



SAFETY-RELATED PROFESSIONAL INFORMATION NOTIFICATIONS (SR-PINs)

This guideline is intended to provide recommendations [information](#) to applicants wishing to submit applications for [regarding safety and safety-related amendments to the Professional Information](#) of a registered ~~essier of a medicine~~ [by notification process](#). It represents the South African Health Products Regulatory Authority's current thinking on the safety, quality and efficacy of medicines. The Authority reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. SAHPRA is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

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1 Introduction

The Professional Information [for a medicine](#) is a legal document [which must be approved by](#) and requires [the](#) South African Health Products Regulatory Authority (SAHPRA). ~~approval to be valid.~~ The purpose of this document [guideline](#) is to provide a process whereby ~~certain~~ safety and safety-related changes [amendments](#) to Professional Information ~~could~~ [can](#) be implemented ~~without review by SAHPRA but by~~ structured a notification process.

This process is intended for the implementation of safety-related changes to the Professional Information after notification to SAHPRA within a defined time period if no response is received from SAHPRA. ~~The~~[This](#) process is referred to as Safety- Related Professional Information Notifications (SR-PINs).

2 General SR-PIN Application Requirements

2.1 All proposed SR-PIN applications must be submitted as proposed Professional Information amendments, and include all supporting [source/reference](#) documentation, ~~as is required by the current system in place to~~ [substantiate/support the proposed safety or safety related amendment\(s\). Documentation must include an assessment report as to why the proposed safety information amendment\(s\) to the Professional Information will not change the already known benefit risk profile of the medicine.](#) All proposed SR-PINs submitted should contain a [cover letter which lists all the proposed safety related amendment\(s\) to the Professional Information as well as a](#) declaration, signed by [both](#) the Chief Executive Officer (CEO) and the Responsible Pharmacist, [or on their behalf by their deputies](#), that the [application](#)/submission is compliant with the requirements of the SR-PIN guideline. The code CCC-SRN is used for [a](#) SR-PIN [application](#)/submissions [is](#) "CCC-SRN".

2.2 ~~Any change to approved Professional Information which significantly changes the balance of the clinical benefit to risk ratio of a medicine is not acceptable as an SR-PIN.~~

2.3 ~~Any SR-PIN change~~ [amendment\(s\)](#) to ~~medicine~~ Professional Information must simultaneously be applied to the ~~medicines~~ patient information leaflet [of that medicine as well as](#) and to the Professional Information [and patient information leaflet](#) for any [a similar](#) medicine, registered, but [currently](#) not marketed, ~~and included in the submission by the applicant.~~

2.4 ~~Changes made to the Professional Informations and/or patient information leaflets without prior review which are not in line with the defined criteria of an SR-PIN will be regarded as unapproved.~~

2.5 An accompanying letter should state

- the type of safety-related amendment
- that the submission is in line with the requirements for an SR-PIN

2.6 ~~If the application (submission) does not comply with the requirements~~ [of the SR-PIN guideline](#), it ~~must~~ [will](#) be rejected [as a SR-PIN application](#) by SAHPRA within 60 working days of receipt at SAHPRA, [which is regarded as the date on the date stamp which serves as proof of delivery of the SR-PIN application, coded as CCC-SRN.](#) If there is no rejection [response](#) from SAHPRA after 60 working days [of the date, serving as proof of delivery of](#) the SR-PIN [application / submission](#), ~~it~~ [it](#) can be regarded as [that the SR-PIN application / submission has been approved / accepted by SAHPRA.](#) ~~The time period for the response starts on the day of receipt at SAHPRA (not necessarily the date recorded on the cover letter of the applicant).~~

2.7 ~~A Professional Information amended according to this process must be printed and included in the pack of the first batch produced after 120 days of acceptance at SAHPRA.~~

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2.4 Safety related Professional Information amendments approved by the SR-PIN process, must be implemented, and the amended Professional Information/patient information leaflet included in medicine packages as soon as possible, but not later than 120 working days following the approval/acceptance thereof by SAHPRA. The holder of the certificate of registration (applicant) should inform SAHPRA of the date of inclusion of the amended Professional Information/patient information leaflet in medicine packages, and provide SAHPRA with a copy of the SR-PIN amended Professional Information and patient information leaflet.

