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Quality Dossier (Module III)

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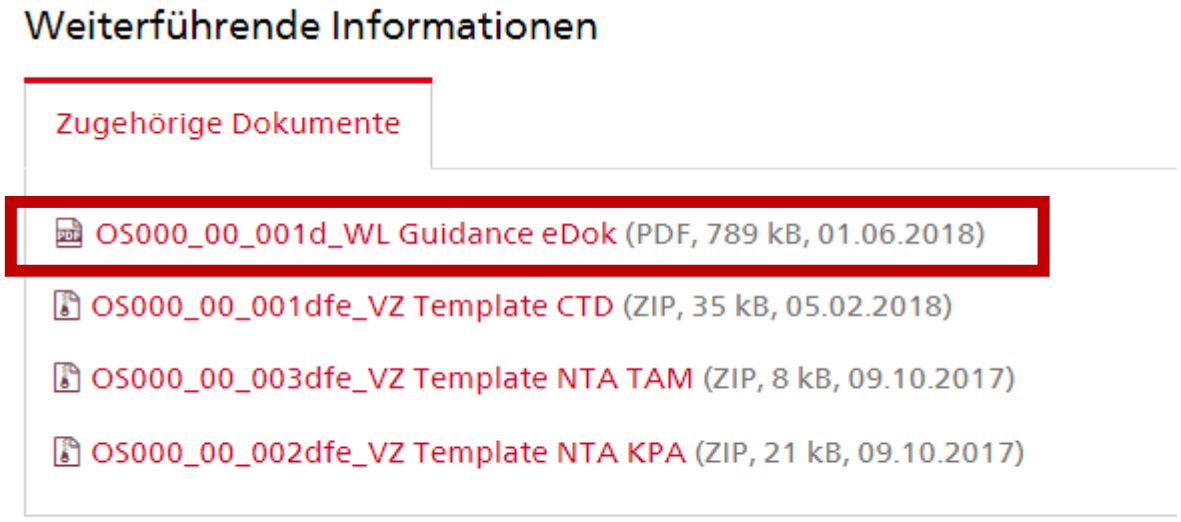
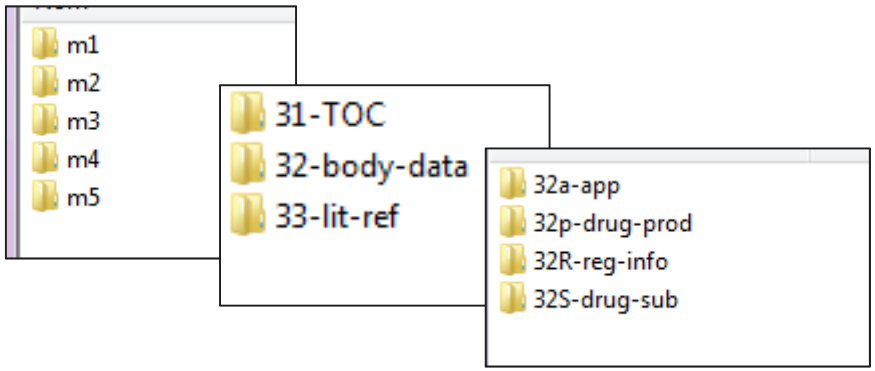
CTD submission: Where do I find the information?

https://www.swissmedic.ch/swissmedic/de/home/services/submissions/papiereinreichung---edok.html



CTD submission Module III: Right formatting is important

(content to be compliant with Ph. Eur. and Ph. Helv.)



