Change history

Version	Valid and binding as of:	Description, comments (by author)	Author's initials
01	**01.04.2015**	**QM ident. changed** **old:** **BW101_10_005e_AL_Guidance_Pharmaceutical_Quality_Dossier** **new:** **BW101_10_006e_AA_Guidance_Pharmaceutical_Quality_Dossier**	**sel**
	30.07.2014	Dropdown field inserted in the header	wis
	30.06.2014	Telephone and fax numbers updated, link revised, new change history inserted in the document	sel

Part Quality

Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document may be acceptable provided they are supported by adequate justification. As a corollary to the above, it is equally important to note that Swissmedic reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Agency to adequately assess the pharmaceutical quality of the investigational medicinal product.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

The objective of this guidance document is to specify the pharmaceutical quality data to be provided by the sponsor before implementing a clinical trial.

2.1.S DRUG SUBSTANCE
2.1.S.1 General Information
2.1.S.1.1 Nomenclature

Provide INN, chemical or other Name (e.g. code).

2.1.S.1.2 Structure

For chemical substances and if applicable biological and biotechnological substances indicate the following: structural formula, molecular weight.

For biological and biotechnological substances: specify the primary structure, higher order structures, post-translation modifications as appropriate.

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2.1.S.1.3 General Properties

Indicate the main physico-chemical characteristics (e.g. pH / pK, melting point, solubility, physical form).

2.1.S.2 Manufacture

2.1.S.2.1 Manufacturer(s)

Indicate the manufacturer(s) name(s) and address(es).

2.1.S.2.2 Description of Manufacturing Process and Process Controls

For chemical substances: provide a flow chart of manufacture. Indicate at least for the last steps of synthesis the starting materials, intermediates, solvents and reagents used.

For biological and biotechnological substances: provide a description of the cell culture system, the purification steps applied and information regarding storage of intermediates.

2.1.S.2.3 Control of Material

All material used in the manufacture (agents, solvents and any other materials) including the purity grade should be listed.

For biotechnological substances: provide information on the genetic development, which led to the selection of the processing strain. Describe the cell bank system and their control (identity, purity, stability).

2.1.S.2.4 Controls of Critical Steps and Intermediates

Provide information as available.

2.1.S.2.5 Process Validation and/ or Evaluation

2.1.S.3 Characterization

2.1.S.3.1 Elucidation of structure and other characteristics

For chemical substances briefly summarize available results. For phase II studies, data and methods are to be provided on request.

For biological and biotechnological substances: provide any information, which can contribute to establish the primary structure, higher order structures, biological activity, post translational modification or any other transformation.

2.1.S.3.2 Impurities

This paragraph should be used to discuss potential impurities arising either from synthesis of chemical substances or from degradation.

For biological and biotechnological substance a distinction between process- and product related impurities is required.

Typical levels of impurities observed should be listed.

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2.1.S.4 Control of Drug Substance
2.1.S.4.1 Specification

This paragraph should provide the specification of the drug substance including methods used and the acceptance criteria applied.

Upper limits are to be set for impurities. They can be preliminary and have to be justified taking the safety of use into account.

2.1.S.4.2 Analytical procedures

Refer to Pharmacopoeias or provide a brief summary of the non-compendial methods used. For phase II studies, data and methods are to be provided on request.

2.1.S.4.3 Validation of Analytical Procedures

The suitability of analytical methods needs to be demonstrated.

2.1.S.4.4 Batch Analyses

Batch results, preferably in tabular format, or certificates of analysis are to be provided for the active substance batches used in non-clinical studies and for actual batch(es) or representative batch(es) of the Drug Substance to be used in clinical trials.

The batch number, batch size, manufacturing site, manufacturing date, testing methods, acceptance criteria and test results are to be listed.

2.1.S.4.5 Justification of specification

Justify the choice of specification at this stage of development. Include methods used and the acceptance criteria applied. The limit of individual and total impurities should be explained with a reference to related preclinical results. For genotoxic impurities refer to the guidance EMEA/CHMP/QWP/251344/2006.

2.1.S.5 Reference standarts or materials

Not required.

2.1.S.6 Container and closure system

A brief description should be provided.

2.1.S.7 Stability

Stability data including results (also from forced degradation studies for phase II studies) are to be summarized in tabular form. Re-test period for chemical substances and storage conditions are to be defined.

