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Attention:
Senior Manager: Inspectorate and Regulatory Compliance and
Office of the Chief Regulatory Officer

Per email to: Deon.poovan@sahpra.org.za and gontse.moutloatse@sahpra.org.za

4 April 2025

SAHPRA'S INTENTION TO DECLARE MEDICINES COMPOUNDED CONTAINING GLP-1 OR GLP-1/GIP AGONISTS UNDESIRABLE

Dear Mr. Poovan and Mrs. Moutloatse,

Novo Nordisk welcomes the opportunity to comment on the announcement entitled "Intention to Declare Medicines Compounded in terms of Section 14(4) Containing GLP-1 or GLP-1/GLP Agonists Undesirable in terms of Section 23 of The Medicines and Related Substances Act, Act 101 of 1965, as Amended".

The submission below aims to support the intention of SAHPRA to protect the public, in accordance with its objectives as set out in section 2A of the Medicines Act, namely, in the public interest, to "monitor … investigate, inspect … and control of medicines". Section 2B further requires action in relation to adverse events, and compliance with existing legislation.

We applaud SAHPRA in undertaking this measure, and will render any support necessary, and provide any information required by SAHPRA in fulfilling these mandates.

The concern relating to the compounding, on the one hand, and counterfeiting on the other, of GLP-1s are also applicable to other settings, and we urge SAHPRA to consider, in a different

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publication, to re-iterate the principles underpinning lawful manufacturing, lawful compounding and lawful advertising and sale of medicines.

We suggest that action by SAHPRA goes hand in hand with action with liaison, in terms of its mandate in section 2B(2)(a), with other statutory bodies, as the activities related to -

- the prescription of medicines is governed by the Health Professions Council of South Africa, and more specifically the requirements of ethical rules 23 and 27A; and
- the compounding of products by retail / community pharmacists, and the licensing category of pharmacies (retail or community, versus wholesale, versus manufacturing) under the Pharmacy Act and regulations fall within the mandate of the Pharmacy Council, including matters of contract manufacturing.

Please find below our specific comments on how the Declaration could be enhanced through clarification- and enforcement statements.

Kind regards,

Signed by:

Signer Name: Sara Norcross
Signing Reason: I am authorized to sign on behalf of the company
Signing Time: 03-Apr-2025 | 4:28 PM CEST

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Sara Norcross

General Manager

Guideline Title	INTENTION TO DECLARE MEDICINES COMPOUNDED IN TERMS OF SECTION 14(4) CONTAINING GLP-1 OR GLP-1/GIP AGONISTS UNDESIRABLE IN TERMS OF SECTION 23 OF THE MEDICINES AND RELATED SUBSTANCES ACT, ACT 101 OF 1965, AS AMENDED
Due date for comments	5 April 2025

Commenter Details: **Novo Nordisk (Pty) Ltd.** **90 Grayston Drive** **Sandton Gauteng**	**E-mail address of contact person:** **EUPI@novonordisk.com**
Date submitted:	

Current text or reference to paragraph	Proposed Amendment	Rationale
Covering letter attached hereto	• Kindly see covering letter for our general approach to this matter.	
General comments	• We encourage an even stronger messaging that this is ultimately about patient and public safety. A specific suggestion is to remove the 'potential' in the conclusion in relation 'potential safety risk'. • The public should be informed of the lawful processes relating to medicines supply, medicines advertisements and the mandatory nature of prescriptions in section 22A, and as set by the HPCSA for schedules 3 and higher medicines. • Healthcare professionals and the public should be reminded of the mandatory nature of reporting adverse events, irrespective of how or where the medicine was obtained, and the details required by SAHPRA for such a report.	
Additionally, compounded GLP1 or GLP1/GIP agonist medicines may not undergo the stringent quality control testing	• It is recommended that SAHPRA clearly defines and differentiate between the different kind of unapproved products, including compounded and counterfeit/falsified products, with	• We appreciate that the guideline may in fact impact all types of unapproved products, but we should flag that declaring compounded GLP-1's undesirable will not necessarily

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procedures before their release for patient usage, as are required for registered biological medicines. This increases the risk of patients being exposed to substandard, counterfeit or falsified products	clear definitions of what a counterfeit product is, and what unlawful compounding is, to avoid misunderstandings. • "Counterfeit medicine", as defined in the General Regulations, should be included in the statement, i.e. *a medicine in respect of which a false representation has been made about its contents, identity or source by any means including its' labelling and packaging*. A counterfeit medicine can be the same molecule, but is not authorised by the owner of that molecule and/or SAHPRA, as the case may be, to be reproduced, and it may be, but is not necessarily a fake version of that molecule or ingredient. • The following definitions are proposed to be included: ○ *"Lawful compounding" means compounding strictly in accordance with the prescripts of section 14(4) of the Act and regulation 3 of the General Regulations* ○ *"Fake" means not real or genuine, i.e. portraying to be one thing, whilst being another.*	address the increasing and similar risk associated with counterfeit and falsified products. • We support SAHPRA taking actions to address any illicit products or products which may put the safety of patients and the general public at risk. • Compounding may be a vehicle by which counterfeit products are produced. • A counterfeit product may, or may not be "falsified" in the sense that it contains different ingredients, or even inactive ingredients.
Lawful compounding	• Related to the above comment on definitions, it is recommended to make clear what *lawful* compounding is. • It is recommended that the statement include reference to the fact that compounding cannot be used as a way to avoid the controls associated with a licenced entity that manufactures and imports medicines (i.e. to avoid the application of section 22C).	• Section 14(4) sets the criteria for lawful compounding as follows: ○ For a *particular* patient ○ In the quantity as prescribed (which prescription must then be in compliance with regulation 33, as well as the HPCSA rules on prescriptions) ○ The product is not advertised ○ The "active component" appears in a registered medicine, which, of course has to not be counterfeit or

