SAHPRA
South African
Health Products
Regulatory Authority

COVID-19: Regulatory guidance

Business for South Africa Medicines Working Group

May 2020

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Pharmaceuticals and Vaccines Suppliers for Covid-19 pandemic

SAHPRA and B4SA under the Pharmaceutical and Vaccines working stream are collaborating on providing industry with regulatory guidance to ensuring essential Covid-19 related medicines supply in both the public and private sector are well managed in a clear and transparent manner.

To this end, the regulatory guidance is now available and we request that industry follow this process in order for SAHPRA to have co-ordinated efforts to address the South Africa public health medicines needs for Covid-19.

Yours faithfully

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Pharmaceutical supply chains are likely to face a number of near- and mid-term challenges, resulting in potential regulatory interactions

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API & RM[1] supply

80% of API supplied from China or India

- Inventory on hand typically 3 months for API and 5 months for RM
- Risk that API shortage could translate to potential product risk ~10-11 months from time of shutdown based on average inventory
- Risk of increased pricing (e.g., RM have shown price increases 10-20%)

Manufacturing

~70% of mfg sites in 11 countries

- Risk of wide-spread reduction in production capacity due to shutdowns (e.g., Italy, France, India)
- To date, production disruptions have totaled ~30-40 days based on length of country shutdown and time to ramp up
- Risk of shortage linked to inventory (typically 5 months to 3.5 years) and new demand patterns (e.g., COVID-usage)

Warehousing

Increased containment & government stockpiling

- Stockpiling largely driven by export stoppages – India has limited export of 2 dozen drugs, Germany has banned export of respirators and masks
- Additional actions could further limit inbound and outbound deliveries

Distribution

Limitations in air freight and local transport

- Transportation in & out of local warehouses may be disrupted
- High-quality distribution capabilities likely limited in the interim (e.g., cold chain)
- Continued logistics disruption given trucker shortages, road closures, and potential price increases

Overcoming disruptions likely to involve regulatory interactions in short-term to mitigate COVID-19 crisis

1. Raw materials

The B4SA Medicines Dashboard provides visibility of gaps and enables a structured process to mitigate gaps, including regulatory interactions

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Last resort process with potential S21 applications

Context

There are **4 archetypes of gaps that can be interpreted from the B4SA Medicines Dashboard**

The dashboards are **dynamic and updated regularly**

A gap is defined as a **potential shortfall in next 3 months** based on surge demand forecasts, and does not necessarily imply an actual or imminent shortage

Archetypes

Actions B4SA and industry pursue to resolve gaps[1]

1 Identified public sector gap can be covered by existing private sector stock

Applies only to public sector gaps

- Identify local private sector sources with surplus availability through weekly data request to industry
- Provide NDoH with visibility of sources through dashboard for order placement

2 Identified public or private sector gap can be covered by local manufacturing / registered import ramp-up

- Identify local private sector ramp-up capacity (manufacturing and registered imports) through weekly data request to industry
- Provide demand creators (incl. NDoH) with visibility of sources through dashboard for order placement

3 Identified public or private sector gap cannot be covered locally

- Provide demand creators (incl. NDoH) with visibility of persistent gaps with no local coverage and potential global sources through dashboard
- B4SA Regulatory Team provides guidance to importers on regulatory processes (incl. Section 21s) where necessary
- Explore therapeutic alternatives and clinical usage guidelines with clinician associations

4 No gap

- Continuous monitoring of supply and demand by Nerve Centre to ensure no gap emerges

1. Excludes parallel NDoH processes that are pursued to close gaps

What is the appropriate regulatory channel for different scenarios, and what is the application process for COVID-19 related medicines?

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Deep dive on next page provides further details

