

**Veterinary Drugs Directorate (VDD)**

**Health Products and Food Branch (HPFB)**

**Quality Overall Summary (QOS)**

**(New Drug Submissions/Abbreviated New Drug Submissions)**

**Foreword**

The Quality Overall Summary (QOS) template should be completed to provide a condensed summary of the key quality information for New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs) containing drug substances and their corresponding products of synthetic or semi-synthetic origin that are filed with Health Canada pursuant to Part C, Division 8 of the Food and Drug Regulations.

The QOS constitutes part of the submission package when filing with the VDD. The structure of this template for the Quality section is consistent with that used for NDS and ANDS filed in Canada. Sponsors are encouraged to organize submission data using the QOS structure; this would assist in expediting the screening and review process.

Abbreviations should not be used in the QOS unless initially defined and consistently used (e.g., N/A = Not applicable), or unless they represent well-established scientific abbreviations (e.g., HPLC, UV, etc.).

It is also important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this guidance, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

To accommodate variability in the types of studies and products described in veterinary drug submissions, the tables included in the QOS template may be modified as necessary. If scanned images are incorporated into the document (e.g., synthetic schemes, molecular structures), sponsors should ensure that a low resolution is used to avoid files that are excessively large.

When completing the QOS template for the VDD, this **Foreword** page should be deleted prior to submitting.

**Quality Overall Summary – QOS (NDS/ANDS)**

|  |  |
| --- | --- |
| **SUMMARY OF PRODUCT INFORMATION** | |
| Proprietary (Brand) Name of Drug Product |  |
| **Non-Proprietary (or Common) Name of Drug Product** |  |
| **Non-Proprietary (or Common) Name of Drug Substance (medicinal ingredient)** |  |
| **Manufacturer name (fabricator)** |  |
| **Manufacturer name (sponsor)** |  |
| **Dosage form(s)** |  |
| **Strength(s)** |  |
| **Route(s) of administration** |  |
| **Species** |  |
| **Submission Type** |  |
| **REFERENCE PRODUCT INFORMATION**  **(for generic product submissions only)** | |
| **Brand Name of the Reference Product:** |  |
| **Dosage Form(s) and Strength(s):** |  |
| **Market Authorization Holder’s Name:** |  |

# S Drug substance (name, manufacturer)

Note: Include the information on the drug substance in the open part of the Master File (MF) in the appropriate sections.

## S.1 General Information (name, manufacturer)

### S.1.1 Nomenclature (name, manufacturer)

|  |  |
| --- | --- |
| **International non-proprietary name (INN):** |  |
| **Compendial name or other relevant names or codes (e.g., company code):** |  |
| **Chemical Abstracts Service (CAS) Number:** |  |
| **International non-proprietary name (INN):** |  |
| **Compendial name or other relevant names or codes (e.g., company code):** |  |
| **Chemical Abstracts Service (CAS) Number:** |  |

### S.1.2 Structure (name, manufacturer)

|  |  |
| --- | --- |
| **Structural formula (including relative and absolute stereochemistry, salt form and solvate moieties):** |  |
| **Molecular formula:** |  |
| **Molecular mass:** |  |

### S.1.3 General Properties (name, manufacturer)

|  |  |
| --- | --- |
| **Physical description (e.g., appearance, colour, physical state):** |  |
| **Physical form (e.g. polymorphic form, solvate, hydrate):** |  |
| **Solubility over the physiological pH range (e.g., pH 1.2-6.8):** |  |
| **Solubilities in relevant solvents:** |  |
| **pH and pKa values:** |  |
| **Polymorphism:** |  |
| **Particle Size Distribution:** |  |
| **Other (e.g., partition coefficients, melting or boiling points, optical rotation, refractive index (for a liquid), hygroscopicity, UV absorption maxima and molar absorptivity):** |  |

## S.2 Manufacture

### S.2.1 Manufacturer(s)

1. **Name, address, and responsibility of each fabricator, including contractors, and each production site or facility involved in fabrication and testing of the drug substance:**

|  |  |  |
| --- | --- | --- |
| **Manufacturer’s Name** | **Site** | **Responsibility** |
|  |  |  |

1. **List of referenced Master Files (MFs) and MF Numbers if applicable:**

### S.2.2 Description of manufacturing process and process controls (name, manufacturer)

1. **Flow diagram of the manufacturing process(es):**
2. **Brief narrative summary of the manufacturing process:**
3. **Alternate processes and explanation of their use:**
4. **Reprocessing steps and justification:**