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		fake • Lawful compounding also requires compliance with the relevant sections of the Good Pharmacy Practice (GPP) rules of Pharmacy Council and the provisions of that Act and its corresponding regulations. Notwithstanding the above, it is an important principle of statutory interpretation and the application of the law, that one section (e.g. section 14(4) cannot be used to avoid the application of section 22C (licensing of manufacturers and distributors of medicines). Therefore, lawful or unlawful compounding should not be used in a manner that avoids the application of the GMP- and SAHPRA licensing criteria. Not only the scale, but also the processes, sites and sales activities of compounding pharmacies would indicate intention to act *in fraudem legis*.
Pre-emptive compounding	• It is recommended that the statement refers to pre-emptive compounding as envisaged by regulation 3, and the boundaries thereof.	• The inclusion of pre-emptive compounding as included in regulation 3(c) of the General Medicines regulations, 2017, has had the unintended effect that compounding takes place at a scale that undermines section 22C. • The phrase “retail sale” in regulation 3(c) creates the impression that both compounding under section 14(4)(a) and (b) can be “anticipatory”, which is not in line with the empowering Act. This again raises the issue of *fraus legis*.
Good Compounding Practice Guidelines	• It is recommended to include the fact that compounding can also not serve as a guise under which biosimilars or generic medicines,	• The Good Compounding Practice Guideline that was issued in June 2023 has not been finalized. • Regulation 3(3)(g) envisages

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	which would otherwise be subject to registration, are manufactured.	such a Guideline, and we urge SAHPRA to re-start efforts to finalise such a guideline.

Importation of materials / substances	• Section 14(4) refers to the importance of the active ingredient in any compounded medicine being *registered*.
	• Section 14(4) however cannot be construed to authorize:
	  ○ the importation of any such ingredient in contravention of section 22C(b); and/or
	  ○ the importation of a counterfeit or fake version of such an ingredient.
	• A section 22C(b) importation licence must comply with GMP, GDP and any other "quality assurance principles" set as conditions by SAHPRA. It is recommended that SAHPRA issue such conditions for entities importing ingredients for use under section 14(4) specifically.
	• Where an importer is also a wholesale-seller to pharmacies for purposes of compounding, the provisions of section 22H(1) still apply, namely that such a wholesaler can only procure the medicine from the "original manufacturer" or "primary importer".
		• The SAHPRA statement is silent on the importation of scheduled substances used in compounding (section 22C) and the application of section 22H by wholesalers in supplying to compounding retail pharmacies.

Reference to GLP-1's and GIP's as ''biological medicines'' through out.	• It is recommended that it is explicitly stated that the section 36A declaration applies to **all** GLP1- or GLP-1/ GIP compounded medicines.	• Section 14(4) refers to "ingredients" in registered medicines. • It is not limited to biologics or synthetic versions thereof, both being large molecules. These ingredients are classified as complex polypeptide medicinal products, being synthetically manufactured biological molecules. • This highlights the complexity of manufacturing processes, which

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		SAHPRA acknowledge in its regulation of biosimilar medicines. • The associated quality- and patient safety concerns remain, irrespective of what type of GLP1- or GLP-1/ GIP is at stake
Enforcement in relation to ''No person may sell any medicine declared as undesirable in terms of Section 23 of the Medicines Act.''	• It is recommended that SAHPRA add more clarity on the specific contraventions of the Act (as we set out in the rationale), and how this draft note will be enforced, if implemented.	• This important step from SAHPRA will only have limited impact, if does not come without intentions, plans and resources to enforce the position. • Contraventions of section 14(1), 18, 20, 22A, 22C, 36A of the Act are offences in terms of section 29 and it is suggested that this be highlighted in the notice. Statements that are false or misleading are, similarly prohibited. • The consequences for non-compliance as set out in section 30, should be included i.e. imposition of fines or imprisonment. • Counterfeit medicines can be seized by SAHPRA in terms of regulation 51, and contraventions in relation to the regulations relating to importation are offences under regulation 55.
Marketing (online and social media)	• It is recommended that SAHPRA broadens the guideline to comprehensively address the relevant activities related to the publics access to unapproved products, including compounded GLP-1's and GIPs, in continuation of the point on enforcement above and to protect all root causes of access to dangerous unapproved medicines, including: • **Advertisement**: Clear reiteration of the ban on any direct-to-consumer advertisement of prescription only medicines, including online and on	• Advertising and marketing are not included in the statement, although it is pertinent in section 14(4), and an important part of the provisions on false and misleading communications (sections 18 and 20).

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	social media; and to re-iterate the prohibition on advertisements of compounded medicines, also to authorized prescribers.
	• **Prescription and dispensing**: No compounding or dispensing without a lawful prescription –
	  • having to precede the compounding and dispensing process (section 14(4)),
	  • complies with the HPCSA rules of a physical examination prior to an informed consent process and the issuance of prescription based on those processes being completed (ethical rule 23);
	  • complies with regulation 33 of the General Regulations.	