S A Pharmaceutical Regulatory Affairs Association
P O Box 2909
Randburg 2125
R.S.A.

Telephone: + 27 (0) 11 852 5252
Telefax: + 27 (0) 865044927

Date: 06 August 2018

To:

- **Chief Executive Officer: Botswana Medicines Regulatory Authority, Dr. Ghanie**
- **Deputy Chief Executive Officer: Botswana Medicines Regulatory Authority, Dr. Selelo**

August 2018: Questions & Answers
Botswana Medicines Regulatory Authority

1. Communication from Botswana Ministry of Health & Wellness dated 17May2017, stated that DRU was working on transition to establish the Medicines Regulatory Authority
    a. Has this process been finalised? – By November 2018, there will be clarity regarding the BOMRA suspension of new applications which was to catch up the backlog.
    b. What effect does this have on medicine registration processes? Registration process is on-going
    c. Will DRU hold workshops or invite comment from industry regarding imminent changes or roll-out? Changes will be communicated with Industry regarding changes and roll-out.

    d. What are the structural changes that have occurred from the BOT DRU TO THE BoMRA? Organograms/ processes etc
    Refer to presentation-Organogram

    e. What are all evaluation process - NEW APPLICATIONS (NCE's/Generics & Variations) in terms of timelines and fees?
    New timelines will be determined and communicated with all stakeholders. The Fee structure is still in draft and under development for finalisation.

    Variation for API site is a longer evaluation – timelines to be communicated later on.
    Only sections for variations must be submitted, i.e. only the hybrid as per guideline

2. Will Medical Devices/Complementary meds/ Health Supplements/Cosmetics (with medicinal claims) etc. be regulated and if yes what is our point of reference for guidelines etc.? Yes, these will be regulated going forward after finalisation of resources.

3. Please provide an updated contact list with telephone numbers and e-mails of all appropriate people at BoMRA

   At present all the work is still done by DRU and queries and questions can be sent to dunit@gov.bw. It is expected that all correspondence will be directed to MRA by November. This will be communicated.
   Contact details: Botswana Medicines Regulatory Authority
   Private Bag 2
   Gaborone Station
   Gaborone. Botswana
   Telephone: +267 3186730
   Email: sselelo@bomra.co.bw

4. What changes can be expected in respect of guidelines and fees...NDA's, Variations, etc.?
   Current CTD guidelines still apply.
   Submit variations according to Botswana guideline, which was adopted from WHO variation guideline. Inclusion of a variation approval from a reference regulatory authority can be used to motivate for fast tracking at the DRU.

5. We understand that BOTSWANA MRA has placed a “HOLD” on all submissions:
   a. When will DRU start accepting new drug applications & Variations? Support comment: (In the past we were advised by our Botswana agent and the DRU not to submit variation applications. When will the DRU start accepting variation applications)? New applications are expected to be received by end of 2018, the date will be communicated.

   b. Are variations/amendments being evaluated and are applicants informed of the outcomes? Timelines for variation approvals? Assessment is on-going and decisions are communicated

6. How should we address variations that had to be implemented despite not being reviewed or approved by the DRU?
   Major and minor variations (as per Botswana guideline) need to be approved before implementation

7. What has happened to variation applications that were submitted to the DRU in the past 10 - 15 years?
Applications are either: In process, some rejected, some approved, work in progress.

8. Considering Botswana's alignment with other SADC countries eg. Namibia, Zimbabwe, South Africa, Zambia, what harmonization and mutual agreements, if any, have been adopted by the DRU eg. wrt GMP Inspections, Abbreviated reviews of applications, etc.? DRU uses a risk based approach thus leveraging on efforts of others such as PICs authorities and joint inspections through zazibona.

9. Other than the ZAZIBONA initiative, is there any initiative to harmonise with SAHPRA? SADC has a bigger program on harmonisation and zazibona is one of the initiatives. SAHPRA is part of the program

10. The Botswana guidelines, make 5 year renewals a requisite for MA's. This did not happen due to the DRU not accepting applications or even reviewing submissions. What is the status of these MA's and will the DRU be expecting renewal applications to be submitted for these applications in future.....Also considering the huge workload on applicants and the DRU is this becomes a requirement. The 5 year renewal has not been implemented, the MA remains valid until further notice. DRU was in deviation from the law, which will be rectified in future.

