ABEX
PHARMACEUTICA (PTY) LTD

# eCTD Go-live in South Africa

## Experiences from Pilot from Industry perspective

***18 & 19 October 2016***

# Important principles

ABEX PHARMACEUTICA (PTY) LTD

- Early planning and preparation
- Know and understand the *current* guidelines, specifications & validation criteria
- Pay attention to lessons learnt
- Purchase and implement the right tools for your environment
  - Make friends with your IT department
- Quality control

# Early planning and preparation

ABEX PHARMACEUTICA (PTY) LTD

- Planning down to document level is crucial for eCTD submissions
- Get it right first time!
  - Paper is forgiving – can slot in extra pages or replace documents just before submission
  - eCTD is not forgiving
    - No last minute changes of documents possible without a delay in submission
    - Last minute changes can lead to checking of hyperlinks, re-validation, re-export
- The ZA eCTD content will be different from e.g. EU / US eCTD's
  - Local requirements in modules 2 to 5 have to be complied with
  - Regional requirements - Module 1 and 3.2.R

# Early planning and preparation

ABEX PHARMACEUTICA (PTY) LTD

- Coordination with principals / parent companies / outsourced partners important
- Take time to understand the eCTD structure and how it applies to your product and submission, especially with
  - Multiple manufacturers
  - Dosage strengths
- Life Cycle Management
  - Keep life cycle in mind when deciding on granularity
  - Initial submission is first step of LCM, incorrect use may cause problems later in LCM
  - Granularity once chosen cannot be easily changed
    - Only entire documents can be replaced in eCTD, not sections or pages within a document

# Know & understand guidelines

ABEX PHARMACEUTICA (PTY) LTD

- Know your guidelines – they provide valuable insights into the needs of evaluators
- Requirements for the content of the ZA eCTD is the same as for the ZA CTD
  - Know and use the guidelines
  - Know the CTD outline
  - Follow the content requirements for each section/document
  - Watch for inconsistencies
- Avoid “garbage in, garbage out”
  - Not following guidelines will put garbage into your eCTD and result in a garbage submission to MCC
  - Getting your paper system in order is the first step toward a quality eCTD

# Pay attention to lessons learnt

ABEX PHARMACEUTICA (PTY) LTD

- Ensure the CD/DVD burning session is closed
- Run validation on CD/DVD after burning, in addition to running it on the eCTD on the file share/server
- Letter of application (1.0) and application form (1.2.1) must be searchable (OCR scanned)
- Ensure correct use of related sequences in the envelope
- Ensure the virus check statement is included and that it is confirmed that the submission is virus free
- Include printout of MD5 checksum that is signed and dated and that product name, application number, and relevant sequence are indicated
- Ensure correct information is included in the envelope

# Pay attention to lessons learnt

ABEX PHARMACEUTICA (PTY) LTD

- Don’t change the footers on official forms (e.g. application form and validation template)
- Include sufficient navigation tools to assist evaluators to locate information:
  - Leaf titles should be descriptive and meaningful
  - Include sufficient and correct hyperlinks & bookmarks
  - Ensure PDFs are electronically rendered or OCR scanned
- Ensure that Section 3.2.R is structured according to the correct granularity and that the node extensions are numbered according to the relevant section

# Software solutions

ABEX PHARMACEUTICA (PTY) LTD

- It is not feasible to produce an eCTD without a software solution
- One size doesn’t fit all - choose a software solution that fits corporate structure, IT strategy and processes
  - Complex integration with document management systems running on central servers
  - Standalone systems running on PCs utilising a shared area
- The software solution should take care of all the technical issues, leaving regulatory people free to focus on content
- Close cooperation with IT department and very good IT support is very important!

# Points to consider in selecting a software vendor

ABEX PHARMACEUTICA (PTY) LTD

- Does the software support the current South African Specification and how will updates be handled?
- Is there proven compliance with South African validation criteria (actual testing has been performed)
- Can you perform validation at any stage in the software tool?
- Are hyperlinks supported and to what extent?
- Does the software take care of file and folder naming conventions?
- Does the software take care of PDF requirements?
- Does the software support various submission types, e.g. paper CTDs, eCTDs, other dossier formats?
- Ease of use of software
- What support, escalation mechanisms and training are available?

# Quality control

ABEX PHARMACEUTICA (PTY) LTD

- Do a quality check on your application prior to submission
- Use a QC process or checklist to help ensure submissions don’t contain formatting issues
- Use the Validation template to ensure the submission is complete
- Good planning and being proactive can help you avoid the need to respond to queries, send resubmissions, and send additional corrective submissions to fix formatting issues!