### S.2.3 Control of materials (name, manufacturer)

1. **Summary of the quality and controls of the materials (e.g., raw materials, starting materials, solvents, reagents, catalysts) used in the manufacture of the drug substance:**

Note: To be completed if the sponsor / drug product manufacturer is also the drug substance manufacturer.

| **Material** | **Test** | **Acceptance Criteria** | **Analytical Procedure** |
| --- | --- | --- | --- |
|  |  |  |  |
|  |  |  |  |

1. **For drug substance(s) manufactured with materials / reagents obtained from sources that are at risk of transmitting Transmissible Spongiform Encephalopathy (TSE) agents including Bovine Spongiform Encephalopathy (BSE), a letter of attestation with supporting documentation should be provided confirming that the material is not from BSE/TSE affected country/area, and/or data should be submitted to demonstrate that the material is not at risk of transmitting TSE (e.g. an EDQM Certificate of Suitability). The product information (pi) template in the Master Volume (1.5 Application Form) should reflect the animal origin ingredient information, when applicable.**

### S.2.4 Controls of critical steps and isolated intermediates (name, manufacturer)

Note: To be completed if the sponsor / drug product manufacturer is also the drug substance manufacturer.

1. **Summary of the controls performed at critical steps of the manufacturing process:**
2. **Summary of quality control testing of intermediates:**

### S.2.5 Process validation and/or evaluation (name, manufacturer)

Note: To be completed if the sponsor / drug product manufacturer is also the drug substance manufacturer.

**Description of process validation and/or evaluation studies (e.g. for drug substances using aseptic processing or sterilization):**

### S.2.6 Manufacturing process development (name, manufacturer)

Note: To be completed if the sponsor/drug product manufacturer is also the drug substance manufacturer.

**Description and discussion of the significant changes made to the manufacturing process of the drug substance during clinical development:**

## S.3 Characterization (name, manufacturer)

### S.3.1 Elucidation of structure and other characteristics

1. **List of studies performed (e.g., IR, UV, NMR, MS, elemental analysis) and a brief summary of the interpretation of evidence of structure:**
2. **Discussion on the potential for isomerism and identification of stereochemistry (e.g., geometric isomerism, number of chiral centres and configurations):**
3. **Summary of studies performed to identify potential polymorphic forms (including solvates):**
4. **Summary of studies performed to identify the particle size distribution of the drug substance:**
5. **Other characteristics:**

### S.3.2 Impurities (name, manufacturer)

1. **List of potential and actual potential drug-related impurities arising from the synthesis, manufacture and/or degradation (e.g., starting materials, by-products, intermediates, chiral impurities, degradation products), including chemical name, structure, and origin:**

| **Drug related impurity**  **(chemical name or descriptor)** | **Structure** | **Origin** |
| --- | --- | --- |
|  |  |  |
|  |  |  |

1. **List of process-related impurities (e.g., residual solvents, reagents, catalysts), including compound name and step used in synthesis:**
2. Discussion on the basis for setting the acceptance criteria for impurities:
   * 1. **VICH GL10 Reporting/Identification/Qualification Thresholds for drug-related impurities, and concentration limits (ppm) for process-related impurities (e.g. residual solvents):**
     2. **Results of impurities detected in drug substance batches used in toxicological, clinical, and comparative studies (include in tabular form the impurity, acceptance criteria, and results):**

| **Impurity**  **(drug-related and process-related)** | **Acceptance**  **Criteria** | **Results**  **(include batch number and use)**  **(e.g., nonclinical, clinical, comparative)** | | |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  |  |  |  |  |

* + 1. Justification for impurities specified and their acceptance criteria:

## S.4 Control of Drug Substance (name, manufacturer)

### S.4.1 Specification (name, manufacturer)

**Specification(s) for the drug substance, including specification number and version, as well as test method number(s) and version(s) are required:**

Note: An QC-approved and dated copy of the release and stability testing site should be provided.

| **Standard claimed (e.g., Professed, USP, Ph. Eur., BP, other)** | |  |
| --- | --- | --- |
| **Specification approved date** | |  |
| **Specification reference number and version** | |  |
| **Test** | **Acceptance Criteria** | **Analytical Procedure**  **(Type/Source/Version)** |
|  |  |  |
|  |  |  |