11. Will GMP inspections be conducted by the DRU/BoMRA in future or will the DRU/BoMRA accept GMP Certificates issued by other authorities? DRU uses a risk based approach thus leveraging on efforts of others such as PICs authorities, however some inspections will need to be done by BoMRA

12. Is there any intention to regulate medical devices in the near future? Currently not regulated. This is one of the new group of products to be regulated in future as provided for by the law.

13. The IPASA PV working group have sent a letter to the DRU for comment regarding recently published draft PV guidelines. IPASA have not yet received any feedback regarding the letter so any opportunity to discuss or receive feedback would be greatly appreciated. IPASA to resubmit the letter as it has not been received.

14. Botswana Drugs and Related Substances Act 2013: Section 23 (3) Exemption from registration. Would section 23 be applicable considering the above suspension? Exemption from registration is provided for patients where there is no alternative or for clinical trials. Motivation should be made by practitioners registered in Botswana.

15. The CPP issued by SAHPRA is valid for 1 year only. It is a mandatory requirement on the Botswana New Dossier Submission Checklist. How does DRU overcome the issue of validity considering the above delay in screening? If CPP was valid at time of submission- DRU did not penalize,

16. Copies of executed and/ blank master production records for commercial production batches. Would DRU accept a justification for not submitting this? DRU requires this for assessment of applications without exception. A way around the challenge of companies unwilling to submit, such as viewing at site during inspection, can be explored.

17. Does DRU require submission of the SMF? How is the SMF number allocated? Refer to the Application form. SMF reference number & version, from manufacturer, is referred to here. This is to guide inspectorate as to when inspection is to be undertaken.

18. Is the QOS not considered a duplication especially where information is already available in the CTD? Does it add value to the dossier? This is particularly related to 2.3.R.2 Analytical Procedures and Validation Information Summaries QOS Is a WHO requirement and was adopted from WHO to be used in generating the assessment report

    Abbreviated validation and analytical information is required and the summaries are required, especially for an abbreviated assessment.

19. How are Dossier registration Renewals handled? Refer to Quest 11 above.

20. The guidelines state that the QOS should not be more than 40 pages (max 80 pages for more complex processes). If the Botswana regulator can clarify on how much detail is required in the QOS, especially with the Analytical Procedures and Validation Information summaries at the end of the QOS, it will be of much appreciation. Summaries of results with discussion and conclusion will suffice.

21. Is there a deadline by when applications for all B-listed products must be submitted?
    GUIDELINE 2015 TO CONVERT B-LISTED TO BOT NUMBER should be used.
    No cut-off time frame to convert the B-listed products to BOT numbers with dossier submission

22. Are CAMS products regulated in the country or not yet? Are they still classified as dietary supplements?

    Complementary medicines include herbal, homeopathic products, supplements and some vitamins in low doses.
    There are guidelines for registration of complementary medicines.

23. What is the format of submitting CAMS or powder supplements for registration in Botswana? The same format as medicine application? Or what documentation is required? There is a different guideline for these, the same to be used for B listed products

24. Can registration application for new products be submitted directly from SA applicant holder for products imported into Botswana? The Act states that the application should be made by a company resident in Botswana

25. What are the requirements for promotional material in Botswana and are any guidelines in this regard available? All promotional and advertising materials must be approved by the MRA. Advertising to the public applies to GSL medicines only, others may only be advertised to professionals

26. Products with B-Numbers:
    a. Please provide update on variation submission process for details impacting the Blue book (e.g. product name change, applicancy change) Variations are being received and processed

    b. Please confirm that a complete new submission dossier/renewal is required for product registration for all products with B numbers. Is there a separate approval process or will the product enter the same path as a new product? i.e. do we expect same evaluation and approval timelines? Refer to Question 24 above

27. Complementary medicines/supplements:
    a. Process for registration or notification for new CM's?
    b. Update on previous call up to register/list current CM's on the market. Are these listings finalised? Can we expect registration certificates? A database of approved CM is available

       Registration certificates to be issued when BoMRA is settled in near future

28. General:
    a. Update on when suspension of new product submissions will be lifted
    b. Update on new DRU structures after legislation change.
    Refer to questions and answers above

29. Please clarify the fees required for all submissions? Since 1992, fee structure has been the same, but a new fee structure is still to be finalised.

30. Please confirm whether only soft e-copies of submissions must be made OR both hard paper copies submitted with an e-copy? E-copies, must these be on a USB or CD-ROM as new technology moves away from CD-ROMs. The application form for original signature is still required in hard copy, rest of dossier can be electronic. CDROMS are preferable.