Supplier scenario	Regulatory channel	Submission process – in all cases see sahpra.org.za for latest detailed guidance	Typical turnaround time[2]
I would like to **import medicine from another manufacturer to my currently registered medicine to overcome a local shortage**[1], OR I would like to **import API from a different source** to that currently on the dossier for my registered medicine given unavailability of usual API source	**Expedited variance application**	• **Email request for application number** to PriorityQvariations@sahpra.org.za for Quality changes, PriorityIvariations@sahpra.org.za for Inspectorate • **Email variations@sahpra.org.za** for access to document upload system • **Labelling exemption S36** – if required • **Submit application online via document upload**, including: – Cover letter – Proprietary name – Applicant details (name, email, contact number) – Nature of variation – Motivation (e.g., supplier country in lockdown) – API DMF	~1-7 working days
I would like to **temporarily import medicines not registered in South Africa** (and not similar to another of my registered products[1]) to overcome a local shortage	**Section 21 approval (bulk/ institution, not named patient)**	• **Email shortages@sahpra.org.za and section21@sahpra.org.za** motivation for S21 review. Upon SAHPRA response, • **submit online application online** to SAHPRA including: – completed application form and product brochure containing relevant, chemical, pharmaceutical, pre-clinical pharmacological, toxicological data where applicable, human or animal pharmacological, clinical data; – details of medicines registration or pending registration with any other regulatory authority – Medical professional or Responsible pharmacist overseeing the process – evidence of compliance of the manufacturer of the medicine with Good Manufacturing Practice standards as determined by the Authority – Certificate of analysis – reasons why a South African registered medicine cannot be used; – any other information as may be required by the Authority (will depend on current position in the product development cycle)	~ 7 working days
There is a **critical shortage requiring immediate alleviation**, with other channels exhausted or only **the product labelling** does not comply with regulation 9 /10	**Section 36 exemption**	• **MoH can override regulatory requirements to exempt a drug from having to follow normal processes, allowing immediate import** • **S36:** "The Minister may, on the unanimous recommendation of the members present at any meeting of the Authority, by notice in the Gazette, exclude, subject to such conditions as he may determine, any medicine from the operation of any or all the provisions of this Act, and may in like manner amend or withdraw any such notice." • **Labelling exemption S36:** Regulation 9 and 10	~21 working days
I would like to **temporarily import medicine not registered in South Africa** (and not similar to another of my registered products[1]) to overcome a local shortage	**Expedited registration of new medicine**	• **Email request for an application number** to applicationnumbers@sahpra.org.za • **Email newmedicines@sahpra.org.za** for access to document upload system • **Submit application via document upload**, including: – Basic information as per 2.58 formatting guidelines – Motivation (e.g., COVID-19 treatment; no local supply) – Name and address of API/medicine source – Information on manufacturer, packer, laboratory – cGMP certificates for sites	~28 – 42 working days
I would like **exemption from post-importation testing for my medicine (excl. vaccine)** to expedite time to market	**Post-importation testing exemption (PITE)**	• **Post-importation testing required for all vaccines (no exemptions)** • **For Biologicals submit application** to biologicals@sahpra.org.za (biologicals). Data from a minimum of five temperature printouts are required, giving an account of the same product or five different biological products, provided that the products require the same storage conditions, and provided that the products are dispatched from the same site but by different shipments • **Request for Post-importation testing exemption refer to SAHPRA guideline on PITE submit** to susan.khoza@sahpra.org.za (small molecules) • Application for PITE should include: – Application letter on company letterhead with motivation – Module 1 application 1.2.1 – Proof of payment – **CoA, temperature loggers, release documents, stability data**	~3 working days

CONTENT DOES NOT CONSTITUTE REGULATORY ADVICE AND SHOULD BE VERIFIED WITH REGULATOR

1. See SAHPRA variation guidelines for variation criteria. 2. Stop clock principle applies and subject to the extent and nature of the submission

DEEP DIVE: the Section 21 process for COVID-19 related medicines differs depending on whether it is bulk or named patient, on- or off-label usage, and OTC or prescription

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~7 working days

I would like to **temporarily import medicines not registered in South Africa** (and other options i.e. Variation changes have been exhauasted[1]) to overcome a local shortage

Section 21 approval (bulk/ institution, not named patient)

Email to section21@sahpra.org.za **and** shortages@sahpra.org.za **with subject line including "Covid-19 product shortage"** with motivation for S21 submission

SAHPRA will send Section 21 application form (https://www.sahpra.org.za/unregistered-products/ for applicant to complete.

Build application documentation, including

- completed application form with oversight of medical professional;
- product brochure containing relevant chemical, pharmaceutical, pre-clinical pharmacological and toxicological data and where applicable, human or animal pharmacological and clinical data with the medicine concerned;
- details of registration or pending registration of the medicine with any other regulatory authority;
- evidence of compliance of the manufacturer of the medicine with Good Manufacturing Practice standards as determined by the Authority
- certificate of analysis
- reasons why a South African registered medicine cannot be used (e.g., shortage in market)
- Quantity and lead time of order
- Medical professional overseeing the process
- Distribution in order to ensure batch tracing details
- Any additional documents as requested by SAHPRA

Process for Section 21:

SAHPRA will email applicant the form or

Access the Section 21 form www.sahpra.org.za/unregistered-products and complete **online portal**

Make payment and scanned all supportive documents and email to SAHPRA section21@sahpra.org.za

SAHPRA will review and advise

Only when SAHPRA issues **a formal approval letter** can products can be imported into South Africa

Promotion and marketing of unregistered medicines are prohibited

Process outlined here is for private sector. Public sector follows separate existing process through NDoH, in collaboration with SAHPRA.

- Covid-19 medicines (aligned with NICD clinical management: https://www.nicd.ac.za/wp-content/uploads/2020/03/Clinical_management_of_suspected_or_acute_COVID_V1.1_13.03.20_updated.)
- For OTC medicines, application form to be signed by Responsible Pharmacist (RP)
- For prescription medicines and off label use of Covid-19 medicines, application to be signed off by Medical Doctor or RP

Exceptions:

- Where drug is for emergent therapy patient to be enrolled in RTC or if none is available, prescribing doctor to make S21 patient named application and seek patient consent

Note that SAHPRA will prioritize according to internal mechanism based on level of criticality of application