### S.4.2 Analytical procedures (name, manufacturer)

**Summary of the analytical procedures (e.g., HPLC, GC methods including key method parameters, conditions, system suitability testing):**

| **Method Name** |  | | | |
| --- | --- | --- | --- | --- |
| **Method Type** | HPLC | | **Method Code** |  |
| **Column** | |  | | |
| **Mobile Phase** | |  | | |
| **Detector** | |  | | |
| **Flow rate** | |  | | |
| **Injection volume** | |  | | |
| **Sample solution concentration** | |  | | |
| **Reference solution concentration** | |  | | |
| **System suitability solution concentration** | |  | | |
| **System suitability tests** | |  | | |

| **Method Name** |  | | | |
| --- | --- | --- | --- | --- |
| **Method Type** | GC | | **Method Code** |  |
| **Column / temperature program** | |  | | |
| **Carrier and auxiliary gas (type / flow rate)** | |  | | |
| **Detector (type / temperature)** | |  | | |
| **Injection (volume / temperature)** | |  | | |
| **Sample solution concentration** | |  | | |
| **Reference solution concentration** | |  | | |
| **System suitability solution concentration** | |  | | |
| **System suitability tests** | |  | | |

### S.4.3 Validation of analytical procedures (name, manufacturer)

**Summary of the validation information including validation parameters and results:**

Note: The validation of analytical procedures should be performed by designated testing facility (e.g. the drug product manufacturer) which is GMP compliant

| **Validation Summary** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method Code** | |  |  |  | |
| **Analytes** (e.g. assay of drug substance, related substances, residual solvents) | |  |  |  | |
| **Typical retention times (RT) or response factors (RF)** | |  |  |  | |
| **Relative response factor (RFImp./RFDr.Sub.)** | |  |  |  | |
| **Specificity** | |  |  |  | |
| **Linearity:** | **Number of concentrations:**  **Range:**  **Slope:**  **Y-intercept:**  **Coefficient of determination (r2):** |  |  |  | |
| **Accuracy:** | **Conc.(s):**  **Number of replicates:**  **Percent recovery (avg/RSD):** |  |  |  | |
| **Precision / Repeatability:** | **Conc.(s):**  **Number of replicates:**  **Result (avg/RSD):** |  |  |  | |
| **Intermediate Precision:** | **Parameter(s) altered:** |  |  |  | |
| **Result (avg/RSD):** |  |  |  | |
| **Limit of Detection (LOD):** | |  |  |  | |
| **Limit of Quantification (LOQ)** | |  |  |  | |
| **Robustness:** | **Stability of solutions:**  **Other variables / effects:** |  |  | |  |
| **Typical chromatograms or spectra may be found in:** | |  |  | |  |

### S.4.4 Batch analyses (name, manufacturer)

1. **Description of the batches:**

| **Batch Number** | **Batch Size** | **Date and**  **Site of Production** | **Use (e.g., nonclinical,**  **clinical, comparative)** |
| --- | --- | --- | --- |
|  |  |  |  |
|  |  |  |  |

1. **Summary of results for relevant batches (e.g., nonclinical, clinical, comparative). Use ranges if several batches included (include test, results and acceptance criteria):**

|  |  |  |
| --- | --- | --- |
| Test Parameter **(Method Number / Revision)** | Clinical Study Batches | Comparative Batches |
|  |  |  |
|  |  |  |

1. **Summary of analytical procedures and validation information for those procedures not previously summarized in S.4.2 and S.4.3 (e.g., historical analytical procedures):**

### S.4.5 Justification of specification (name, manufacturer)

1. **Justification of the drug substance specification (e.g., evolution and inclusion of tests, analytical procedures, and acceptance criteria, differences from compendial standard):**

## S.5 Reference Standards (name, manufacturer)

1. **Source of reference standards or reference materials (e.g., House, USP, BP, Ph. Eur.):**
2. **Characterisation and evaluation of non-official (e.g., non-compendial) reference standards or reference materials (e.g. calibration against an official standard). Indicate source, lot number, date of fabrication, confirmation that a certificate of analysis has been included, and provide a summary of differences in fabrication process from that described in section S.2.2:**

## S.6 Container closure system (name, manufacturer)

1. **Description of the container closure system(s) for the storage and shipment of the drug substance including materials of construction:**
2. **Summary of the specifications for the container closure system(s) components:**
3. **Discussion of the suitability for the intended use:**

