Feedback from RA workshop
2 June 2011
Lisa Urio – Pharmacist
Botswana DRU

HILDE RODSETH

Participants:

- BOTSWANA DRU: Lisa Urio
- PIASA: Kirti Narsai
- IMSA: Ilse Cukrowski & Marianne Zenon
- SMASA: Merle Scher & Eunice Mogotloane
- NAPM: Nerine Du Plessis
- SAPRAA EXCO: Salma Ismail, Hilde Rodseth, Yolanda Peens
- PHARMISA: Jenny Gedye, Sandra Abreu
- SAAPI: Salima Mahomed
- OTHER: Denzel Koopman

Q1: Best method for communication with DRU, e.g. phone, email, fax?

- DRU not own website – see Ministry of Health & under clinical services for guidelines
- Emails checked at least every 3 days (but sometimes server problems)
- Pharmacists do check email boxes of absent colleagues
- Phone if response to email not forthcoming
- Regulatory officers of DRU have been assigned specific company portfolios (we have requested copy of list to email to SAPRAA members/SAPRAA website)

Q2: Is CTD format now also accepted? If yes, is the ZA CTD format acceptable?

- DRU is moving towards the CTD, but EU CTD NOT ZA CTD
- Applicant still to complete MH 2048 with cross reference to CTD (for now)
- Pre-registration evaluation checklist and new Summary of the dossier in WORD still required

Q3: Could the DRU please consolidate all requirements into one document? Now: guideline + eval form + screening

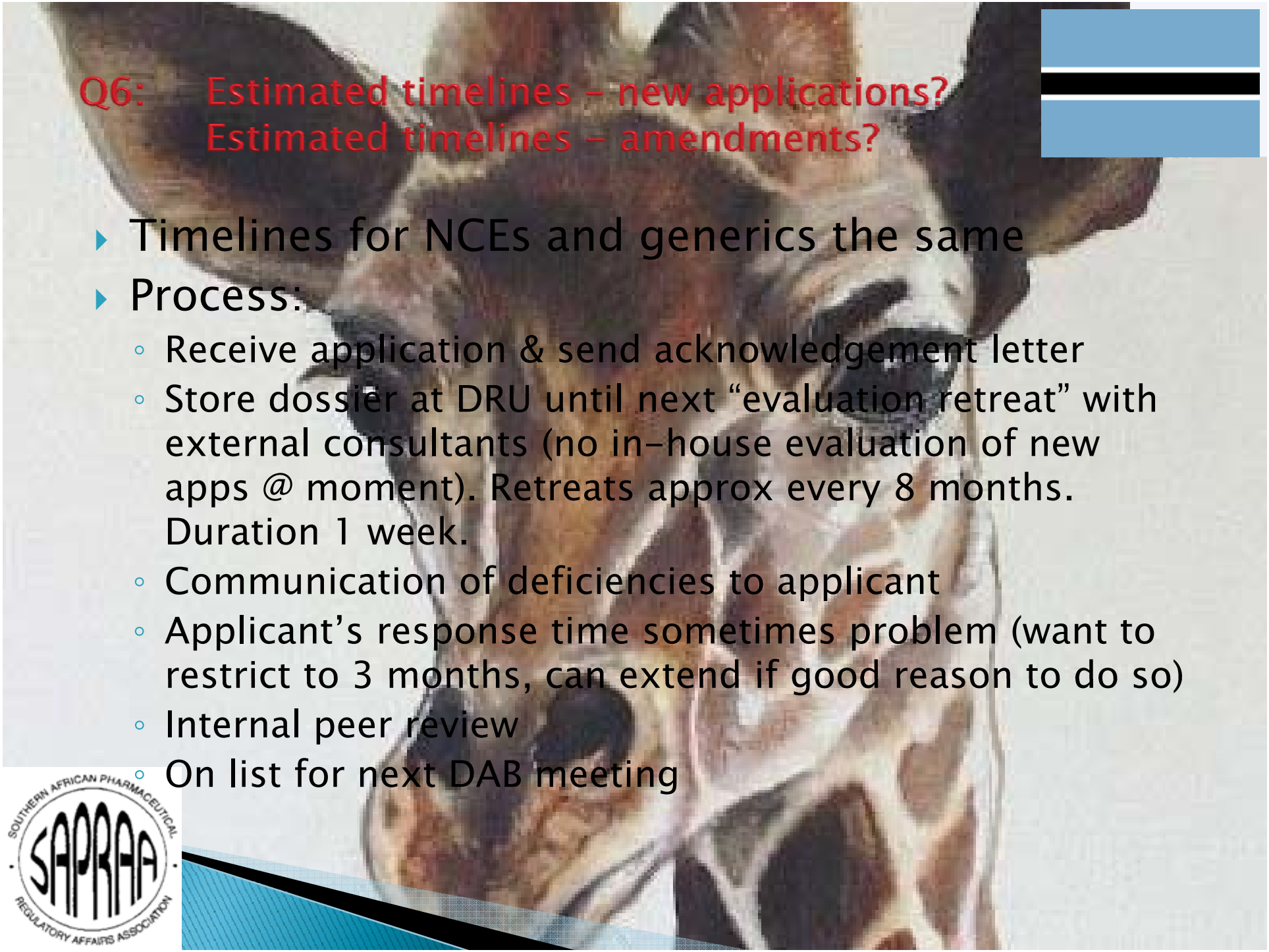
- The DRU does not see this request as feasible

Q4: Could DRU update application form to include all req? When working with form, applicant can find all related requirements for that section

- DRU is of the opinion that this would make the application form too bulky
- The current situation of having separate documents likely to remain in place

Q5: Please confirm whether DRU needs hard copy and/or electronic copy and how many copies? What is mandatory, what is optional?

