SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

COMMUNICATION TO STAKEHOLDERS

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Renewals Frequently Asked Questions

This document is set to provide the summary of the frequently asked questions regarding the Medicine Registration Renewals Process ensuring a consistent approach to benefit all stakeholders to ensure quality, efficacious and safe products are available to the public.

The document covers specific questions in relation to but not limited to the following:

- Inactive Products/un-marketed products
- Products registered before 2017 and not yet registered (old medicines)
- Variations review during renewal
- PI/PIL, GMP approval and CPP, PQRs, QIS and QOS
- Risk Benefit assessment report
- Product Schedule during renewal process
- Process timeline
- Renewals Workstream structure and Schedule

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

INDUSTRY DISCUSSION – RENEWALS GUIDELINE FREQUENTLY ASKED QUESTIONS

FAQ / Applicant Questions	Response from Authority
1. Are the timelines provided for submission of applications for the review process prior to expiry date in working days or calendar days?	The timelines provided are in working days, i.e., 120 days. This corresponds to 6 months prior to the expiry date.
2. Will the timeline, in terms of days, allocated for each step in the process be included in the process map?	The timelines for the different steps will be established and refined during the pilot process. A more granular process map which will include the number of days for each step would be published once the pilot is completed.
3. Will a Portfolio Co-ordinator be linked to a company as was done in the Backlog Project?	The PC appointed in the Renewals workstream will be responsible for the end-to-end coordination of the process. The PC will not be linked to a specific portfolio of companies.
4. Which SAHPRA portal will be used for this submission of renewal applications?	Renewal applications should be submitted via the FTP system until further notice.

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5. Considering that veterinary medicines applications were required to be converted to CTD from 1st Jan 2022, are applicants expected to convert the veterinary medicines to eCTD for the renewal applications?	From Jan 2022, all veterinary applications should be submitted in CTD format. Applicants should submit renewal applications in eSubmission CTD format via the FTP platform. Submissions for renewal of veterinary products will not be in eCTD format for now, until further notice.
6. What is the scenario regarding dormant medicines for the renewal process	Dormant medicines are required to be renewed. Failure to do so will result in them being cancelled. The Renewal process is applicable to all registered products, regardless of their marketing status.
7. Will the Type IA and IB be managed by DVP portal which cannot handle eCTD submissions? And once we submit the renewals in eCTD format, how will we manage those variations, will the DVP portal be updated or how will those Type IA and IBs be managed after the eCTD roll out?	SAHPRA is in the process of procuring a Regulatory Information Management System and the tool that we envisaged to deploy and we will be managing all of the documents through one of the industry tools. In future, variations will be submitted in eCTD format to then be recorded as the sequences on this software platform so that we have got all of the life cycle management and we have got all the information in eCTD format through this tool.

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8. Should applicants submit Modules 1-5 or Modules 1-3 when it pertains to the submission of a full eCTD baseline dossier?	Module 1-5 will be required fora baseline dossier for all applications that are currently not in eCTD format. An application for renewal which will be a follow-up sequence should only consist of the information that is requested in the Renewals Guideline.
9. Please advise of a solution in the case of TOAs where new applicants do not have visibility of previous submissions on the DVP but are required to provide a history of amendments in the application for renewal of the relevant products. .	This will be well taken care of by the RIMS which will ensure we have all the history in one place provided we have received a baseline dossier in cases where we do not have. Amend to include statement from Communication
10. Are eCTD baseline dossiers only required for those products not in eCTD format?	All applications submitted in 2017 and prior where we do not have eCTD baseline dossiers will be required to have baseline dossiers submitted in eCTD format.
11. What is the consensus regarding old medicine where Module 4 and Module 5 information is not	At this point the old medicines will not comply with Module 4 / 5 and this will be discussed in the consultation sessions that will be starting next year as the framework is firmed up.

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available?	
12. How do we submit baseline dossiers in eCTD format if applicants have already submitted a variation in eSubmission format?	Applicants are required to convert the variations in eSubmission format to eCTD and submit the eCTD as a baseline.
13. What is the process regarding grandfathered/ old medicines that do not meet the requirements for application for a renewal	Further information regarding grandfathered/old medicines will be communicated in due course.
14. What measures will be in place to ensure that we do not have Backlog of applications for renewal?	The roadmap spans across 13 years and accounts for the large number of products that would have to be reviewed. The applications will not be processed at one go. The roadmap allows SAHPRA to start with products registered in2018, then 2019, then 2020 and so on. We will then slowly build up capacity internally to ensure that we do not start running into a backlog. We would have enough time to bring relevant resources on board and train them so they can look after the renewals on an ongoing basis. This is something that will happen over the course of 13 years as there will be step changes at different intervals. The key is to make sure that the renewals requirements and the renewals evaluation process is very streamlined but still