## S.7 Stability (name, manufacturer)

### S.7.1 Stability summary and conclusions (name, manufacturer)

1. **Summary of forced degradation (stress) studies (e.g., heat, humidity, oxidation, light, acid/base hydrolysis) and results:**
2. **Summary of accelerated, intermediate (if applicable) and long-term testing (e.g., studies conducted, protocols used, results obtained):**

| **Batch Number/ Batch Size(s)** | **Manufacturing Date** | **Storage Conditions**  **(Temp °C, % RH)** | **Container Closure System** | **Completed (and Proposed) Test Intervals** |
| --- | --- | --- | --- | --- |
|  |  |  | same as described in S.6 |  |
|  |  |  |  |  |
|  |  |  |  |  |

1. **Proposed storage conditions and re-test period (or shelf life, as appropriate):**

|  |  |  |
| --- | --- | --- |
| **Container Closure System** | **Storage Conditions** | **Re-test Period/Shelf life** |
|  |  |  |

### S.7.2 Post-approval stability protocol and stability commitment (name, manufacturer)

Note: The stability protocol used for long term studies for the stability commitment should be the same as that for the primary batches, unless otherwise scientifically justified (VICH GL3)

1. **Stability protocol for primary batches to continue stability studies if available data do not cover the proposed re-test period or shelf life:**

*<<delete table if not applicable>>*

| **Protocol Parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

1. **Stability protocol for production scale commitment batches**

| **Protocol Parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

1. **Stability protocol for continuing (i.e., ongoing) batches**

| **Protocol Parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

# P. Drug Product

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

1. **Description of the drug product *(For generics: include a discussion on the pharmaceutical equivalence of the proposed product with the Canadian Reference Product)*:**
2. **Composition of the drug product:**
   1. **Composition, i.e., list of all components of the dosage form, and their amounts on a per unit basis:**

| **Component and Quality Standard (e.g., USP, Ph. Eur., BP, other)** | **Function** | **Strength (label claim)** | | | |
| --- | --- | --- | --- | --- | --- |
| *Strength 1 (e.g., mg, mg/mL)* | | *Strength 2 (e.g., mg, mg/mL)* | |
| **Quantity per unit** | **% (w/v, w/w)** | **Quantity per unit** | **% (w/v, w/w)** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **Total** |  |  |  |  |  |

* 1. **Composition of all components that are mixtures (e.g., colourants, coatings, capsule shells, imprinting inks):**

**(c) Description of accompanying reconstitution diluent(s), if applicable:**

**(d)** **Description of container/closure system used for the accompanying reconstitution diluent, if applicable:**

**(e) Description of accompanying dosing devices, if applicable:**

## P.2 Pharmaceutical Development (name, dosage form)

### P.2.1 Components of the drug product (name, dosage form)

#### P.2.1.1 Drug substance (name, dosage form)

1. Discussion of the compatibility of the drug substance with excipients listed in P.1:
2. Discussion of the key physicochemical characteristics (e.g., water content, solubility, particle size distribution, polymorphic or solid state form) of the drug substance that can influence the performance of the drug product:
3. **For combination products, a discussion of the compatibility of drug substances with each other:**

#### P.2.1.2 Excipients (name, dosage form)

**Summary and discussion of the studies conducted to develop the formulation including the selection of excipients and their concentrations, as well as their characteristics that can influence that drug product performance:**

### P.2.2 Drug product (name, dosage form)

#### P.2.2.1 Formulation development (name, dosage form)

1. **Summary describing the development of the drug product (e.g., route of administration, usage):**
2. **Discussion of the differences in the formulations for the batches used the in the *in vivo* studies (e.g., pivotal clinical, comparative bioequivalence) and the formulation described in P.1:**
3. **For scored tablets, provide rationale/justification for scoring:**

#### P.2.2.2 Overages (name, dosage form)

**Justification of overages in the formulation(s) described in P.1:**

#### P.2.2.3 Physicochemical and biological properties (name, dosage form)

**Discussion of the parameters relevant to the performance of the drug product (e.g., pH, ionic strength, dissolution, particle size distribution, polymorphism, rheological properties) (*For generics: Include a discussion on the comparative physiochemical and/or biological properties of the proposed product and the Canadian Reference Product)*:**

### P.2.3 Manufacturing process development (name, dosage form)

1. **Discussion of the development of the manufacturing process of the drug product (e.g., optimization of the process, summary of studies conducted to demonstrate homogeneity of the medicated feed (i.e. mixing studies), selection of the method of sterilization):**
2. **Discussion of the differences in the manufacturing process(es) for the batches used the in the *in vivo* studies (pivotal clinical, comparative bioequivalence) and the process described in P.3.3:**