31. If hard copies are submitted, may these be in lever arch files? No, only pronged files accepted.

32. Will BOMRA be looking to e-CTD submissions and if yes when and what software program is being considered? Yes in future, not at this point in time.

33. For new people within the regulatory affairs environment, please clarify the difference between B numbered medicines and BOT numbers?
B listed products are those that were on the market before regulation, BOT products are those that have undergone an evaluation and registration process. They are both allowed to be marketed in the country

34. Considering that most products enter Botswana through South Africa, please clarify whether you will accept Multi-market label. (Also note that the package insert states ATC classification and we have historically utilised the ZA system- What added value is the ATC providing?) Multi market labels have been approved in the past provided they have English as one of the languages and covers all the areas specified in the law, regulations and guidelines.

35. Please discuss the Labelling regulations and how these may be harmonised for multi-market products (e.g. Bots requires name/address of mnf)? Work has been underway at SADC to harmonise labelling

36. When will BOMRA issue registration certificates? After BOMRA is settled and functionalities are in place.

37. What are the requirements for an in-country representative? For e.g. are there any specific qualification/registration/licencing requirements?
Act says the applicant is a company resident in Botswana.
Qualifications to be confirmed by Dr Selelo as to what is required by law.

38. The website does not contain the latest updated Blue Book/registration status of products. Where this can be obtained?

    Blue book obtained at a cost of 50 pula. The database is then sent via e-mail by DRU. There is a separate database for CAMS

39. What mechanism and platform are there for direct face to face engagement of an applicant with the DRU for unique queries and circumstances?
    Meetings are able to assist and engage industry where relevant. Appointments for meeting with agenda should be made.

40. What are the requirements for promotional material in Botswana and are any guidelines in this regard available?
    MML labels allowed, ATC classification not a deal breaker
    Manufacturer details are required

41. New product registration - With recent new product approval received, discrepancies have been noted between the product applications submitted to DRU and approval letters issued, e.g incorrect trade name approved, strengths not applied for approved, packaging not applied for approved. These discrepancies are costly to the industry as they delay product launch of critical molecules. Is there a way in which the MRA and industry can work together closely to minimize the occurrence of such issues?
    BOMRA requests that the specific companies to communicate directly with Dr Selelo to iron out the discrepancies.

42. Is there possibility to consider email address for PV Communication, especially considering the requirement to receive acknowledgement receipt from authority with respect to CIOMs? CIOMS received by e-mail so there is currently, a direct e-mail communication to DRU

43. PBRER acceptable, how should this be presented – electronic or paper?
    - PBRER's may be sent via e-mail however may be too large,
    - File size for email needs to be confirmed by Dr Selelo for BOMRA.
    - BoMRA is currently setting up IT systems that will facilitate improved communications, including Electronic submissions.

44. The issue relating to sampling, donations and bonusing are not covered in the Act/ Regulations/ Guidelines. Does the MRA allow sampling/bonusing/donation of products? If yes, what are the allowable instances?
    Sampling and bonusing is not provided in the law but a statement may be included in the regulations.
    Industry -Direct selling companies would need to engage regarding bonusing and sampling

Public sector donations have to go through Central Medical Stores.

Private sector donations are PRE-authorized via BoMRA – A QC, ID test may be conducted on the product

General:

ZAZIBONA looked at over 200 applications, whilst Botswana reviewed approximately 50 applications. Zazibona applications must be submitted in at least 2 participating countries.

Biosimilar:

- Biosimilar evaluations have not yet been conducted as there was no capacity at DRU, however, going forward the WHO guideline would be used by BoMRA.
- Suggestion that Zazibona would be an excellent route to submit a biosimilar.

Veterinary:

Previously no registrations with veterinary medicines, however going forward BoMRA will have to implement a way forward for a smooth transition in order not to hamper access to veterinary products. Guidelines will be similar to human medicines for Quality & safety sections

Clinical Trials:

- The Health research and development committee (HRC) must approve clinical trials
- Not many applications processed in Botswana.
- ADR'S must be reported.
- Safety updates for newer products must be submitted

Question from Dr Selelo: Why companies register products and then not market: this greatly compromise access

The implementation of retention fees might assist to decrease product evaluation and registration which lies dormant and not marketed. A suggestion was made for implementation of a "Sunset clause", however another suggestion was that BOMRA to send out a communication regarding "withdrawals" of dossiers wherein industry notifies BoMRA with a suitable notification of withdrawal of product dossier.