~~2.85 The An applicant must submit all final printed Professional Information and/or PILs that were submitted for SRPINs in an must submit an annual report to SAHPRA by the end of the first quarter (31 March) of every each year. The annual report should take the format of line- listing, which includes the date of the SRPIN submission, and the type of safety-related amendment in a dated and chronological order, all SR-PIN applications approved or rejected by SAHPRA.~~

~~2.9 Inclusion of any statement/information in addition to that which qualifies the submission as an SR-PIN, will render the submission invalid as an SR-PIN.~~

~~2.10 A list of all submissions of SR-PINs made in the period between the last and the next Central Clinical Committee (CCC) meeting must be presented as an agenda item at every CCC meeting.~~

3 Safety-related Professional Information notifications (SR-PINs) Sources/References that can be used to support and/or substantiate a SR-PIN application

3.1 Clinical studies;

3.2 Most recently updated SAHPRA approved innovator Professional Information, and if medicine is no longer marketed, the most recently updated SAHPRA approved interchangeable multisource medicine Professional Information;

3.3 Most recently updated Professional Information of medicine which has been approved by a Regulatory authority with which SAHPRA aligns itself. The data/information which prompted the updating of the relevant section(s) of the Professional Information should also be submitted;

3.4 Most recently updated Company Core Data Sheet (CCDS). The data/information which prompted the updating of the relevant section(s) in the CCDS should also be submitted;

3.5 Expert reports with data/information relevant to the section(s) to be amended in the Professional Information;

3.6 Relevant published scientific literature;

3.7 Relevant excerpts from most recent editions of internationally available textbooks e.g. USPDI, Martindale (for safety issues) and Goodman & Gilman (pharmacology); and

3.8 Relevant acts and/or regulations, guidelines/guidance documents published by SAHPRA or relevant guidelines/standards published by relevant competent bodies.

~~3.1 Information relating to safety including alignment with regulations as well as Professional Information standardised text (wording) as determined by the Authority from time to time for inclusion in the Professional Information, which is applicable to all products containing a specific substance or applicable to a class of medicines, may be implemented without review.~~

~~A submission for a proposed Professional Information amendment together with all supporting documentation, however, is still required from the applicant to inform SAHPRA that the change to the Professional Information is being made. The wording of standardised text as determined by the Authority must be used. If the applicant makes any changes to the wording that may alter the meaning or intensity of the information, a submission with information in support of the deviations must be made.~~

- ~~3.2 Amendments that concern the inclusion of safety related information and adverse reactions under the headings Warnings and Special Precautions, Interactions, Side Effects, and Known Symptoms of Overdose, in line with the most recent "global" company core data sheet (CCDS) update and other reputable sources, provided they do not affect the risk:benefit balance of the medicine. In cases where the risk:benefit balance is affected, amendment will require full review and approval by SAHPRA prior to implementation.
A submission must include the reference CCDS together with the information on which the CCDS update is based and information from other reputable sources. Such amendments may be implemented if the applicant has had no response from the secretariat within 60 working days of the date of submission to SAHPRA offices.~~
- ~~3.3 All other safety related amendments or amendments which do not comply with the above will be subject to the current process in place, whereby submissions will be reviewed in turn as received.~~

4 Amendments requiring full review and approval by SAHPRA that do not qualify for the SR-PIN process

- [4.1 Inclusion of any statement/information other than or in addition to, what is allowed by the SR-PIN guideline.](#)
- 4.1.2 Addition of a new indication or a change to an approved indication.
- 4.1.2.3 Changes to the dosage and directions for use.
- ~~4.3 Inclusion of a Contraindication.~~
- 4.4 Changes to the composition/formulation. ~~(These will be dealt with by the Post-Registration Amendments Unit of the Directorate: Medicines Evaluation & Research.)~~
- 4.5 Any [safety or safety related](#) amendment to the [approved](#) Professional Information that [which](#) changes the [clinical](#) benefit-risk profile [for the use](#) of the medicine, [or softens any safety or safety related information already in the Professional Information or removal of safety or safety related information from the Professional Information.](#)
- 4.6 Any safety or safety related issues, that have given rise to significant correspondence/interaction between the applicant and Regulatory Authorities with which SAHPRA aligns itself, Dear Healthcare Professional (DHCP) letters, public health advisories, press releases or similar safety alerts, or other significant communications to the public or health care professionals in any other countries. ~~(see USRN guideline).~~

5 Update History

Date	Reason for update	Version & publication
2008	Published for comment	October 2008
July 2012	Released for piloting	v1, November 2012
March 2014	Guideline name changed. Amendment to sections 1, 2.6, 3.2, 3.3 Addition of new 2.10, 4.6	v2
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September 2016	Version 3 published for comment Amendment to sections 1, 2.1, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 4, 4.2, 4.4, 4.5, 4.6, 4.12 Deletion of sections 3.3, 3.4, 3.5, 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11	v3, November 2016
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June 2017	Version 3 finalised Amendment to sections: Purpose of the guideline, 1, 2, 2.1, 2.3, 2.6, 2.8, 4, 4.1, 4.5, 4.6 Deletion of sections: 2.2, 2.4, 2.5, 2.7, 2.9, 2.10, 3, 3.1, 3.2, 3.3, 4.3 Addition of new section 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 4.1	v3, August 2017
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