# Quality control

ABEX PHARMACEUTICA (PTY) LTD

- In eCTD format, QC includes e.g.
  - Check all hyperlinks and bookmarks
  - Check lifecycle functions (new, append, delete, replace)
  - Technical validation
  - Ensure no file names are truncated
    - Typically occurs when the path exceeds limits
  - Correct validation errors before submission
  - Ensure the media contains the submission and doesn't have defects
  - Ensure the submission is virus free

# Quality control

ABEX PHARMACEUTICA (PTY) LTD

- Check the hyperlinks before submitting
  - Are references in documents (tables, figures, images, sections, inter-document links, etc) hyperlinked?
  - Are the ToCs hyperlinked to the corresponding sections in the document?
  - Are there any broken hyperlinks?
  - Do all hyperlinks go to correct destinations?
  - Are all external hyperlinks removed (eg web links, e-mail links)?
  - Do hyperlinks appear as blue text or blue box links if blue text isn't possible?
  - Are hyperlinks set to Inherit Zoom?
  - ....

# Quality control

ABEX PHARMACEUTICA (PTY) LTD

- Check the bookmarks before submitting
  - Does the bookmark name indicate the bookmark's destination/content?
  - Is the bookmark way too long?
  - Are bookmarks provided for the ToC items?
  - Does the bookmark match the description/title showing on the ToC?
  - Will someone who is unfamiliar with the application know what content they'll see before they click on the bookmark?
  - Are bookmarks set to Inherit Zoom?
  - ....

# Quality control

ABEX PHARMACEUTICA (PTY) LTD

- Is the leaf title short, meaningful and indicative of the document's content?
- Will someone who isn't familiar with the application know what the document is from the leaf title only without having to open the document?
- Think like an evaluator and choose self-explanatory names

# Before you submit, ask...

ABEX PHARMACEUTICA (PTY) LTD

- If I was an evaluator, could I…….?
  - Easily locate the information/document
  - Easily copy and paste from the document
  - Easily differentiate between same type documents displayed in the eCTD
  - Easily navigate and access references in documents via bookmarks, links and the Table of Contents
- The ultimate goal is to provide an evaluator-friendly eCTD:
  - Focus of evaluation should be content, not format
  - More efficient reviews

# Conclusion

ABEX PHARMACEUTICA (PTY) LTD

- Steep learning curve
  - Same content as ZA CTD, but lots of new terminology & technical requirements
  - Regulatory affairs need new, more IT orientated competencies
  - Working processes need to be adapted
- Think carefully before jumping in…
  - Once eCTD, always eCTD
  - Are all concerned divisions in the company aware and ready?

# Wishes for the future

ABEX PHARMACEUTICA (PTY) LTD

- Extent to which ink signatures are required in Module 1 to be reconsidered, e.g. for all declarations, letter of application in 1.0, application form in 1.2.1, electronic copy declaration in 1.2.2.4, each page of proposed, annotated PI & PIL (1.5.5) and final PI & PIL in 1.3.1.1 & 1.3.2, etc.
- Extent to which the submission date is required within documents contained in Module 1, e.g. on every page on the final PI/PIL and annotated versions of these, validation template to be reconsidered
  - Suggestion to use the sequence number rather than the date

# Wishes for the future

ABEX PHARMACEUTICA (PTY) LTD

- Guidance to be provided for submission of e.g. PSURs, Section 36 exemption applications, once-off amendment applications.
  - Should these be handled within or outside the eCTD?
- Application numbers will be valid for a period of 4 weeks
  - What should an applicant do if there is an unplanned delay in submission to prevent cancellation of the application number?

# Acknowledgements


- Laura Magnus, Teva
- Robyn Black, Boehringer Ingelheim
- Quality eCTD submissions, Rubinstein, SB et al (http://www.regulatorycomp.com/resources/ectd_article.pdf)
- The introduction of eCTD in Switzerland in 2010, Alfonso, D (https://www.swissmedic.ch/aktuell/00283/00399/01667/01740/index.html?)

ABEX
PHARMACEUTICA (PTY) LTD

# Thank you!

**Contact details:**
Anita Smal
Abex Pharmaceutica (Pty) Ltd
Professional partners of EXTEDO in South Africa
Phone: +27 12 997 6974
Fax: +27 86 511 9636
E-mail: asmal@abexpharm.com