### P.2.4 Container Closure System (name, dosage form)

**Discussion of the suitability of the container closure system (described in P.7) used for the storage, transportation (shipping), and use of the drug product (e.g., choice of materials, protection from moisture and light, compatibility of the materials with the dosage form):**

### P.2.5 Microbiological attributes (name, dosage form)

**Discussion of microbiological attributes of the drug product (e.g., preservative effectiveness studies):**

### P.2.6 Compatibility (name, dosage form)

**Discussion of the compatibility of the drug product (e.g., with reconstitution diluent(s) or dosage devices, co-administered drugs):**

## P.3 Manufacture (name, dosage form)

### P.3.1 Manufacturer(s) (name, dosage form)

1. **Name, address, and responsibility of each site, including contract sites, involved in the manufacturing, packaging, labelling, testing, importing/release, storage, and distribution of the drug product:**

| **Site** | **Responsibility** |
| --- | --- |
|  |  |
|  |  |

1. **List of referenced Drug Master Files (DMFs) and DMF Numbers (copies of DMF letters of access should be located in Part 1:**
2. **Attestation and/or confirmation that all facilities involved in the production have a Good Manufacturing Practices (GMP) compliance rating and/or an Establishment License (EL) (GMP and/or EL information should be located in Part 1):**

### P.3.2 Batch formula (name, dosage form)

**List of all components of the dosage form to be used in the manufacturing process, and their amounts on a per batch basis, including those removed during the production process.**

Note: Indicate the use of overages and justification, if applicable.

| **Strength (label claim)** |  |  |
| --- | --- | --- |
| **Master Production Document reference #, version #** |  |  |
| **Batch Size(s) (number of dosage units)** |  |  |
| **Component and Quality Standard (e.g., USP, Ph. Eur., BP, other)** | **Quantity per batch** | **Quantity per batch** |
|  |  |  |
|  |  |  |
|  |  |  |
| Total |  |  |

### P.3.3 Description of manufacturing process and process controls (name, dosage form)

1. **Flow diagram of the manufacturing process:**
2. **Narrative summary of the manufacturing process, including amounts of ingredients, equipment type and working capacity, and process parameters:**
3. **Justification of reprocessing of materials:**

### P.3.4 Controls of critical steps and intermediates (name, dosage form)

**Summary of controls performed at the critical steps of the manufacturing process and on isolated intermediates:**

### P.3.5 Process validation and/or evaluation (name, dosage form)

**Summary of the process validation and/or evaluation studies conducted or a summary of the proposed validation protocol for the critical steps or critical assays used in the manufacturing process (e.g., protocol number, parameters, results):**

## P.4 Control of Excipients (name, dosage form)

### P.4.1 Specifications (name, dosage form)

1. **Summary of the specifications for non-compendial excipients and for compendial excipients which include supplementary tests not included in the monograph(s):**
2. **Confirmation that none of the excipients which appear in the drug product are prohibited for use in drugs by the Canadian Food and Drug Regulations:**
3. **List of referenced Master Files (MFs), if applicable (copies of MF letters of access should be located in Part 1):**

### P.4.2 Analytical procedures (name, dosage form)

**Summary of the non-compendial analytical procedures:**

### P.4.3 Validation of analytical procedures (name, dosage form)

Summary of the validation information for the non-compendial analytical procedures:

### P.4.4 Justification of specifications (name, dosage form)

**Justification of the specifications (e.g., evolution of tests, analytical procedures, and acceptance criteria, exclusion of certain tests, differences from compendial standard):**

### P.4.5 Excipients of animal origin (name, dosage form)

**(a) List of ingredients that are of animal origin (including country of origin):**

**(b)** **Summary of the information (e.g., origin, specifications, country of origin, BSE status of country of origin, viral safety data) regarding animal sourced ingredients:**

**(c)** **A TSE Certificate of Suitability and/or a science-based risk assessment when appropriate may be found in:**

### P.4.6 Novel excipients (name, dosage form)

**Summary of the details on the fabrication, characterization, specifications including methods and validation with cross references to supporting safety data (nonclinical and/or clinical) on novel excipients (i.e., those used for the first time in a drug product or by a new route of administration):**

## P.5 Control of Drug Product (name, dosage form)

### P.5.1 Specification(s) (name, dosage form)

Note: Provide an attested, QC-approved and dated, copy from the designated release and stability testing site(s).