- Administrative requirements are as follows:
  - Original covering letter – must itemise submission – not bound into application volumes
  - One hard copy MH 2048 (copy of covering letter attached to each volume)
    - Rigid plastic binders preferred – no lever arch files
  - One hard copy proof of payment
  - One hard copy signed pre-registration evaluation checklist
  - One hard copy signed "Declaration by the Applicant"
  - One CD (CD does not have to re-writable) containing:
    - MH2048 (pdf)
    - WORD version of Summary of the dossier

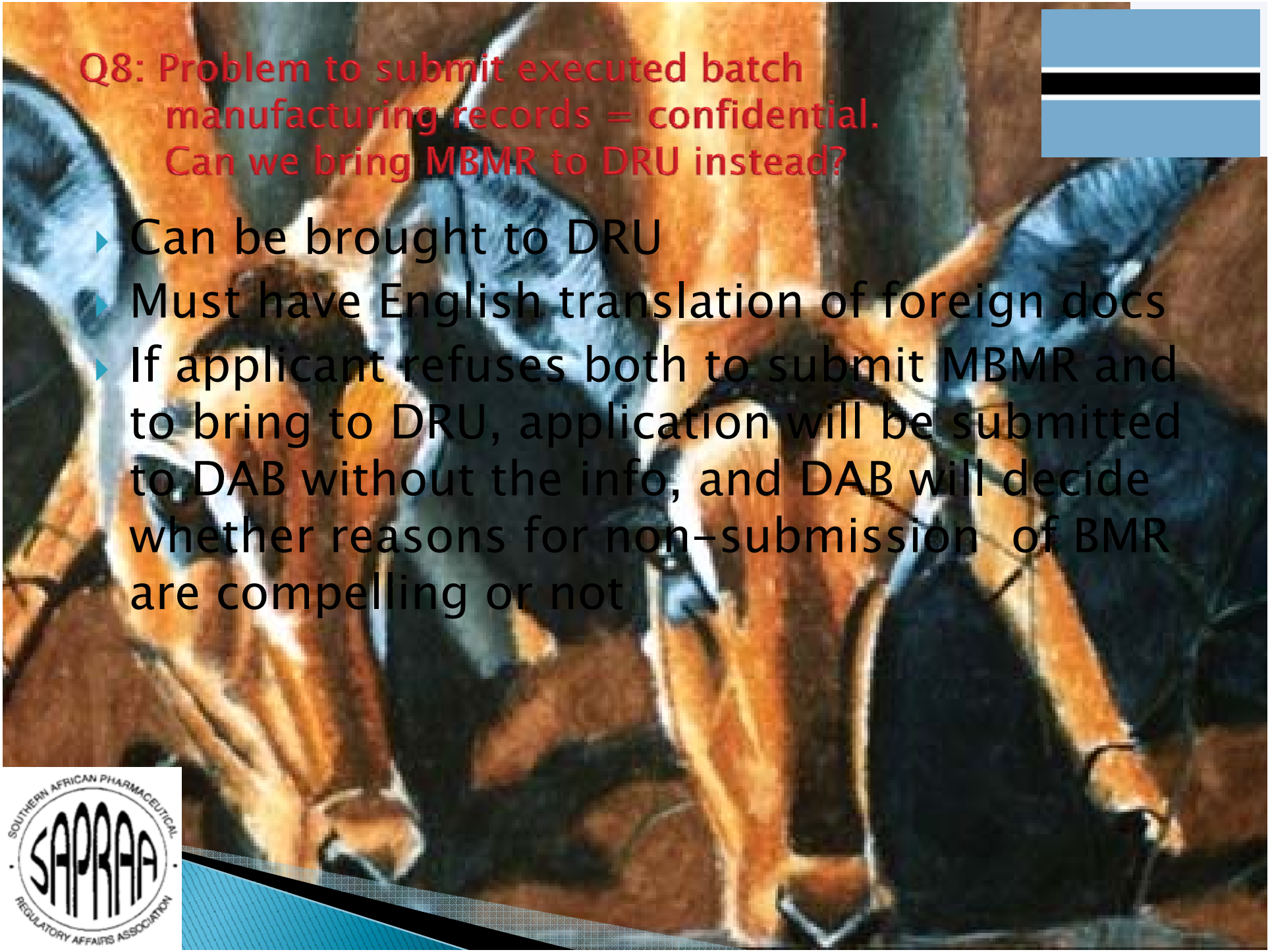


Q6: Estimated timelines – new applications? Estimated timelines – amendments?

- Timelines for NCEs and generics the same
- Process:
  - Receive application & send acknowledgement letter
  - Store dossier at DRU until next "evaluation retreat" with external consultants (no in-house evaluation of new apps @ moment). Retreats approx every 8 months. Duration 1 week.
  - Communication of deficiencies to applicant
  - Applicant's response time sometimes problem (want to restrict to 3 months, can extend if good reason to do so)
  - Internal peer review
  - On list for next DAB meeting

Q7: Estimated timelines – new applications? Estimated timelines – amendments?

- Aim for DAB meetings every 2 months, but sometimes have to be postponed if full quorum not available
- DRU in-house staff only deal with variations & responses day-to-day, eval. of new applications done at "retreats" (paired with ext. expert)- next one in Aug 2011 & Dec 2011 (TBC based on funds)
- At moment 160 applications pending evaluation
- Major amendments: 7-8 months to approve



Q8: Problem to submit executed batch manufacturing records = confidential. Can we bring MBMR to DRU instead?

- Can be brought to DRU
- Must have English translation of foreign docs
- If applicant refuses both to submit MBMR and to bring to DRU, application will be submitted to DAB without the info, and DAB will decide whether reasons for non-submission of BMR are compelling or not

Q9: If we can bring MBMR to DRU, to be arranged how long after submission of new product application?

