SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY

Private Bag X828, PRETORIA, 0001

15 May 2019

Dear industry partners,

BACKLOG CLEARANCE PROGRAM – NEWSLETTER UPDATE

Our progress towards the launch of the Backlog Clearance Program is evidenced by key achievements across SAHPRA over the past month. As always, thank you for your cooperation as we work towards go-live in August 2019. Please see below an update on seven key aspects of our preparation for the Program.

1. Recruitment for the Backlog Clearance Team

We have officially launched recruitment for the Backlog Clearance Team! SAHPRA is hiring experienced, contract evaluators across Clinical, Pharmaceutical and Analytical (quality and bioequivalence), Inspectorate, and Names and Scheduling. In addition, opportunities include 19 posts for contract services personnel such as Portfolio Coordinators, Evaluator Coordinators, and Project Office Managers. The closing date for applications is 24 May 2019. Please see the detailed announcement on our website (here) for more information on how to apply, as well as job descriptions for the various positions.

2. Application Survey and resubmission windows

Over the past couple of months we have been hard at work checking applicants' new registration application survey submissions against SAHPRA's internal databases to ensure the integrity and validity of the backlog application database. We have now completed this review and to finalise the database, we will this week be publishing (by application number only with no other identifying characteristics) the comprehensive list of new registration applications that will be evaluated as part of the Backlog Clearance Program. Any application that is not reflected on this list will be considered formally withdrawn and will not be evaluated by SAHPRA, as per the 'backlog applicant declaration' signed by each company's General Manager / CEO.

In a spirit of partnership with industry, SAHPRA will open a two-week query period to resolve any outstanding issues before the list of backlog applications is deemed final. Detailed instructions will be issued along with the list. No late queries will be accepted and after this period ends, no further correspondence will be entered into regarding withdrawn backlog applications.

During the Application Survey, SAHPRA also requested preliminary information regarding any relevant Transfers of Applicancy for those applications. SAHPRA will be contacting applicants directly to obtain proof of these transfers. Importantly, only finalised Transfers of Applicancy will be recognized. This is to ensure that, going forward, we communicate with the applicant who has legal authority over an application, and will ultimately be the holder of the certificate of registration.

Your cooperation is vital in submitting timeous queries regarding the backlog application database and Transfers of Applicancy. These quick turnaround times will enable us to plan the work schedule and finalise the resubmission windows as soon as possible.

As previously mentioned, the resubmission windows will be driven by therapeutic areas and APIs of the highest public health need, as determined by a consultative process with the National Department of Health. The resubmission windows will be published in the next month, to enable you to start preparing your applications. For each resubmission window, we will include:

- Preliminary timeframe (i.e. when and how long the window will be)
- Therapeutic areas included in each window, defined by a list of APIs
- Types of medicines included in each window (e.g. NCEs or Generics)

3. Draft guidelines for comment

Thank you to those companies who submitted comments on the first tranche of draft guidelines published in April. The comment window for these closed on 15 May 2019. We have also released a second tranche of draft documents for comment, which included:

- Guidelines (eCTD and eSubmission)
- Validation Templates (eCTD and eSubmission)
- Variations Addendum for Orthodox Medicines

Based on feedback, we have extended the comment window for this second tranche of documents to 28 May 2019. We recognise that the comment period is relatively short, but these quick turnaround times are vital for us and our digital system vendor to meet the August go-live date.

We sincerely appreciate your engagement in reviewing these documents. Once all comments have been incorporated, we will publish final versions prior to resubmission. To re-emphasise from my previous communication, each company will need to invest in additional training for staff to ensure compliance to the new guidelines. We will be taking a stringent approach to non-compliant applications.

4. GMP inspection update

Thank you to everyone who participated in the GMP survey conducted earlier this year. In preparation for go-live, SAHPRA's Inspectorate team is carrying out a revised inspection schedule to clear the backlog that has developed over numerous years. Many companies will be receiving requests for an inspection; should the team reach out to you, please ensure that you respond timeously and that the inspection goes ahead on the arranged date. Please note that non-replies and rescheduling of inspections will be a significant disruption. Meeting this schedule is a vital requirement to ensure go-live at 1 August.

5. New Variations process

Thank you to everyone who joined us at the Industry Variations Workshop held in mid-April. To re-cap, SAHPRA has decided to adopt the European Union (EU) Variation Classification Guideline in full for orthodox (small molecule) human and veterinary medicines with specific exceptions. This includes Clinical variations, replacing the draft Clinical Variations Guideline that was previously published for comment. The EU Variation Classification Guideline provides a risk-based approach to evaluations enabling SAHPRA to focus capacity on applications requiring evaluation. It provides a simplified guideline across units and aligns SAHPRA with global best practice. Administrative burden on SAHPRA of redrafting a guideline will be reduced should the EU amend their guideline.

