

Preparing for the CTD (and more)

SAPRAA – Midrand

Michael S. Schultz
Director Sales
Middle East - Asia Pacific - Africa
Email: mschultz@lorenz.cc



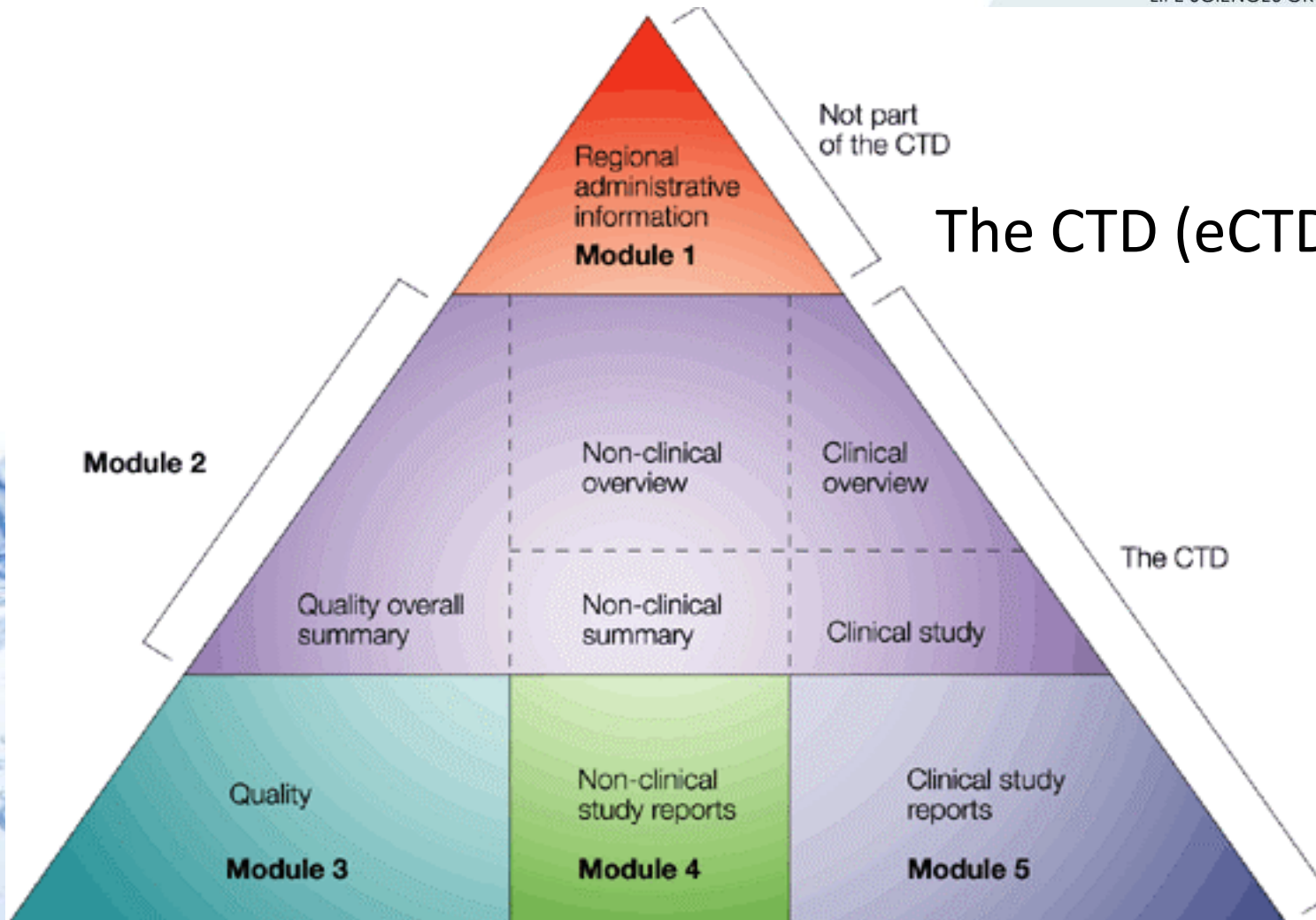
LORENZ Life Sciences.
Get a Lifecycle.™

Common Technical Document

The International Conference on Harmonisation (ICH) agreed upon a structure for the organization of paper submissions. The common technical document (CTD) provides a well-defined table of contents, divided into five modules. CTD was quickly adopted and provided a long-lasting basis for future standards to come.