- Only to be brought to DRU after receipt of a request for submission – cannot be done pro-actively
- Contact DRU pharmacist responsible for your company to arrange review

Q10: Submission of reference standards req? Does DRU actually use these to test? Biologicals a problem (temp. control, diff methods)

- DRU submits reference standards to Drugs Quality Laboratory for testing
- Previously DRU informed us to only submit these on request
- Ask company representative to alert DRU when submission of cold-chain samples and/or reference standards are planned

Q11: Guideline addendum = dossier summary requirement. Virtually another dossier! Are all details really required? Why summary required?

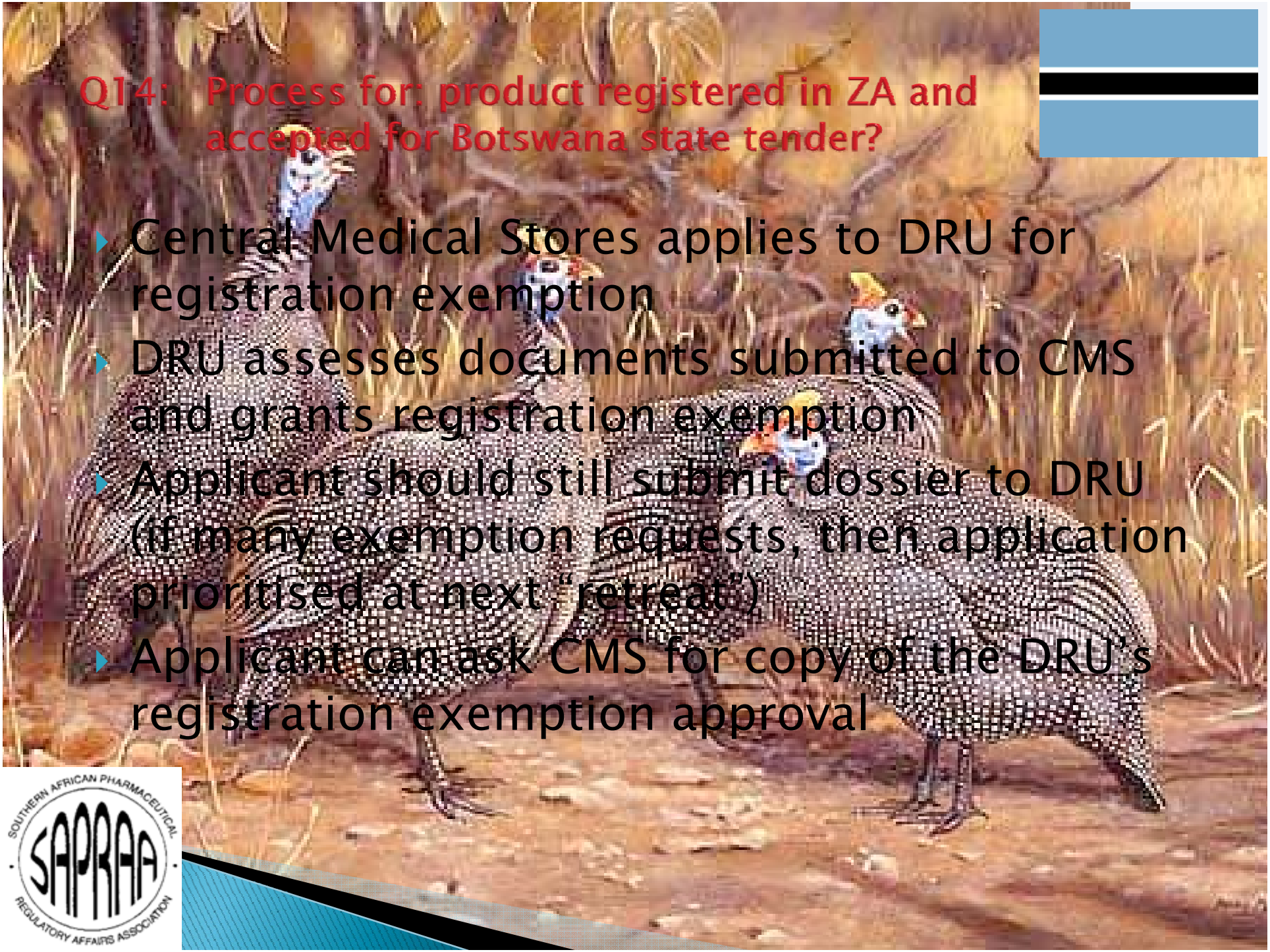
- Summary document is used to prepare evaluation report of application for the Drugs Advisory Board
- SAPRAA requested a blanked out "model summary report" so that we can get better feel for level of detail required

Q12: For dossier summary, will DRU accept cross-ref to dossier, since electronic version of dossier also provided? WORD format a problem

- WORD text required as they edit the text
- Cross-reference to dossier not practical as report goes to DAB

Q13: Why can we not pay via EFT (= traceable and secure)? Some applicants find cash fees a problem.

- Payments go into Ministry of Health account, not DRU specific account
- DRU cannot trace payments even if proof of payment provided
- DRU advise us to get local agent/representative to pay cash and we reimburse them
- A receipt is issued immediately by DRU
- Companies complained that they have corporate governance problems with cash payments, but no other way



Q14: Process for: product registered in ZA and accepted for Botswana state tender?

- Central Medical Stores applies to DRU for registration exemption
- DRU assesses documents submitted to CMS and grants registration exemption
- Applicant should still submit dossier to DRU (if many exemption requests, then application prioritised at next "retreat")
- Applicant can ask CMS for copy of the DRU's registration exemption approval

Q15: Timeline and fees to register product as per Q:14?

- Fee same as for any new registration application
- Registration timeline not applicable as registration exemption given to CMS, so product may be supplied on tender without delay
- Application will follow normal course at DRU in parallel
- Process mainly used for TB, HIV & oncology medicines

Q16: Registration samples as commercial pack required but product not registered yet in ZA. Can we submit overseas commecial pack? If so, which countries preferred?