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	exercise due diligence in terms of renewing certain critical information and obviously ensuring patient safety.
15. It is not always possible to plan variation in advance of the process, Are there any exceptions With regards to variations submissions being made together with a renewal application	Variations should not be submitted together with a renewal application. Variation applications should be submitted as a follow up sequence via the FTP system.
16. How far in advance can an applicant submit for renewal, e.g. is 6 to 12 months in advance accepted?	Renewals should be submitted at least 120 working days (6 months) prior to the expiry date, which corresponds to 6 months.
17. Issue on the interface between eSubmission which were in CTD format but not on eCTD but in sort of NEES format, so far there is a lot of practical examples where bit	For variations where eCTD baseline have been submitted before, if there are these kind of variations coming through now, the requirement is for the baseline to be submitted along with the variation. For instance, if SAHPRA have got something that was previously submitted in a CTD or eSubmission format, if there is any significant variations right now, normally is eCTD baseline plus the sequence.

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Type II variation has been submitted in eSubmission format and now suddenly we are faced with providing a baseline eCTD. And the issue for us then is do we go backwards and take out that variation because the timing of the renewal is not something that we can control. So the practical issue for the industry is where you have that transition; you have got very big Type II eSubmission which is already in the system and now you suddenly faced with baseline eCTD and what we were hoping would be entertained is that huge variation will be able to be integrated into the baseline eCTD. So this is the sort of the special case that we are going to have in many cases because of the eCTD baseline issue?	Pending variations in eSubmission format –applicant should submit the renewal application once the variation is approved since the formats are different and to manage life cycle of the product information.

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18. If the applicant submits a renewal application, then it is understood that applicants can still send the variation through the FTP/DVP in parallel if for example, Type IA/Type IB quality variation comes up from the manufacture?	To re-confirm that, yes, that is the case. We then allow the normal process of amendments/variations to carry on and that also gives colleagues a period where we move to the good software platform that will allow us to have visibility across the teams and also to see amendments across the teams amendments that pending or has been reviewed etc. Yes indeed we will still allow for those amendments to run through the normal process whilst we are busy doing the renewal in the other work stream.
19. If baseline have already been submitted, does the renewal date move out?	Baselines submission do not have an impact on the original registration date, therefore, the renewal due date will also be not impacted by baseline submissions.
20. Is the EU also enforcing this renewal program or is it already in place?	Renewal process is already in place at EMA.
21. Can we submit the PI/PIL as was 5 years ago and the current one; and then attach all Labelling Variations which were submitted and	Amendment schedule will be sufficient showing all the variations in the previous 5 years and must be submitted together with the current approved PI/PIL.

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approved?	
22. Which PI/PIL are we supposed to use SmPC or not?	Will stick with the SmPC while we are sorting out the regulation issue.
23. If the PI is in the SmPC format, does the PIL also have to be in the new format given that the regulations are not yet updated?	The current format of the approved PIL will be accepted until the regulations are updated and published for implementation.
24. Where a manufacturer source country no longer issue the GMP certificate, what would be a suitable substitute?	A suitable substitute will be a certificate from the Recognized Regulatory Authority (RRA) or from SAHPRA itself as per the GMP guidelines.
25. Does the resolution letter have an expiry date?	The resolution letters have an expiry date, it is noted in the resolution how long that resolution letter is valid for. Should you have any concerns around that and is affecting your renewal, you need to contact the inspectorate in order to say that the inspection needs to be planned for that particular site or if you have the reliance certificate that meet requirements in terms of GMP, you can submit that as well.

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26. FDA does not issue GMP certificates and nor letters, please advise?	FDA does have the Establishments Inspection Reports (EIR) which we use for reliance. These reports, from the FDA, should be included in the application for the relevant sites.
27. Will the QIS and QOS replace the SCoRE?	Yes, the QIS and QOS (if the SCoRE has not been submitted already for the product) should be submitted for renewal applications.
28. Where in the CTD dossier will the QOS and QIS be inserted?	In Section 3.2.R.8
29. With regards to the PQRs, the requirement is that we need to conduct a review of 10 or 25 consecutive batches, in cases this is not possible, and will it be acceptable to use batches that were manufactured or maybe just released for other markets and not necessarily in SA?	The review should be conducted for export products as well, so we talking about the principal manufacturing in the country they are in and they are required to do periodic quality product review and the reason for this review is to verify the consistency of the existing process, the current specifications for both starting materials, finished products and to highlight any trends. So it would be value adding if you did include those batches because then it would give the Regulator an idea of whether the processes controlled at the point of manufacture.