Drug Substance

- 32s1-gen-info
- 32s2-manuf
- 32s3-charac
- 32s4-contr-drug-sub
- 32s5-ref-stand
- 32s6-cont-closure-sys
- 32s7-stab

"Cold" and "hot" part

Drug Product

- 32p1-desc-comp
- 32p2-pharm-dev
- 32p3-manuf
- 32p4-contr-excip
- 32p5-contr-drug-prod
- 32p6-ref-stand
- 32p7-cont-closure-sys
- 32p8-stab

"Hot" part

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Main focuses of quality review – cold part

- Drug Substance: Manufacture incl. raw materials
- Drug Substance: Characterization incl. impurities
- Drug Substance: Control of Drug Substance

- Drug Product: Pharmaceutical development
- Drug Product: Manufacture incl. validations and in process controls
- Drug Product: Control of excipients
- Drug Product: Container closure system

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LoQ – What is frequently missing or object to concerns

- Quality of the maintenance of the CTD module 3
  - appendices are missing
  - descriptions are not detailed enough
- Characterization of Drug Substance: counter ions, important characteristics (e.g. solubility) are missing
- Characterization and quantification of impurities are insufficient
- Rationale for specifications are insufficient, e.g. no accordance with Ph.Eur. or the existing data

However:
No questions for approx. 50% of the Quality variations concerning the cold part of the documentation

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Main focuses of quality review – hot part

- Specifications and their justification
- Validation of analytical methods (guideline BAG in progress, 2018)
- Synthesis modules: evaluation of solvents and individual components
- Limits for radiochemical purity, tests for possible impurities
- Batch data (comparative data old-new submission)
- Batch data covering full range of radioactivity concentrations
- Stability data
- SPC (Summary of Products Characteristics / "Fachinformation")

  → Kit radiopharmaceuticals, quality control

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LoQ – What is frequently missing or object to concerns?

- Wrong layout of submission (CTD is obligatory for module III)
- Specifications of impurity limits not justified
- Limits of radiochemical purity too low (compliance Ph.Eur.; Ph.Helv.)
- Insufficient validation of quality control methods
- Batch data or/and stability data are incomplete (End of shelf-life)
- Data provided is not covering the range of radioactivity concentrations
- SPC instructions for RCP testing are not complete/clear

In progress: SGRRC Guide for Module III submission

www.sgrrc.ch

SGRRC SSRCR

Schweizerische Gesellschaft für Radiopharmazie / Radiopharmazeutische Chemie
Société Suisse de Radiopharmacie / Chimie Radiopharmaceutique
Società Svizzera di Radiofarmacia / Chimica Radiofarmaceutica
Swiss Society of Radiopharmacy / Radiopharmaceutical Chemistry

Radiopharmaceutical Categories:

- Classic diagnostics
- PET diagnostics
- Therapeutics
- Generators

→ List of minimal information to provide in module III

	A	B	C	D	E	F
1	**Checkliste zur Begutachtung CTD Qualität classic diagnostics**					
2						
3		nuklide		Tc-99m		In-111
4		compound	Generator			
5	**MODULE 3 : QUALITY**					
6	3.1.	TABLE OF CONTENTS OF MODULE 3				
7	3.2.	BODY OF DATA				
8	3.2.S	DRUG SUBSTANCE				
9	3.2.S.1	General Information				
10	3.2.S.1.1	Nomenclature				
11	3.2.S.1.2	Structure				
12	3.2.S.1.3	General Properties				
13	3.2.S.2	Manufacture				
14	3.2.S.2.1	Manufacturer(s)				
15	3.2.S.2.2	Description of Manufacturing Process and Process Controls				
16	3.2.S.2.3	Control of Materials				
17	3.2.S.2.4	Controls of Critical Steps and Intermediates				
18	3.2.S.2.5	Process Validation and/or Evaluation				
19	3.2.S.2.6	Manufacturing Process Development				
20	3.2.S.3	Characterisation				
21	3.2.S.3.1	Elucidation of Structure and other Characteristics				
22	3.2.S.3.2	Impurities	Radionuklidreinheit			
23	3.2.S.4	Control of Drug Substance				
24	3.2.S.4.1	Specification				
25	3.2.S.4.2	Analytical Procedures				
26	3.2.S.4.3	Validation of Analytical Procedures		echte Validation		

classic diagnostics | PET diagnostics | therapeutics | notes class diagn | notes tx | notes PET