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2.1.P DRUG PRODUCT

2.1.P.1 Description and Composition of the Drug Product

Provide the qualitative and quantitative composition of the Investigational Drug Product. In case of reconstitution, a description of the diluents used is necessary.
The declared formula should be the formulation of the batches used in the concerned clinical trial.

2.1.P.2 Pharmaceutical Development

Briefly describe the suitability of the selected dosage form to its intended use.

2.1.P.3 Manufacture

2.1.P.3.1 Manufacturer(s)

Indicate the manufacturer(s) name(s) and control site(s) name(s) and address(es).

2.1.P.3.2 Batch formula

Not required.

2.1.P.3.3 Description of Manufacturing Process and Process Controls

A flow chart should be provided.

2.1.P.3.4 Control of critical steps and intermediates

In case of sterile products, the means or strategy used to guarantee product sterility have to be described.

2.1.P.3.5 Process Validation and/ or Evaluation

Only for non-standard dosage forms required as available.

2.1.P.4 Control of Excipients

2.1.P.4.1 Specifications

Refer to Pharmacopoeias or, if not described there, attach a certificate of analysis.

2.1.P.4.2 Analytical procedure

Refer to Pharmacopoeias or provide a brief summary of the non-compendial methods used.

2.1.P.4.3 Validation of analytical procedure

Not applicable.

2.1.P.4.4 Justification of specifications

Not applicable.

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2.1.P.4.5 Excipients of Human or Animal Origin

Provide necessary details with standard formular ZL000_00_010e_FO Substances of animal or human origin

2.1.P.4.6 Novel Excipients

If applicable, provide detailed information as outlined for Drug Substance.

2.1.P.5 Control of Drug Product

2.1.P.5.1 Specifications(s)

This paragraph should provide the specifications of the Investigational Drug Product including methods used and the acceptance criteria applied.

Upper limits are to be set for impurities. They can be preliminary and have to be justified taking the safety of use into account.

2.1.P.2 Analytical procedures

Refer to Pharmacopoeias or provide a brief summary of the non-compendial methods used. For phase II studies, data and methods are to be provided on request.

2.1.P.5.3 Validation of Analytical Procedures

The suitability of analytical methods needs to be demonstrated.

2.1.P.5.4 Batch Analyses

Batch results, preferably in tabular format, or certificates of analysis are to be provided for actual batch(es) or representative batch(es) of the Investigational Drug Product to be used in clinical trials.

The batch number, batch size, manufacturing site, manufacturing date, testing methods, acceptance criteria and test results are to be listed.

2.1.P.5.5 Characterisation of the Impurities

Only those impurities must be described here, which have not been mentioned under 2.1.S.3.2.

2.1.P.5.6 Justification of Specification(s)

Justify the choice of specification at this stage of development. Include methods used and the acceptance criteria applied. The limit of individual and total impurities should be given here.

Upper limits are to be set for impurities. They can be preliminary and have to be justified taking the results of the preclinical studies into account.

2.1.P.7 Container Closure System

Briefly describe the packaging and labeling of the investigational drug product and if applicable for the diluents for reconstitution.

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2.1.P.8 Stability

Results from stability studies should be summarised in a tabular form. Conclusions of all stability tests performed so far should be drawn. An evaluation of the available data and justification of the proposed shelf-life to be assigned to the Investigational Drug Product in the clinical study should be provided.

Information presented should include the proposal for the assigned shelf-life of Investigational Drug Product. Criteria based on which the shelf life will be extended during an ongoing study need to be defined.

In the case batches of the Investigational Drug Product do not meet specifications requirements throughout the entire period of uses, the Agency should be informed of the situation, including any corrective action proposed.

2.1.A Appendices
2.1.A.2 Adventitious Agents Safety Evaluation

TSE Safety: Provide detailed information on minimization of TSE risk or avoidance of TSE agents.

Viral safety: Information assessing the risk with respect to potential viral contamination should be provided. The risk of introducing viruses into the product and the capacity of the manufacturing process to remove or inactivate viruses should be evaluated.

Other adventitious agents: Detailed information regarding other adventitious agents (bacteria, mycoplasma, fungi) should be provided in chapter 3.2.S.2.3.

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