The classification system consists of four annexes providing the relevant codes for variations:

- A = Administrative changes
- B = Quality changes
- C = Safety, efficacy and pharmacovigilance changes
- D = Plasma Masterfile / Vaccine Antigen Masterfile changes

Each code provides an evaluation procedure that determines the extent of evaluation required for a variation based on the inherent risk of a variation application:

- Type IA procedures are low risk variations that can immediately be implemented with SAHPRA only requiring a notification within a year of implementation
    - Type IAin procedures are a subset that require applicants to wait 30 calendar days before implementing
- Type IB procedures are applications that are not classified as high or low risk applications
    - These applications require 30 days (for Pharmaceutical & Analytical) and 60 days (for Clinical) to provide comment before implementation
- Type II procedures are high risk variations requiring evaluation of the relevant modules

SAHPRA has developed a Variations Addendum that details specific exceptions to the EU guideline. This has been distributed for public comment (as stated above), with feedback due on 28 May. Four types of exceptions are described:

- Exclusions – EU codes, procedures and, documentation that will not be adopted
- Additions – Additional codes, procedures and, documentation created by SAHPRA and not covered explicitly in the EU Variation Classification Guideline
- Alterations – EU codes, procedures and, documentation adopted and adapted by SAHPRA, with a different procedural treatment
- Clarifications – Providing further clarity on the interpretation of a code

SAHPRA's latest CTD guideline will still apply, and take preference where there are common document types between South Africa and the EU.

SAHPRA's current plan is that we will be implementing this Guideline for all outstanding matters. This presents industry with the opportunity to consolidate and update applications as multiple variations may have been submitted for the same registered product. This approach will enable the immediate implementation of Type IA and Type IB variation applications, provided their notification / comment period has lapsed. This applies to the entirety of the inherited backlog. It is envisaged that a digital portal will enable applicants to notify SAHPRA of variation applications.

As Type II variations require evaluation, industry stakeholders will be asked to complete two surveys in parallel to assist SAHPRA in refining estimates of evaluator capacity and expertise required. Similar to pre-registration, all Type II variation applications will be resubmitted in eCTD or eSubmission format. SAHPRA's immediate next steps are to finalise the online portal, as well as surveys for Type II variations.

6. Variation certificates

SAHPRA's re-engineered variation certification process is up and running, and we are seeing significant efficiency gains from the changes implemented. Approximately 600 variation certificates have been signed and collected.

To complete some of the variation certificates, we will need applicants to resubmit documentation (i.e. original dossier and variation documentation) electronically. An email will be sent out to the applicants in question. Your engagement in resubmitting this documentation is appreciated and will help facilitate more progress as we work towards clearing the certification backlog.

7. Project Starburst

Project Starburst is also making progress; to date, 33 products have been registered, with an additional 30 ready to be registered. This is a significant win for the Backlog Clearance Program, as every additional registered product brings us closer to achieving widespread access to medicines for all South Africans. Please note that confirming eligible applications is an ongoing process. SAHPRA is still reaching out to some companies that submitted applications for Starburst to request further documentation to confirm compliance and authenticity for eligible applications. Your timeous response to these queries is vital to help us drive this process forward.

Please note that if you do not receive a query or final recommendation from us (i.e. registration or rejection) by end-June, your application was ineligible for Starburst and will need to be resubmitted electronically as part of the Backlog Clearance Program. We will not be publishing a list of applications to be evaluated in Project Starburst versus those included in the general Backlog Clearance Program. In general, SAHPRA will not respond to individual queries on this matter.

Concluding notes

SAHPRA is developing its harmonisation strategy for business as usual (BAU) – that is all applications received from 1 February 2018. The general principle is that all revised policies and processes that apply to the Backlog Clearance Program will also apply to BAU. Any differences in the management of backlog and BAU will be clearly explained, but for now, the old-SAHPRA guidelines and practices still stand.

Timelines for the reformation of BAU will be duly communicated, but we are aiming to launch the revised processes in September. As previously advised, transition is challenging and so wherever possible please await further communication from SAHPRA about submitting BAU applications. We appreciate your patience and cooperation on the changes to come.

Lastly, please note SAHPRA's new email service and new contact details, for your use going forward:

- For general non-product specific enquiries: enquiries@sahpra.org.za
- For the overall Backlog Clearance Team: backlog@sahpra.org.za
- For Backlog Variation Certificates: backlog.certification@sahpra.org.za
- For Backlog Variations: backlog.variations@sahpra.org.za

There have been many wins over the past few months, and although progress in some areas is slower than hoped for, we are steadily moving forward towards go-live in August 2019. We appreciate your ongoing engagement and patience over this time.

Yours faithfully

Davis Mahlatji

HEAD, BACKLOG CLEARANCE PROGRAM