SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
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COMMUNICATION TO STAKEHOLDERS

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Bioequivalence studies performed by Contract Research Organisation (Synapse Labs Pvt. Ltd)

INTRODUCTION

This document is intended to communicate the South African Health Products Regulatory Authority's (SAHPRA's) position to all applicants/Holders of Certificates of Registration (HCRs) who intend to submit/have submitted applications supported by bioequivalence studies conducted by Synapse Labs Pvt. Ltd, a Contract Research Organisation (CRO) located in Pune, India, and SAHPRA's intention to request information in terms of Section 19(2) of the Medicines and Related Substances Act, Act 101 of 1965, as amended (The Medicines Act).

The recommendation follows a good clinical practice (GCP) inspection by the European Medicines Agency (EMA), which showed critical deficiencies. These findings raised serious concerns about the validity and reliability of data from bioequivalence studies conducted at the CRO. The communication issued by the EMA may be accessed here: https://www.ema.europa.eu/en/medicines/human/referrals/synapse.

Bioequivalence studies are carried out to demonstrate that a generic medicine releases the active substance in the body at the same rate and to the same extent as the reference medicine. However, EMA determined that supporting data generated by the CRO was inadequate or insufficient to demonstrate bioequivalence. The EMA, therefore, recommended the suspension of marketing authorisations for the affected medicines.

A list of medicines authorised using Synapse Labs, is available on the EMA website.

EMA is a reference regulatory authority that SAHPRA relies on. SAHPRA supports and undertakes a similar stance as EMA regarding biostudies performed at Synapse Labs Ltd. Find below SAHPRA's position on applications previously approved and currently under review.

Chairperson: Prof Helen Rees • Vice-Chairperson: Dr Obakeng Khaole • Prof Joyce Tsoka-Gwegweni
Prof Patrick Demana • Dr Xolani Khayelihle Ngobese • Adv Hasina Cassim • Ms Ditaba Lucy Maraka
Mr Itani Elias Mashau • Ms Lerato Mothae • Dr Alfred Kgasi • Prof Johanna Meyer
• Ms Mandisa Skhosana • Mr Faizal Docrat • Prof Yahya Choonara
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SAHPRA Action/Position

New applications/pipeline applications

1. SAHPRA will reject all new applications that have passed screening and are currently in the evaluation phase, where safety and efficacy is supported by studies conducted at the above mentioned CRO.

Note: *If the applicant intends to register the same medicine/s in future, where new BE studies become available, a new application should be submitted.*

2. For all new applications that have not passed screening and are still to be evaluated, where safety and efficacy is supported by studies conducted at the above-mentioned CRO, SAHPRA advises that applicants/proposed HCRs withdraw the current submission and resubmit new applications with new BE study/ies to support efficacy.

3. The non-acceptability of BE studies affects the entire submission, including the quality aspects, as a new BE study will result in a new biobatch that would require a revision of most sections relating to the biobatch.

Registered applications

4. For all registered products, where new biostudies from a compliant CRO **are available**, applicants should indicate such in response to the requested information below in Section: Applicant Responsibility.

5. For all registered products, where new biostudies from a compliant CRO **are not currently available**:

    a. Applicants **who intend to** submit a new BE study through a variation process should indicate such in response to the requested information in Section: Applicant Responsibility.
    b. Applicants **who do not intend to** submit a new BE study should indicate such in response to the requested information in Section: Applicant Responsibility.

6. Submission of new BE study variations should be submitted to SAHPRA within two (2) years of publishing this communication, in line with submission timelines which SAHPRA will communicate at a later stage.

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For further information, applicants can refer to EMA's website:
https://www.ema.europa.eu/en/medicines/human/referrals/synapse

Applicant responsibility

In line with section 19 (2) of the Medicines and Related Substances Act, Act 101 of 1965, as amended, applicants are requested to provide information related to the affected registered products on a spreadsheet with the following headings.

1. HCR/Applicant name
2. Application number
3. Proprietary name
4. API/INN
5. Dosage form
6. Study number
7. Therapeutic class
8. Marketing status (i.e. marketed, not marketed, dormant)
9. Post marketing data (i.e. PSURs)
10. Under tender (Yes/No)
11. Alternative biostudy available (Yes/no, specify timeframe for submitting)

It is the responsibility of the applicants to contact SAHPRA with respect to their affected products and follow the SAHPRA directive on this matter. Companies must submit the above requested information within **three (3) months** of publishing this communication. Under section 29 (c), any person who fails to comply with a notice issued under section 19 (2) shall be guilty of an offence.

Boitumelo Semete-Makokotlela
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SIGNIFLOW

Dr Boitumelo Semete-Makokotlela
Chief Executive Officer (CEO)
SAHPRA

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