- Ideally commercial pack intended to be supplied to Botswana required
- If not reg. yet in ZA, DRU would like artwork (= colour mock up) of ZA pack, plus commercial samples from another country: English label and ICH country
- Expired samples also OK -motivate
- Prefer two different batches, but can motivate if cannot provide

Q17: Why so many registration samples required?

- Needed to accommodate testing at the Drugs Quality Laboratory

Q18: Is the "pre-registration evaluation checklist" still valid/required?

- Yes
- Used as a screening tool to ensure that the application is complete

Q19: Is the variation guideline dated 2009 still valid?

- Yes
- It is available on the Ministry of Health website

Q20: Please provide guidance for submitting variations as the classification (V numbers) and checklist don't match up.

- DRU aware of this
- Only use the guideline for variations & please ignore the checklist! (SAPRAA requested retraction of checklist from website to avoid confusion)
- Only one pharmacist at DRU who deals with all variations: Sekgele Ramoroka
- Separate variations and one cover letter per variation please

Q21: Separation of variations under sep. cover letters problematic, esp. "interlinked" variations. Need exists for more efficiency for companies and DRU

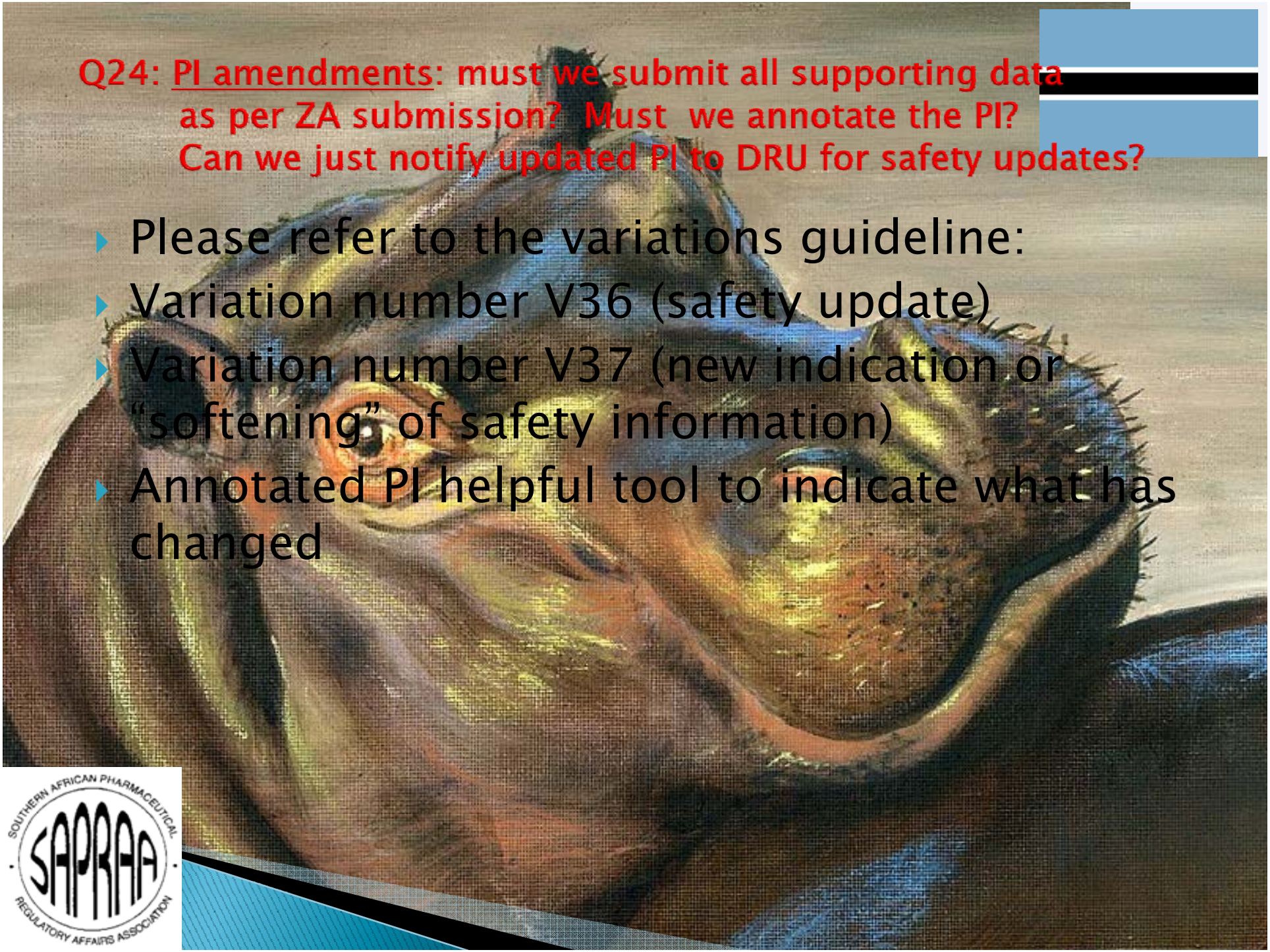
- Some variations have to be linked, but explain clearly in the covering letter why they have to be linked
- Avoid combined variations wherever possible – causes confusion

Q22: Can we just notify DRU of "minor" variations?

- Seems to be what is happening in practice
- Companies are not receiving approval letters routinely for these

Q23: What is approval timeline for "major" variations?