**Specification(s) for the drug product, including specification number and version, as well as test method number(s) and version(s) are required:**

| **Standard claimed (e.g., Professed, USP, BP, other)** | |  |
| --- | --- | --- |
| **Specification approved date** | |  |
| **Specification reference number and version** | |  |
| **Test** | **Acceptance Criteria**  **(release and shelf-life)** | **Analytical Procedure**  **(Type/Source/Version)** |
|  |  |  |
|  |  |  |

### P.5.2 Analytical procedures (name, dosage form)

Note: The validation of analytical procedures should be performed by the designated drug product release and stability, GMP compliant, testing site(s).

**Summary of the analytical procedures (e.g., HPLC, GC methods including key method**

**parameters, conditions, system suitability testing for the drug product, including reconstituted product or drug premix, if applicable):**

| **Method Name** |  | |
| --- | --- | --- |
| **Method Type/Code** |  | |
| **Column** | |  |
| **Mobile Phase** | |  |
| **Detector** | |  |
| **Flow rate** | |  |
| **Injection volume** | |  |
| **Sample solution concentration** | |  |
| **Reference solution concentration** | |  |
| **System suitability solution concentration** | |  |
| **System suitability tests** | |  |

### P.5.3 Validation of analytical procedures (name, dosage form)

1. **Summary of the validation information on methods summarized in P.5.2 including validation parameters and results for the drug product, including reconstituted product or drug premix, if applicable:**

| **Validation Summary** | | | | |
| --- | --- | --- | --- | --- |
| **Method Code** | |  | | |
| **Analytes** | |  |  |  |
| **Typical retention times (RT) or response factors (RF)** | |  |  |  |
| **Relative response factor (RFImp./RFDr.Sub.)** | |  |  |  |
| **Specificity** | |  |  |  |
| **Linearity:** | **Number of concentrations:**  **Range:**  **Slope:**  **Y-intercept:**  **Coefficient of determination (r2):** |  |  |  |
| **Accuracy:** | **Conc.(s):**  **Number of replicates:**  **Percent recovery (avg/RSD):** |  |  |  |
| **Precision / Repeatability:** | **Conc.(s):**  **Number of replicates:**  **Result (avg/RSD):** |  |  |  |
| **Intermediate Precision:** | **Parameter(s) altered:** |  |  |  |
| **Result (avg/RSD):** |  |  |  |
| **Limit of Detection (LOD)** | |  |  |  |
| **Limit of Quantification (LOQ)** | |  |  |  |
| **Robustness:** | **Stability of solutions:**  **Other variables / effects:** |  |  |  |
| **Typical chromatograms or spectra may be found in** | |  |  |  |

1. **Summary of the validation information on other methods (e.g. LAL method for the test of bacterial endotoxins):**

**Template for LAL Method Validation**

**Appendix No.:**

|  |  |  |  |
| --- | --- | --- | --- |
| **LAL Method Validation** | | **Volume/Page:** |  |
| **Method name:** |  | **Method code:** |  |
| **Reference (e.g., USP, FDA):** |  | **Approval date:** |  |
| **LAL reagent source** | |  | |
| **Endotoxins (RSE/CSE) source** | |  | |
| **Bacterial endotoxin limit:** | **K value (EU/kg/hour) used:**  **M value (max dose/kg/hour) used:**  **Calculated limit (K÷M):**  **Limit in specifications:** |  | |
| **Minimum Valid Concentration (MVC):** | **λ (LAL sensitivity) value used:**  **Calculated MVC (λM÷K):**  **Concentration used in test:** |  | |
| **Maximum Valid Dilution (MVD):** | **Concentration of product:**  **Calculated MVD (conc÷MVC):**  **Dilution used in test:** |  | |
| **Describe acceptance criteria used for standardization of CSE against RSE** | |  | |
| **Confirmation of labelled LAL reagent sensitivity:** | **Labelled LAL reagent sensitivity:**  **Dilution series of RSE/CSE:**  **Observed LAL reagent sensitivity:** |  | |
| **Inhibition/**  **Enhancement:** | **Concentration of sample:**  **Dilution series of RSE/CSE:**  **Inhibition/Enhancement observed?**  **If yes, describe further procedures.** |  | |
| **Provide actual results for at least 3 batches:** | |  | |