-ICH M4 Expert Working Group(EWG)

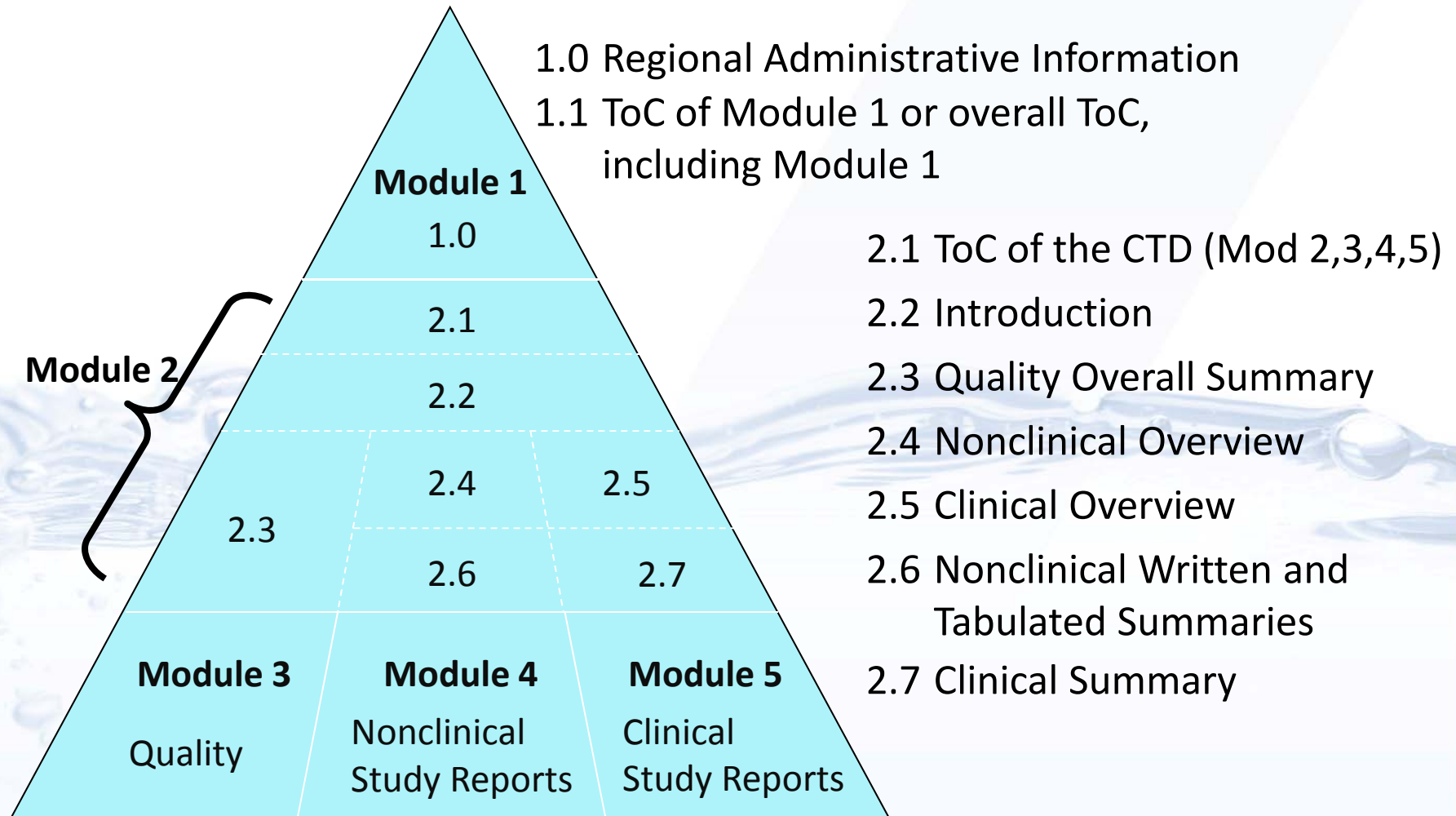




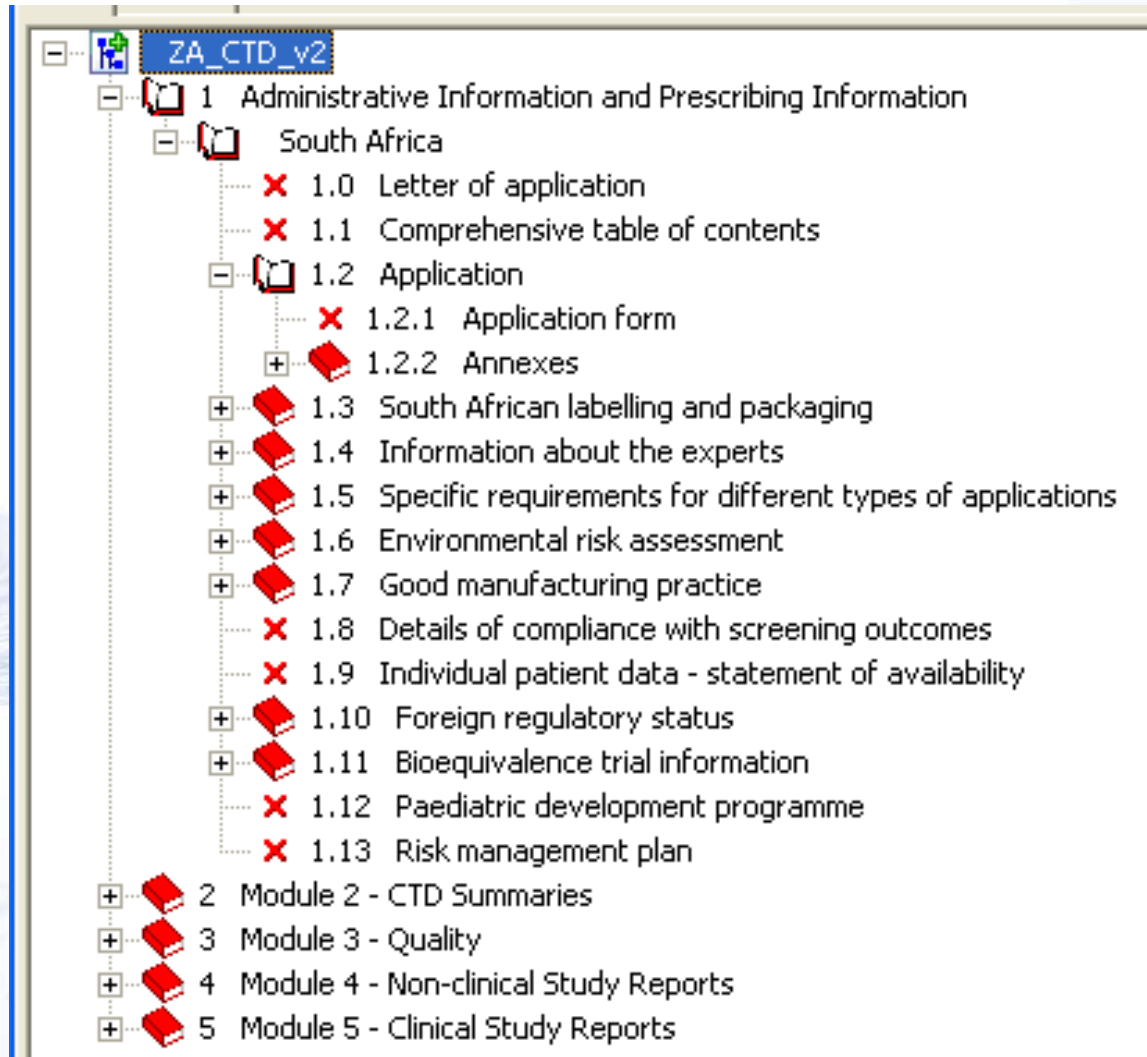
The CTD (eCTD) Triangle



CTD (eCTD) Numbering System



Module 1 – ZA CTD



ZA_CTD_v2

- [-] 1 Administrative Information and Prescribing Information
 - [-] South Africa
 - [-] 1.0 Letter of application
 - [-] 1.1 Comprehensive table of contents
 - [-] 1.2 Application
 - [-] 1.2.1 Application form
 - [+] 1.2.2 Annexes
 - [+] 1.3 South African labelling and packaging
 - [+] 1.4 Information about the experts
 - [+] 1.5 Specific requirements for different types of applications
 - [+] 1.6 Environmental risk assessment
 - [+] 1.7 Good manufacturing practice
 - [-] 1.8 Details of compliance with screening outcomes
 - [-] 1.9 Individual patient data - statement of availability
 - [+] 1.10 Foreign regulatory status
 - [+] 1.11 Bioequivalence trial information
 - [-] 1.12 Paediatric development programme
 - [-] 1.13 Risk management plan
 - [+] 2 Module 2 - CTD Summaries
 - [+] 3 Module 3 - Quality
 - [+] 4 Module 4 - Non-clinical Study Reports
 - [+] 5 Module 5 - Clinical Study Reports

