Full launch resubmission windows

Please note that this section is only relevant for products included in the Backlog Clearance Program (i.e. products with at least one variation application from before 1 February 2018).

In order for SAHPRA to segment and prioritise backlog products with Type II variation applications successfully, applicants will need to adhere to resubmission windows. Every 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 variations is included below.

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. Variation applications submitted either late or in the incorrect window will be considered withdrawn from the Backlog Clearance Program.

SAHPRA will prioritise products falling in the following two categories, which may result in resubmission of a product outside of its associated therapeutic area / pharmacological classification:

1. Stock-out status: Products which are currently stocked out, or expected to be stocked out within 3 months, due to an outstanding variation application
2. Tender status: Products which are unable to fulfil the obligations of a won tender due to an outstanding variation application

The opening of the first backlog resubmission window for backlog Type II variations will coincide with the “full launch” of the Digital Variations Portal, exact dates are subject to change.

NEW REGISTRATION APPLICATION PROCESS

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

Creating a new registration application

- **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 relevant 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.

- **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.

- **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.

- **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.

- **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].

- **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]

- **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.

- **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 biowaiver 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].

- **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

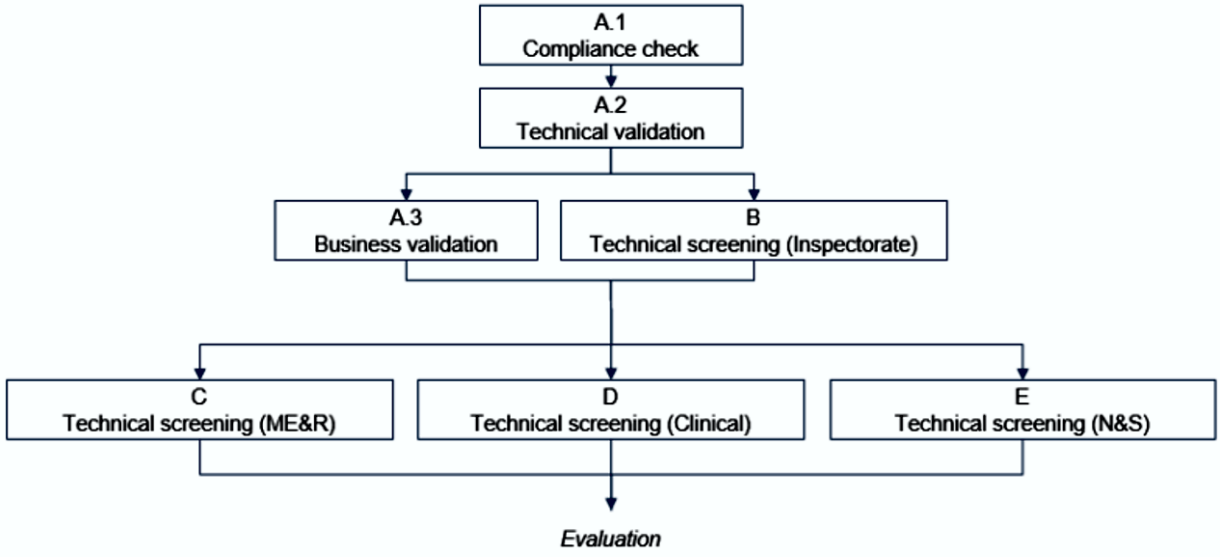
Upon submission, the receipt of the application will be logged and physical proof of receipt will be provided. Applications should be clearly labelled with the words **"BACKLOG – NEW REGISTRATION"** on the front page of the letter of application. SAHPRA will not take responsibility for resubmissions 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 are not required.

- **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.

- **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.

- **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.

Building SAHPRA's human capacity

A further challenge faced at SAHPRA is its limited human resource capacity to effectively fulfil its mandate. According to information provided by SAHPRA's CEO Portia Nkambule in November 2018, SAHPRA then had 178 full-time employees and around a similar number of external evaluators supporting regulatory activities. SAHPRA is seeking to significantly increase its staff capacity to around 450 full-time staff over the next five years and has already initiated a hiring drive, advertising more than 100 new posts in May 2019. SAHPRA has further indicated that staff members were recently transferred from the National Department of Health's Pharmaceutical Trade and Product Regulation programme to SAHPRA under a section 197 transfer agreement and, according to SAHPRA's annual performance plan, the transferred staff will support core programmes responsible for medicines evaluation and registration and authorisation management.

While SAHPRA is seeking to strengthen staff capacity in all of its programmes, the 100 recently advertised posts included 17 new posts for medicines regulation and 19 posts for the backlog clearance project. A key goal of SAHPRA is to build its internal capacity to fulfil its medicines regulatory functions, unlike the MCC which relied heavily on external evaluators. SAHPRA's annual performance plan explains that its reliance on a "dwindling" number of external evaluators creates difficulties in managing and optimising regulatory decision times due to the lack of contractual performance agreements with external evaluators. The annual performance plan clarifies that while SAHPRA hopes to absorb some external evaluators as internal staff, it will also seek to build its internal capacity through up skilling existing staff and recruiting new staff – but notes challenges in attracting and recruiting new internal evaluators.