### P.5.4 Batch analyses (name, dosage form)

1. **Description of the batches:**

| **Strength and**  **Batch Number** | **Batch Size** | **Date and**  **Site of Production** | **Use (e.g., nonclinical,**  **clinical, comparative)** |
| --- | --- | --- | --- |
|  |  |  |  |
|  |  |  |  |

**(b)** **Summary of results for relevant batches (e.g., nonclinical, clinical, comparative) use ranges if several batches are included:**

| Test Parameter | Clinical Study Batches | **Production Batches** |
| --- | --- | --- |
|  |  |  |
|  |  |  |

**(c) Summary of analytical procedures and validation information for those procedures not previously summarized in P.5.2 and P.5.3 (e.g., historical analytical procedures):**

### P.5.5 Characterization of impurities (name, dosage form)

**Information on the characterization of impurities not previously provided in section S.3.2 2 (e.g., summary of actual and potential degradation products, basis for setting the acceptance criteria):**

### P.5.6 Justification of specification(s) (name, dosage form)

**Justification of the drug product specification(s) (e.g., selection of tests, evolution of tests, analytical procedures, acceptance criteria, differences from compendial standard where applicable):**

## P.6 Reference Standards or Materials (name, dosage form)

1. **Source of reference standards or reference materials (e.g., House, USP, BP, Ph.Eur.):**

**(b)** **Characterization and evaluation of non-official (e.g., non-compendial) reference standards or reference materials (e.g., method of manufacture, elucidation of structure, certificate of analysis, calibration against an official standard):**

## P.7 Container Closure System (name, dosage form)

1. **Description of the container closure system (i.e. primary and secondary packaging), including unit count or fill size, container size or volume, and for injectable products indicate the rubber closure formulation number:**
2. **Materials of construction of each primary and functional secondary packaging component:**

|  |  |
| --- | --- |
| **Packaging Component** | **Description and Supplier** |
|  |  |
|  |  |
|  |  |

1. **Summary of specifications of each primary and functional secondary packaging component:**

|  |  |
| --- | --- |
| **Packaging Component** | **Specification** |
|  |  |
|  |  |
|  |  |

**(d)** **List of referenced Master Files (MFs), if applicable (copies of MF letters of access should be located in Part 1):**

## P.8 Stability (name, dosage form)

### P.8.1 Stability summary and conclusions (name, dosage form)

1. **Summary of stress testing and results (e.g., photostability studies, cyclic studies for semi-solids, freeze-thaw studies):**
2. **Summary of accelerated and long-term testing (e.g., studies conducted, protocols used, results obtained):**
   1. **Description of stability study details:**

| **Strength and Batch Number** | **Batch Size** | **Manufacturing Date** | **Container Closure System** | **Storage Conditions (°C, %RH, light)** | **Completed (and Proposed) Test Intervals** |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

* 1. **Summary and discussion of stability study results (including results from in-use stability studies, and stability studies of medicated feed):**

1. **Proposed storage conditions and shelf life (and in-use storage conditions and in-use period, if applicable):**

|  |  |  |
| --- | --- | --- |
| **Container Closure System** | **Storage Conditions** | **Shelf life (and in-use period if applicable)** |
|  |  |  |

### P.8.2 Post-approval stability protocols and stability commitments (name, dosage form)

1. A commitment to continue stability studies on primary batches if available data do not cover the proposed shelf life:

| **Protocol parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches per strength and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

1. Stability protocol for production scale commitment batches (indicate protocol reference number and approval date):

| **Protocol parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches per strength and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

1. Stability protocol for continuing (i.e., ongoing) batches (indicate protocol reference number and approval date):

| **Protocol parameter** | **Description** |
| --- | --- |
| **Storage conditions (including tolerances)** |  |
| **Testing frequency** |  |
| **Number of batches per strength and batch sizes** |  |
| **Container closure system(s)** |  |
| **Tests and acceptance criteria** |  |
| **Other** |  |

1. **Bracketing and matrixing design and justification for commitment and/or continuing (i.e., ongoing) batches, if applicable:**

## P.9 Production Documentation(name, dosage form)

### P.9.1 Executed production documents (name, dosage form)

**Indicate the batches, including strengths, for which executed production documents have been provided (e.g., pivotal clinical and comparative bioequivalence batches):**

### P.9.2 Master production documents (name, dosage form)

**Indicate the blank master production documents provided for each strength, proposed batch size, and fabrication site:**