Module 2 – Summaries

Module 2	
2.1	OVERALL CTD TABLE OF CONTENTS OF MODULES 2, 3, 4, AND 5
2.2	INTRODUCTION
2.3	QUALITY OVERALL SUMMARY
2.3.S	DRUG SUBSTANCE
2.3.S.1	General Information
2.3.S.2	Manufacture
2.3.S.3	Characterization
2.3.S.4	Control of Drug Substance
2.3.S.5	Reference Standards or Materials
2.3.S.6	Container Closure System
2.3.S.7	Stability
2.3.P	DRUG PRODUCT
2.3.P.1	Description and Composition of the Drug Product
2.3.P.2	Pharmaceutical Development
2.3.P.3	Manufacture
2.3.P.4	Control of Excipients
2.3.P.5	Control of Drug Product
2.3.P.6	Reference Standards or Materials
2.3.P.7	Container Closure System
2.3.P.8	Stability

Module 2 – Summaries

Module 2 (Cont.)	
2.3.A	APPENDICES
2.3.A.1	Facilities and Equipment
2.3.A.2	Adventitious Agents Safety Evaluation
2.3.A.3	Novel Excipients
2.3.R	REGIONAL INFORMATION
2.4	NONCLINICAL OVERVIEW
2.4.1	Overview of the Nonclinical Testing Strategy
2.4.2	Pharmacology
2.4.3	Pharmacokinetics
2.4.4	Toxicology
2.4.5	Integrated Overview and Conclusions
2.4.6	List of Literature Citations
2.5	CLINICAL OVERVIEW
2.5.1	Product Development Rationale
2.5.2	Overview of Biopharmaceutics
2.5.3	Overview of Clinical Pharmacology
2.5.4	Overview of Efficacy
2.5.5	Overview of Safety
2.5.6	Benefits and Risks Conclusions
2.5.7	References

Module 2 (Cont.)	
2.6	CONTENT OF NONCLINICAL WRITTEN AND TABULATED SUMMARIES
2.6.1	Introduction
2.6.2	Pharmacology Written Summary
2.6.3	Pharmacology Tabulated Summary (Appendix B)
2.6.4	Pharmacokinetics Written Summary
2.6.5	Pharmacokinetics Tabulated Summary (Appendix B)
2.6.6	Toxicology Written Summary
2.6.7	Toxicology Tabulated Summary (Appendix B)
2.7	CLINICAL SUMMARY
2.7.1	Summary of Biopharmaceutics and Associated Analytical Methods
2.7.2	Summary of Clinical Pharmacology Studies
2.7.3	Summary of Clinical Efficacy
2.7.4	Summary of Clinical Safety
2.7.5	References
2.7.6	Synopses of Individual Studies

Module 3 – Quality

Module 3	
3.1	MODULE 3 TABLE OF CONTENTS
3.2	BODY OF DATA
3.2.S	DRUG SUBSTANCE
3.2.S.1	General Information
3.2.S.2	Manufacture
3.2.S.3	Characterisation
3.2.S.4	Control of Drug Substance
3.2.S.5	Reference Standards or Materials
3.2.S.6	Container Closure System
3.2.S.7	Stability
3.2.P	DRUG PRODUCT
3.2.P.1	Description and Composition of the Drug Product
3.2.P.2	Pharmaceutical Development
3.2.P.3	Manufacture
3.2.P.4	Control of Excipients
3.2.P.5	Control of Drug Product
3.2.P.6	Reference Standards or Materials
3.2.P.7	Container Closure System
3.2.P.8	Stability

Module 3 (Cont.)	
3.2.A	APPENDICES
3.2.A.1	Facilities and Equipment
3.2.A.2	Adventitious Agents Safety Evaluation
3.2.A.3	Novel Excipients
3.2.R	REGIONAL INFORMATION
3.3	LITERATURE REFERENCES

Module 4 – Non-Clinical Study Reports

Module 4	
4.1	MODULE 4 TABLE OF CONTENTS
4.2	STUDY REPORTS
4.2.1	Pharmacology
4.2.2	Pharmacokinetics
4.2.3	Toxicology
4.3	LITERATURE REFERENCES