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30. Will the SAHPRA template be issued for QOS/QIS?	QIS and QOS templates will be published after the pilot has concluded.
31. What are the phases for? Are we getting a list of product to be submitted according to therapeutic use during these phases?	Products registered in specific years and have been bucketed into different year groups which is a phase and within the phases is the subsections per quarter. The schedule will then inform the applicants when the renewal applications should be submitted.
32. If the duplicate registrations renewal date comes up before the master registration, which date will be used to plan for the renewal?	The renewals framework is at a line item level also when a product line has been registered it would then be due for renewal based on its individual registration date.
33. Will the renewal of all applications be once off and not every 5 years that pass, as it is reported that EU will do away with the renewal all together as of Jan 2022?	According to our legislation, that is section 15, subsection 6A, Registration is valid for 5 years, which means renewal applications has to be submitted within 5 years.

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34. Can we consolidate the master and clone into one eCTD baseline?	Yes, the master and the clone can be consolidated into one eCTD baseline, however the Renewal applications will be taken case by case depending on their respective dates of registration.
35. Have we identified the applicants that their products will be involved in Pilot?	Yes, the products for pilot have been identified. And communication with those applicants relating to these specific products will then be shared now after this workshop in early next week so that there will be enough time to set up further discussions with the respective applicants.
36. Based on past experience, the project where innovators and generics were not aligned for clinical, we suggest that innovators be renewed first	The framework specifies what the evaluators should look at. There are specific areas that focus on the safety, quality and efficacy components that the team will look at. The approach is slightly different to what is being done in registration process.
37. Prioritising format, I know that it has been suggested that innovators be looked into first but is there going to be a process maybe, will it be like a FIFO type of thing or will there be a quality and	The renewal process will not follow not follow any priority process but will be processed according to the registration dates as per schedule shared.

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efficacy portion attached to which ones do get reviewed or rather renewed first. So if there is the process, could that be share but if there is still going to be taking it back internally, kindly advice?	
38. Since the renewal include the approved information, does it require approval again or a check from SAHPRA?	Renewal process will not include the re-evaluate approved information. There will be specific areas that evaluators will focus on with respect to safety, quality and efficacy components of the medicine.
39. For products where there is no eCTD baseline for products called up for renewal, will the baseline submission on its own be acceptable for the purpose of renewal to be completed or the baseline need to be submitted with the separate variation sequence?	Baseline, sequence 0000, should be submitted and the renewal information should be submitted in sequence 0001

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40. What file name convention should be used for the renewal submissions?	Application number-REN-Sequence number Example: (i) When converting to eCTD the following naming convention should be used: 540000-REN-0000 (for the baseline) and 540000-REN-0001 (for the renewal information (ii) When the renewal application is submitted as a follow up sequence, the following naming convention should be used: 540000-REN-00XX where XX is the relevant follow up sequence number
41. If the dossier is very outdated, like dossiers in MRF format and it was never updated completely; as it has been said that old information will need to be changed would that not then be a variation? So will we need to put in a variation first before we do renewal or do we make those changes as part of the renewal?	Test methods that changed that are supposed to be submitted as an update and variations to them should have been submitted already in the dossier. What SAHPRA is avoiding is to have to deal with those issues because there are applicants that are not updating this information. At the time for submission for renewal, SAHPRA would require that applicants have updated or brought this in line with the current standards. Even if some of the guidelines requirements have not been met, these are things that should have been brought in line once these guidelines has been changed. In cases where this has not been done, it should be done before hand, ideally for renewals all of this should have been submitted already. These should have already been approved before hand, SAHPRA don't want applicant to have to submit an application where these are not done. If not done, it will results in the renewal being rejected as it will not be aligned to the latest Pharmacopeia.

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42. Please advise where is the guideline for template to be included in the renewal?	The guideline states clearly what will be required for renewal submission. It has stated that Module 1 and also stated the requirements for products dated 2017 prior. And other product from 2018 to date, the information is also indicated in the guideline.
43. At the time of renewal and the variation has not yet been approved by SAHPRA, is it possible to get an extension for renewal submission?	Applicants will be reminded of their renewal 6 months before the renewal due date.
44. Please confirm if the exemption will be retained for non-clinical and clinical data which were exempted at the time of registration?	No change in requirements for Non-clinical and clinical data for renewal. The renewal is based on the basis on which it was registered.
45. Will registration number stay the same on the registration certificate?	The registration number will remain the same.

FAQ / Applicant Questions	Response from Authority
46. On the PI/PIL issue; if the Amendment Schedule Format is not a reasonable Compromise; can we submit the pi/PIL as was 5 years ago and the current one; and then attach all Labelling Variations which were submitted and approved. At least those Variations will be on file with us & SAHPRA can compare the then.	Amendment schedule will be sufficient showing all the variations in the previous 5 years and must be submitted together with the current approved PI/PIL.
47. What if you have amendments during the renewal process?	Variations should not be submitted together with a renewal application. Variation applications should be submitted as a follow up sequence via the FTP system. The Applicant should follow the Priority review request process for urgent variations.
Who should be contacted in case of any queries on the renewals process?	Enquiries can be made to the following dedicated mailbox: renewals@sahpra.org.za