- Depends on the workload at the DRU at any given time
- Estimated to be 7 to 8 months
- Only one pharmacist dealing with variations
- SAPRAA expressed interest in receiving some statistics about the number of variations handled each month

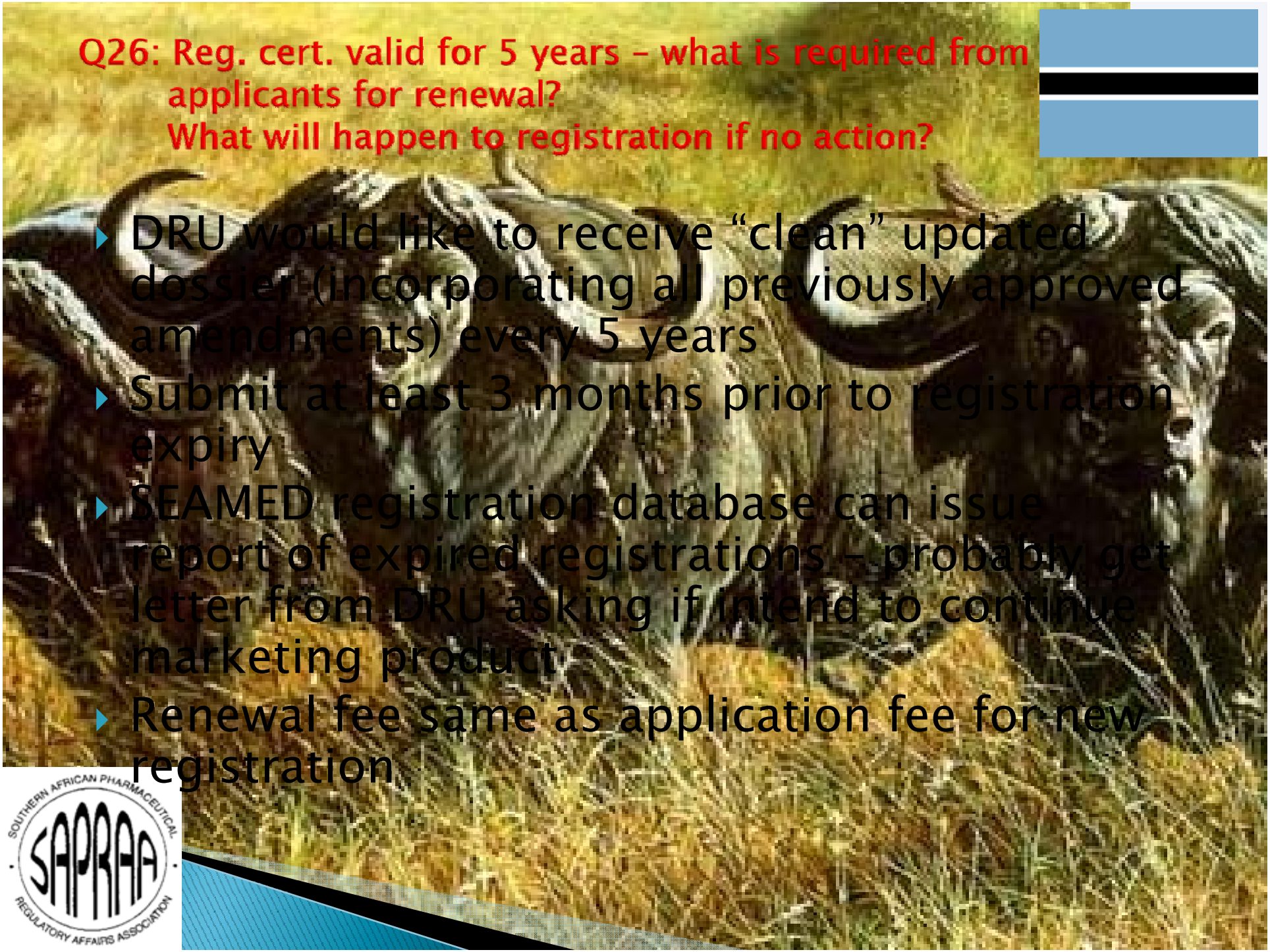


Q24: PI amendments: must we submit all supporting data as per ZA submission? Must we annotate the PI? Can we just notify updated PI to DRU for safety updates?

- Please refer to the variations guideline:
- Variation number V36 (safety update)
- Variation number V37 (new indication or "softening" of safety information)
- Annotated PI helpful tool to indicate what has changed

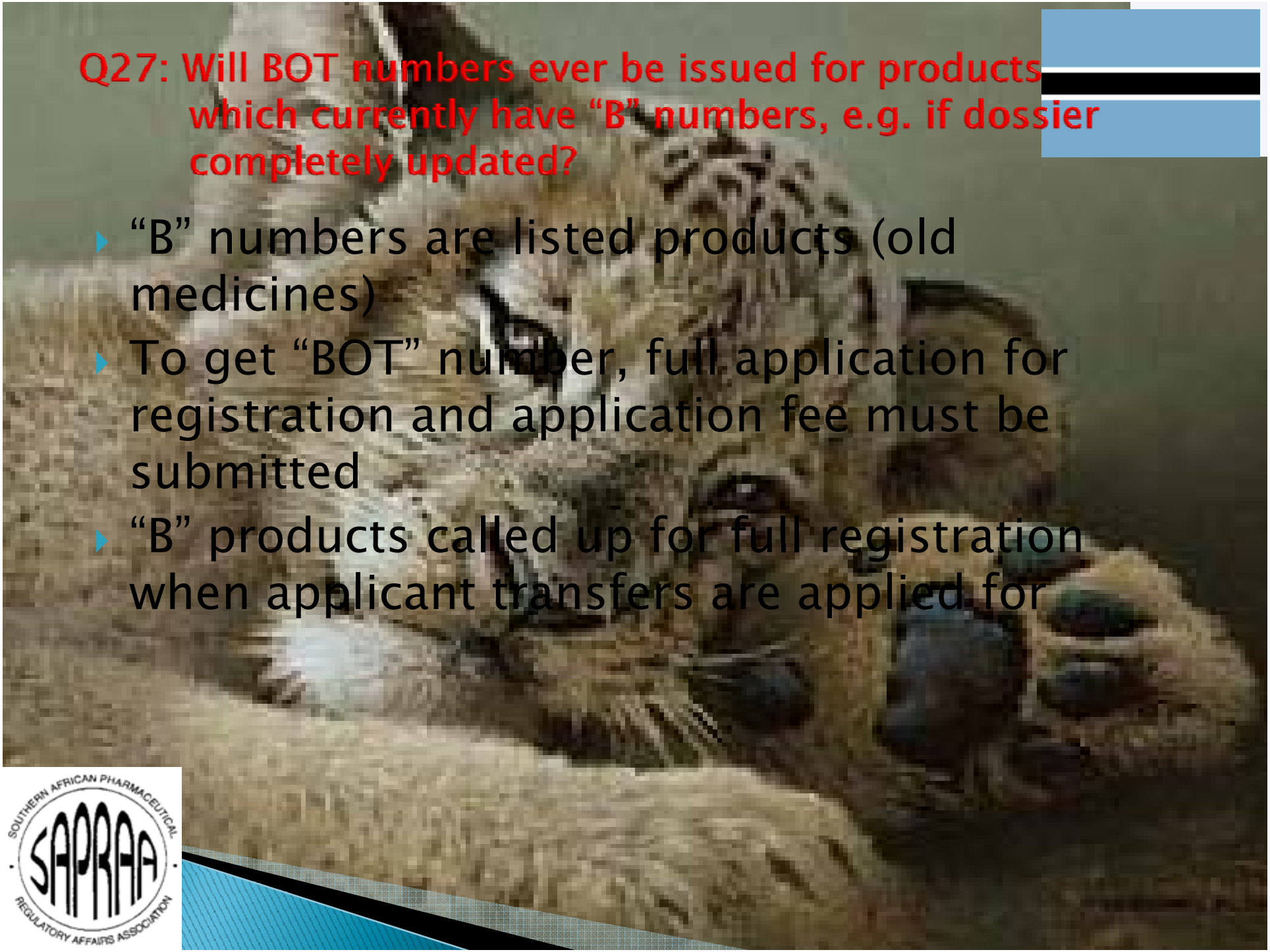
Q25: Requested to submit DMF, but not allowed by principle company. Alternatives?