Module 5 – Clinical Study Reports

Module 5	
5.1	MODULE 5 TABLE OF CONTENTS
5.2	TABULAR LISTINGS OF ALL CLINICAL STUDIES
5.3	CLINICAL STUDY REPORTS
5.3.1	Reports of Biopharmaceutic Studies
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials
5.3.3	Reports of Human Pharmacokinetic (PK) Studies
5.3.4	Reports of Human Pharmacodynamic (PD) Studies
5.3.5	Reports of Efficacy and Safety Studies
5.3.6	Reports of Post-Marketing Experience
5.3.7	Case Report Forms and Individual Patient Listings
5.4	LITERATURE REFERENCES

Submission Management Explained

S U B M I S S I O N M A N A G E M E N T

Document Mgt.

Storage
Versioning
Release Mgt.
Document Audit Trail

Compilation

Hyperlink Management
Pagination & Volumisation
Internal Review
Merging & Reuseability
Submission Audit Trail
Legacy Processing

Publishing

Print
Electronic

Life-Cycle Mgt.

Amendment Mgt.
Agency Communication



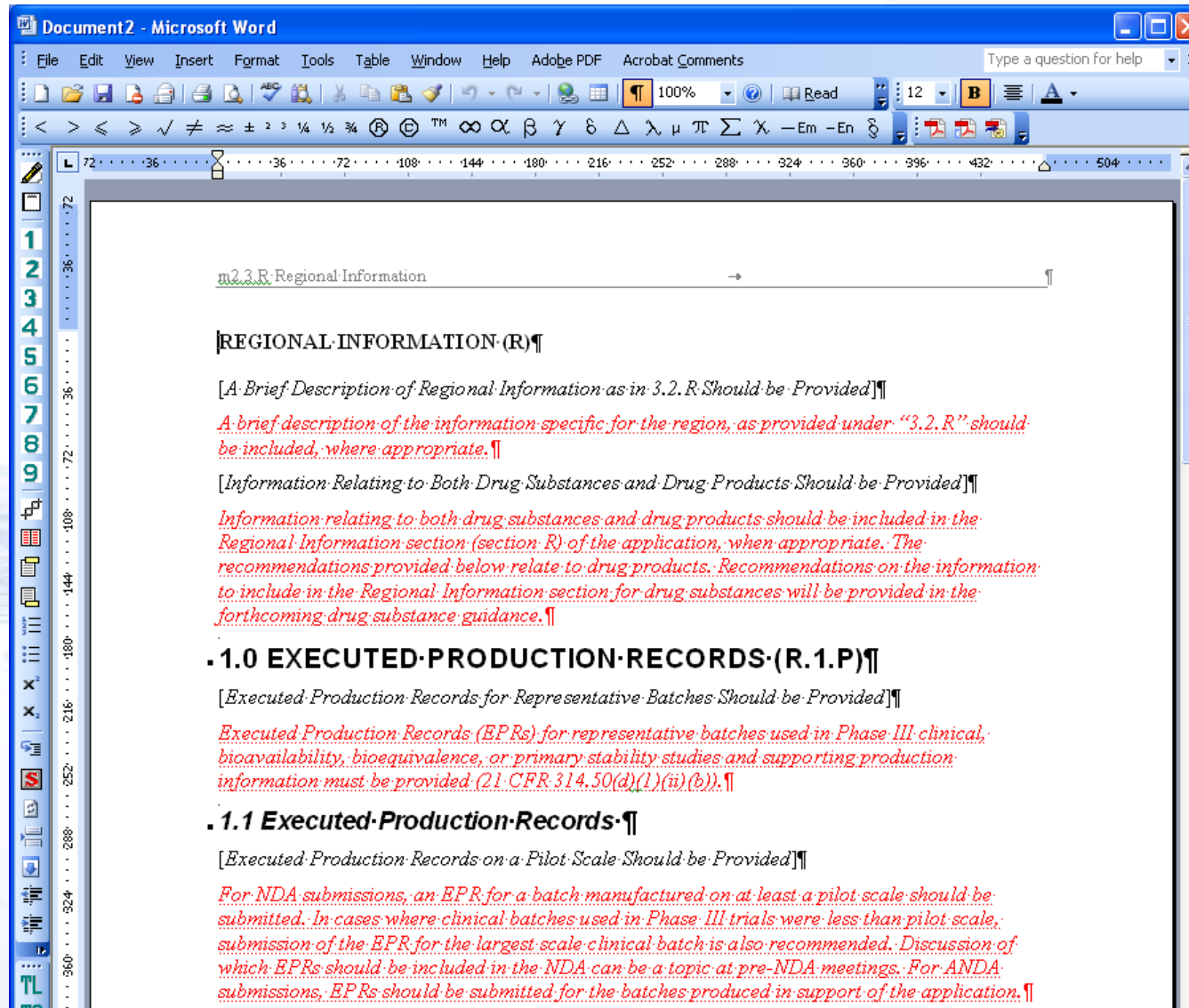
Document Authoring

- **Goal** – Compliant, **Submission-Ready Documents**
 - Table of contents/figures/tables/appendices
 - Bookmarked & hyperlinked
 - Reference citations
- **PDF – Most-used format for documents in electronic submissions**
 - Version 1.4
 - No password protection
 - Intelligent PDFs: Bookmarks & Hyperlinks
 - Optimized for web view
 - Avoid scanning if possible

Document Authoring

- Critical Success Factors:
 - Use of MS Word templates
 - Pre-formatted
 - Standardized for entire organization
 - Generic – no logos!
 - Headers/Footers: YES? NO?
 - Requirements for CROs and contract writers built into RFPs and contract deliverables
 - Provide 3rd-parties who provide you documents templates to use
 - Ask for CTD/eCTD formatted documents from Licensors
 - **Training!!!**

Document Authoring



Document2 - Microsoft Word

File Edit View Insert Format Tools Table Window Help Adobe PDF Acrobat Comments Type a question for help

100% 12 B

m2.3.R: Regional Information

REGIONAL INFORMATION (R)

[A Brief Description of Regional Information as in 3.2.R Should be Provided]

A brief description of the information specific for the region, as provided under "3.2.R" should be included, where appropriate.

[Information Relating to Both Drug Substances and Drug Products Should be Provided]

Information relating to both drug substances and drug products should be included in the Regional Information section (section R) of the application, when appropriate. The recommendations provided below relate to drug products. Recommendations on the information to include in the Regional Information section for drug substances will be provided in the forthcoming drug substance guidance.