Opportunities and challenges for public engagement

SAHPRA has taken significant and commendable steps since its establishment in February 2018 in outlining reform plans and processes to improve its functioning to effectively fulfil its mandate. In addition to the adoption and initiation of a strategy to address the regulatory backlog and its efforts to build its staffing capacity, SAHPRA has developed plans to digitise key processes and implement a new fees model (among other interventions). These steps have been taken despite significant challenges faced by the new regulatory agency in its first year of operations, including staff protests and the closure of its offices in the Civitas building due to unsafe working conditions.

While SAHPRA should be commended for its important work to date, responsiveness to the public and accountability remains a challenge despite the regulators commitments to improving and demonstrating transparency and accountability. Health NGOs in South Africa continue to express frustration due to the non-responsiveness of the regulator following requests for information and engagement.

In December 2018, SAHPRA CEO Nkambule noted that the regulatory authority was seeking to create a culture of transparency and that in the current transitional phase it would prioritise the implementation of a formal communications strategy and systems. SAHPRA's annual performance plan notes that a communications strategy has been drafted and has been approved to be implemented during 2019. The plan further adds that through implementing the communications strategy, SAHPRA will endeavour to (among other goals) "develop mechanisms to allow all stakeholders to communicate easily with the regulator including being able to lodge queries and complaints".

CONCLUSION

At its formation, SAHPRA inherited a backlog of ~16,000 applications – over 8,000 new registration applications and just under 8,000 variation applications. For new registrations, this backlog goes back as far as 1992 and 50% of these applications are at least 5 years old. Generic applications comprise >90% of the new registration backlog. 15 Active Pharmaceutical Ingredients (APIs) comprise 16% of the new registration backlog, each averaging 20 applicants.

Given the magnitude of this inherited backlog, if SAHPRA maintained current capacity and current processes, it would take 8 years to clear the backlog – assuming no new applications. This challenge is compounded by a shortfall in absorption capacity, where SAHPRA's predecessor, the Medicines Control Council, historically received 4,700 applications per year but was only able to register 2,600. Therefore, SAHPRA intends to make an innovative step change to rapidly clear the inherited backlog whilst simultaneously transforming its operating model to improve its on-going absorption capacity.

SAHPRA's Board has committed to clear the backlog within 2 years. This ambition highlights that the backlog is not just an administrative challenge; it represents a public health crisis. There are three pillars to SAHPRA's backlog clearance strategy:
Reduce the number of applications that require evaluation
Segment and prioritise remaining applications
Design and implement new models for evaluation

Given the ambitious timeline to clear the backlog, it is necessary to partner with industry to reduce the number of applications requiring evaluation. Three levers will be used in combination. First, as 50% of new registration applications are at least 5 years old, industry will need to 'opt-in' for applications submitted in 2013 or earlier. These older applications are more likely to be out-of-date / in an old format, of less commercial interest to industry, and / or of less importance to public health. Once this program is launched, industry will have 2 months to notify SAHPRA of their intention to 'opt-in' using a survey template. If no 'opt-in' is received, these older new registration applications will be eliminated from the backlog. Second, for these pre-2014 applications – and for all other new registration and variation applications – applicants will be required to consolidate, update and re-submit these applications to ensure SAHPRA evaluates the most up-to-date information. All variations should be included in this latest information, as should require reliance and summary documents. Finally, all poor quality applications will be rejected. Strict quality standards will be published and made transparent by SAHPRA, similar to other regulators' submission or acceptance checklists.

The second pillar of SAHPRA's backlog clearance strategy is to segment and prioritise all applications by public health need and public health risk. Public health need, according to government priority therapeutic areas and unmet medical need, will determine the order in which applications will be evaluated. Public health risk will determine the evaluation pathway. This will be based upon the type of application and complexity of evaluation required in addition to the level of prior scrutiny by recognised regulators. The third pillar involves new models for evaluation. These new models will also be applied to "business as usual" (beyond the inherited backlog) to improve SAHPRA's absorption capacity going forward. SAHPRA has adopted new evaluation policies and will rely on several stringent regulatory authorities: US FDA; EMA; Japan MHLW; SwissMedic; Health Canada; Australia TGA, and United Kingdom MHRA. SAHPRA will continue to be part of Zazibona and WHO PQ.

SAHPRA will also formalise different processes to operationalise these reliance models: full review, abridged review, verified review, recognition and notification. Implementation of these new policies will be accompanied by a renewed level of operational excellence, including:

- Streamlined processes – upfront administrative and technical screening, batch processing by API, top-down summary-enabled approach to full reviews
- Optimal staffing – with a dedicated backlog clearance team (separate to 'business as usual') and new positions such as Application
- Managers who will have end-to-end responsibility for an application's progress
- Digitally empowered approach to evaluation – all re-submitted / updated applications to be in eCTD or eSubmission format
- Improved transparency and accountability
- Effective change management

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