- DRU representative has not encountered problems with this
- Point 5.1.2. of "Summary document" appears to make provision for applicant to supply letter of access to DMF as an alternative



Q26: Reg. cert. valid for 5 years – what is required from applicants for renewal? What will happen to registration if no action?

- DRU would like to receive "clean" updated dossier (incorporating all previously approved amendments) every 5 years
- Submit at least 3 months prior to registration expiry
- SEAMED registration database can issue report of expired registrations – probably get letter from DRU asking if intend to continue marketing product
- Renewal fee same as application fee for new registration

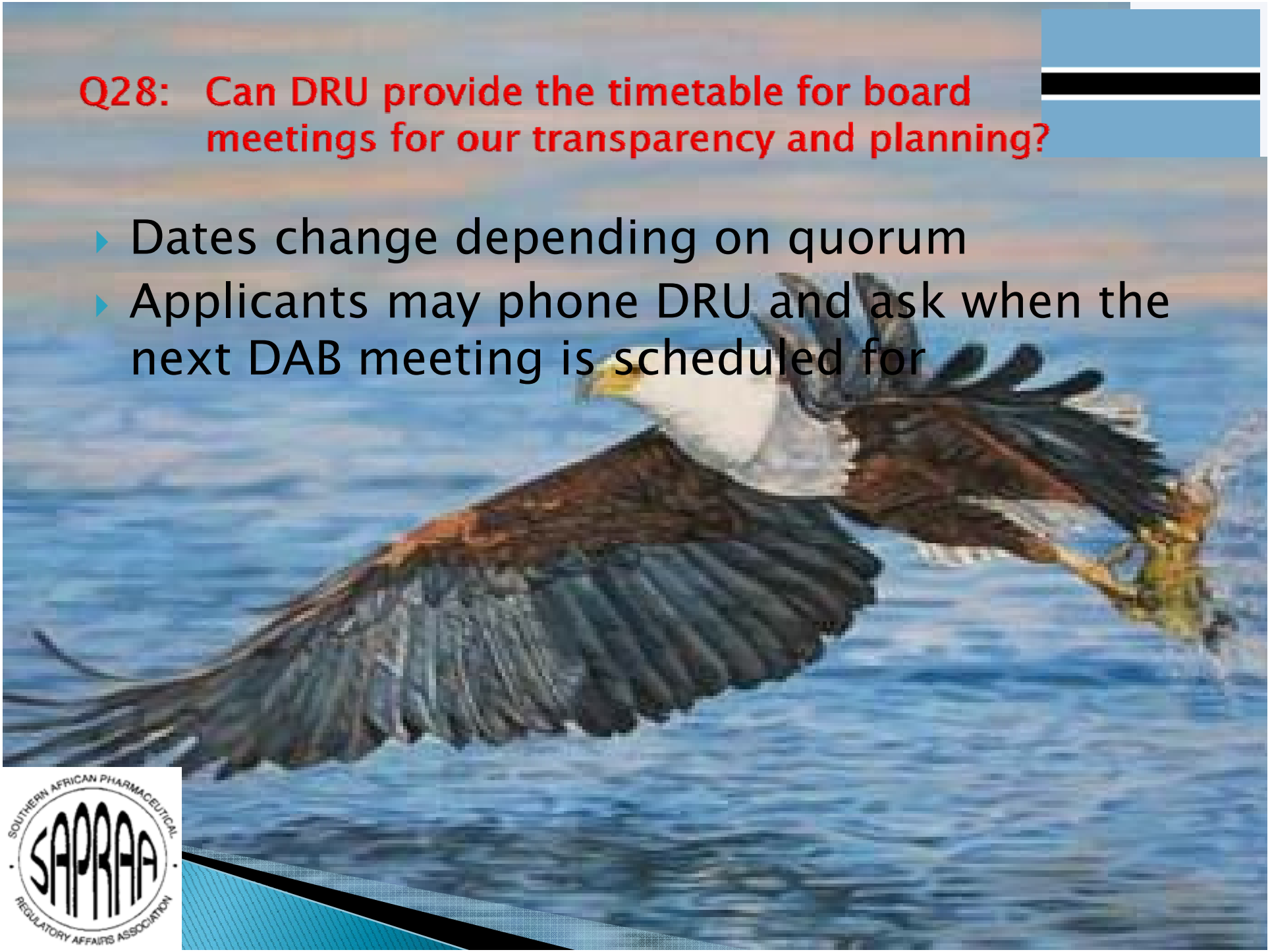


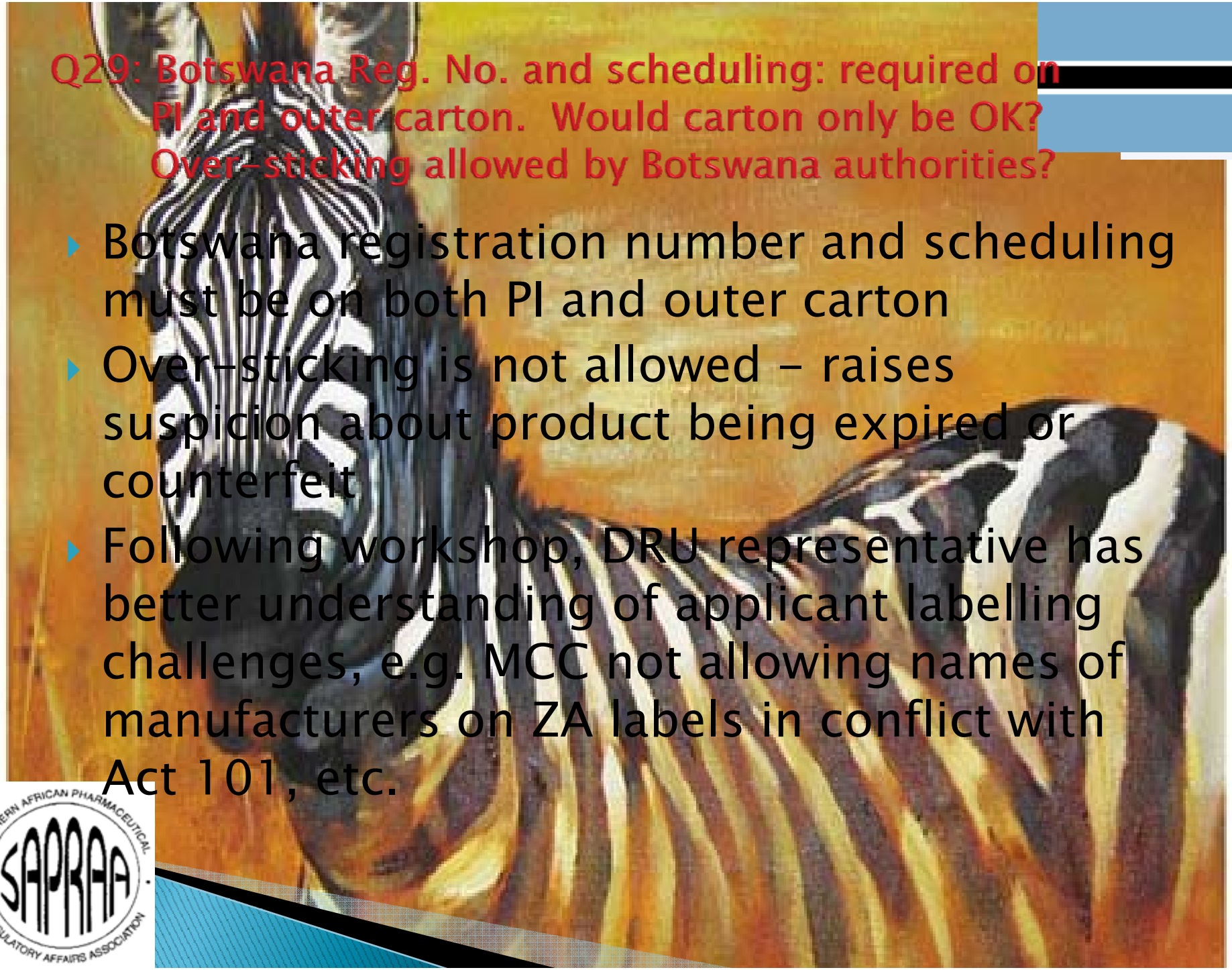
Q27: Will BOT numbers ever be issued for products which currently have "B" numbers, e.g. if dossier completely updated?

- "B" numbers are listed products (old medicines)
- To get "BOT" number, full application for registration and application fee must be submitted
- "B" products called up for full registration when applicant transfers are applied for

Q28: Can DRU provide the timetable for board meetings for our transparency and planning?

- Dates change depending on quorum
- Applicants may phone DRU and ask when the next DAB meeting is scheduled for





Q29: Botswana Reg. No. and scheduling: required on PI and outer carton. Would carton only be OK? Over-sticking allowed by Botswana authorities?

- Botswana registration number and scheduling must be on both PI and outer carton
- Over-sticking is not allowed – raises suspicion about product being expired or counterfeit
- Following workshop, DRU representative has better understanding of applicant labelling challenges, e.g. MCC not allowing names of manufacturers on ZA labels in conflict with Act 101, etc.

Q30: Clinical data: how much detail does the DRU want, especially if product already registered in South Africa?

- Product registration in ZA makes no difference
- DRU accept Clinical Overview plus Clinical Summaries (or Clinical Expert Report) only
- They can request full clinical study report case-by-case

Q31: Is there a Botswana DRU guideline for advertising/promotional material?

- Requirement for pre-approval of advertising mentioned in Act, but presently no dedicated resource at DRU to review these
- Problem is that SABC TV programs viewed in Botswana
- Radio programs more restricted
- No guideline is available
- Until resources at DRU and guideline for applicants available, cannot really implement this aspect of the Act

Q32: Are changes to fees planned in the next 12 months?