1.0 EXECUTED PRODUCTION RECORDS (R.1.P)

[Executed Production Records for Representative Batches Should be Provided]

Executed Production Records (EPRs) for representative batches used in Phase III clinical, bioavailability, bioequivalence, or primary stability studies and supporting production information must be provided (21 CFR 314.50(d)(1)(ii)(b)).

1.1 Executed Production Records

[Executed Production Records on a Pilot Scale Should be Provided]

For NDA submissions, an EPR for a batch manufactured on at least a pilot scale should be submitted. In cases where clinical batches used in Phase III trials were less than pilot scale, submission of the EPR for the largest scale clinical batch is also recommended. Discussion of which EPRs should be included in the NDA can be a topic at pre-NDA meetings. For ANDA submissions, EPRs should be submitted for the batches produced in support of the application.

Document Management

- Folder structure
- Document Types
- Assign Attributes or Metadata to Document Types
- Organize by project
- Search
 - Metadata
 - Full-text search
- Version/access control
- Review & Approval Processes
- Document Audit Control

Recap: Best Practices

Prepare internal SOPs for

- 1) Document Creation: Word > PDF
- 2) Document Level Attributes (metadata)
- 3) Version Control
- 4) Document Distribution for Review & Approval

LORENZ Life Sciences Group



- **Market leader in Regulatory Affairs software products & services**
 - Active since 1987 – over 20 years of experience in Regulatory Affairs
- **docuBridge used by these National Regulatory Authorities:**
 - Health Canada (Canada)  Health Canada
 - JZAMP (Slovenia) 
 - AGES (Austria) 
 - EDQM (France) 
 - BfArM (Germany) 
 - URPL (Poland) 
- **190+ installations of docuBridge (eCTD/CTD Submission Management Solution) around the globe**
- **Over 60% of the eCTDs submitted to FDA & Health Canada are generated using LORENZ's docuBridge application**
- LORENZ' mission is to **engineer the world's most desirable e-regulatory solutions** by providing an exceptional end-to-end customer experience through advanced functionality, facilitated user-interface and deployment, as well as best-in-class customer services

Veni. Vidi. Publicati.



LORENZ Life Sciences.
Get a Lifecycle.™