- Fees prescribed in the Act, therefore difficult to change
- Still 800 Pula for foreseeable future
- However, there are changes proposed to Botswana Medicines Act – hoping to get to parliament by the end of the year (new act will also give DRU more powers, e.g. in inspections)

Q33: What are DRU plans for registraton of veterinary medicines e.g. stock remedies and other veterinary medicines?

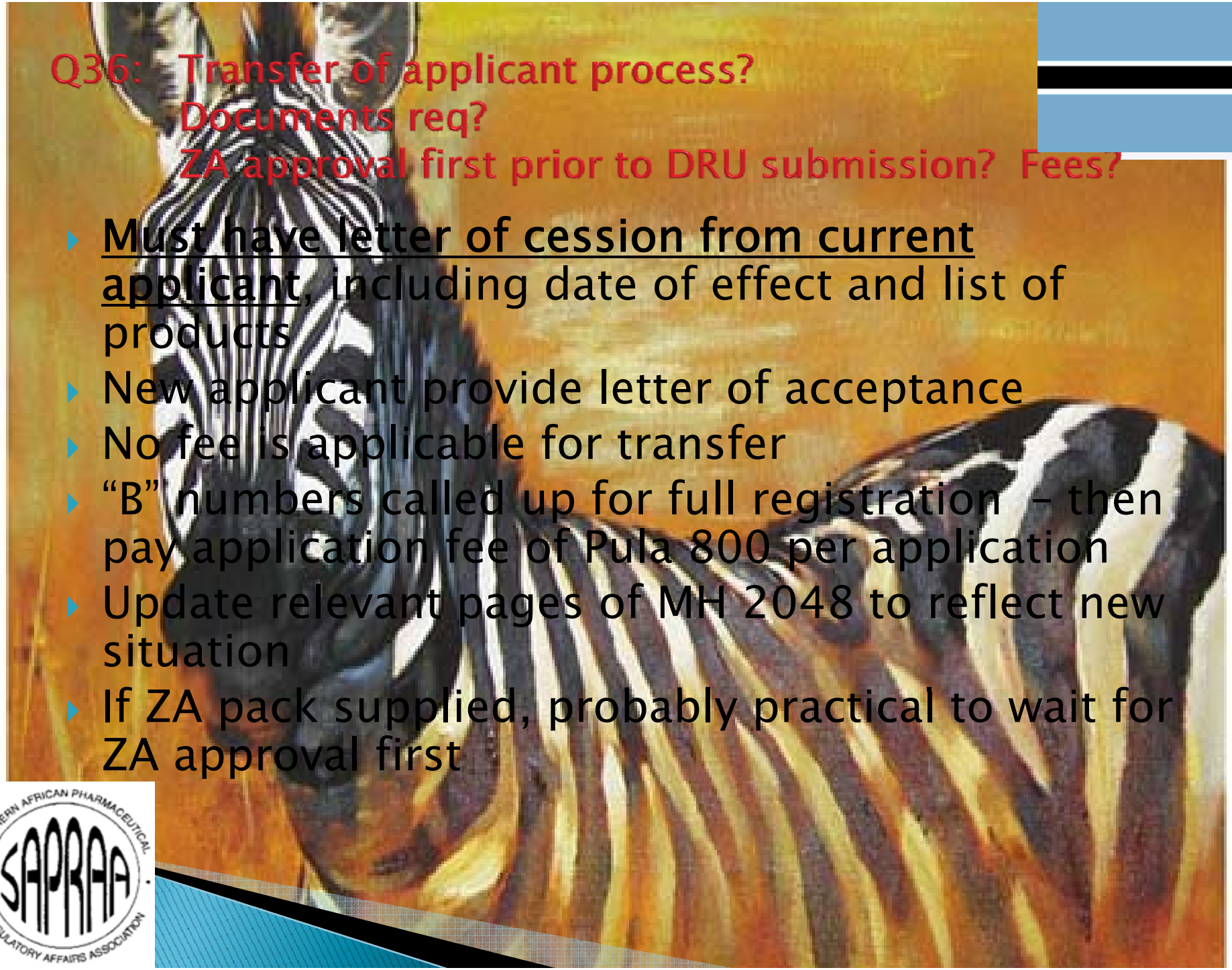
- Regulation of veterinary medicines in the proposed new Medicines Act

Q34: Pharmacovigilance: is there a guideline available now for adverse event reporting? Who is pharmacovigilance contact person in DRU?

- Final guideline is available
- Responsible people at DRU:
  - Tau Mahupu
  - Mrs Tsiu

Q35: Any update regarding issuing of outstanding registration certificates? Why do we get diff. registration No. for each pack size?

- No plans to back track the issuing of registration certificates
- Concentrating on issuing registration certificates for new products moving forward
- Each pack size distinguished (A/B/C,etc. to aid control at the borders & block counterfeits or unregistered products from entering the Botswana



Q36: Transfer of applicant process? Documents req? ZA approval first prior to DRU submission? Fees?

- **Must have letter of cession from current applicant**, including date of effect and list of products
- New applicant provide letter of acceptance
- No fee is applicable for transfer
- "B" numbers called up for full registration – then pay application fee of Pula 800 per application
- Update relevant pages of MH 2048 to reflect new situation
- If ZA pack supplied, probably practical to wait for ZA approval first

Q37: Process for complementary medicines?

- Separate guideline and application for complementary medicines on website
- Submit 2 samples
- DRU grants exemption from registration – valid for 5 years (renewable)
- DRU follow TGA principles with local adaptation case-by-case
- Can contact Lisa Urio to clarify whether a particular product would be classified as complementary

THANK YOU

"Individual commitment to a group effort – that is what makes a team work, a company work, a society work, a civilization work."

- **Vincent Thomas "Vince" Lombardi**
- (June 11, 1913 – September 3, 1970) American Football coach