**QUALITY OVERALL SUMMARY (QIS)**

**INTRODUCTION**

(a) Summary of product information:

|  |  |  |  |
| --- | --- | --- | --- |
| **Non-proprietary name(s) of the finished pharmaceutical product(s) (FPP)** |  | | |
| **Proprietary name(s) of the finished pharmaceutical product(s) (FPP)** |  | | |
| **International non-proprietary name(s) of the active pharmaceutical ingredient(s) (API(s)), including form (salt, hydrate, polymorph)** |  | | |
| **Applicant name and address** |  | | |
| **Dosage form** |  | | |
| **Application & Registration Number(s)** |  |  |  |
| **Strength(s)** |  |  |  |
| **Route of administration** |  | | |
| **Proposed indication(s)** |  | | |
| **Contact information** | Name:  Phone:  Fax:  Email: | | |

(b) Administrative Summary:

|  |  |
| --- | --- |
| **Applicant’s date of preparation or revision of the QIS** |  |
| **Internal version and/or date of acceptance** | *(MRA use only)* |

**Related dossiers (e.g. FPP(s) with the same API(s) submitted to the MRA by the applicant):**

|  |  |  |  |
| --- | --- | --- | --- |
| **Reference number**  (eg A1500001) | **Registered (Y/N)** | **API, strength, dosage form**  (eg. Abacavir (as sulphate) 300 mg tablets) | **API manufacturer**  (including address if same  supplier as current dossier) |
|  |  |  |  |
|  |  |  |  |

**2.3.S DRUG SUBSTANCE (or ACTIVE PHARMACEUTICAL INGREDIENT (API)) (NAME, MANUFACTURER)**

Indicate which option applies for the submission of API information:

|  |  |  |
| --- | --- | --- |
| **Name of API:** | |  |
| **Name of API manufacturer:** | |  |
| □ | Confirmation of API Prequalification document | |
| □ | Certificate of suitability to the European Pharmacopoeia (CEP) | |
| □ | Active pharmaceutical ingredient master file (APIMF) procedure: | |
| □ | Full details in the PD | |

**2.3.S.2 Manufacture (name, manufacturer)**

***2.3.S.2.1 Manufacturer(s) (name, manufacturer)***

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing, storage) of each manufacturer, including contractors and each proposed production site or facility involved in these activities:

|  |  |  |
| --- | --- | --- |
| **Name and address**  **(including block(s)/unit(s))** | **Responsibility** | **API-PQ number /CEP number (if applicable)** |
|  |  |  |
|  |  |  |
|  |  |  |

***2.3.S.2.3 Control of Materials (name, manufacturer) – for API option 4 only***

(a) Name of starting material:

(b) Name and manufacturing site address of starting material manufacturer(s):

**2.3.S.4 Control of the API (name, manufacturer)**

***2.3.S.4.1 Specification (name, manufacturer)***

1. API specifications *of the FPP manufacturer*:

| **Standard (e.g. Ph.Int., Ph.Eur., BP, USP, in-house)** | |  |
| --- | --- | --- |
| **Specification reference number and version** | |  |
| **Test** | **Acceptance criteria** | **Analytical procedure**  **(Type/Source/Version)** |
| Description |  |  |
| Identification |  |  |
| Impurities |  |  |
| Assay |  |  |
| etc. |  |  |
|  |  |  |
|  |  |  |

**2.3.S.6 Container Closure System (name, manufacturer)**

(a) Description of the container closure system(s) for the storage and shipment of the API:

**2.3.S.7 Stability (name, manufacturer)**

***2.3.S.7.1 Stability Summary and Conclusions (name, manufacturer)***

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

|  |  |  |
| --- | --- | --- |
| **Container closure system** | **Storage statement** | **Re-test period\*** |
|  |  |  |
|  |  |  |

\* indicate if a shelf-life is proposed in lieu of a re-test period (e.g. in the case of labile APIs)

**2.3.P DRUG PRODUCT (or FINISHED PHARMACEUTICAL PRODUCT (FPP))**

**2.3.P.1 Description and Composition of the FPP**

1. Description of the FPP (in signed specifications):

(b) Composition of the FPP:

(i) Composition, i.e. list of all components of the FPP and their amounts on a per unit basis and percentage basis (including individual components of mixtures prepared in-house (e.g. coatings) and overages, if any):

| **Component and quality standard (and grade, if applicable)** | **Function** | **Strength (label claim)** | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  | |  | |
| **Quant. per unit or per mL** | **%** | **Quant. per unit or per mL** | **%** | **Quantity per unit or per mL** | **%** |
| <complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection> | | | | | | | |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| Subtotal 1 |  |  |  |  |  |  |  |
| <complete with appropriate title e.g. Film-coating > | | | | | | | |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| Subtotal 2 |  |  |  |  |  |  |  |
| Total |  |  |  |  |  |  |  |

(ii) Composition of all *components purchased as mixtures* (e.g. colourants, coatings, capsule shells, imprinting inks):

1. Description of accompanying reconstitution diluent(s), if applicable:

***2.3.P.2.2.1 Formulation Development***

(b) Information on primary (submission, registration, exhibit) batches including comparative bioavailability or biowaiver, stability, commercial:

1. Summary of batch numbers:

|  |  |  |  |
| --- | --- | --- | --- |
| **Batch number(s) of the FPPs used in** | | | |
| **Bioequivalence or biowaiver** | <e.g. bioequivalence batch A12345> <e.g. biowaiver batch X12345> | | |
| **For proportional strength biowaiver: the bioequivalence batch of the reference strength** |  | | |
| **Dissolution profile studies** |  | | |
| **Stability studies (primary batches)** | | | |
| ‹packaging configuration I› |  |  |  |
| ‹ packaging configuration II› |  |  |  |
| ‹*Add/delete as many rows as necessary*› |  |  |  |
| **Stability studies (production batches)** | | | |
| ‹ packaging configuration I› |  |  |  |
| ‹ packaging configuration II› |  |  |  |
| *(Add/delete as many rows as necessary)* |  |  |  |
| **Validation studies (primary batches)** | | | |
| ‹ packaging configuration I› |  |  |  |
| ‹ packaging configuration II› |  |  |  |
| *(Add/delete as many rows as necessary)* |  |  |  |
| **Validation studies (at least the first three consecutive production batches)**  **or code(s)/version(s) for process validation protocol(s)** |  |  |  |

**Summary of formulations and discussion of any differences:**

| **Component and quality standard (e.g. NF, BP, Ph.Eur, in-house)** | **Relevant batches** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Comparative bioavailability or biowaiver** | | **Stability** | | **Process validation** | | **Commercial (2.3.P.1)** | |
| **<Batch nos. and sizes>** | | **<Batch nos. and sizes>** | | **<Batch nos. and sizes>** | | **<Batch nos. and sizes>** | |
| **Theor.**  **quantity per batch** | **%** | **Theor.**  **quantity per batch** | **%** | **Theor.**  **quantity per batch** | **%** | **Theor.**  **quantity per batch** | **%** |
| <complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection> | | | | | | | | |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Subtotal 1 |  |  |  |  |  |  |  |  |
| <complete with appropriate title e.g. Film-coating > | | | | | | | | |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Subtotal 2 |  |  |  |  |  |  |  |  |
| Total |  |  |  |  |  |  |  |  |

**2.3.P.3 Manufacture**

***2.3.P.3.1 Manufacturer(s)***

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing) of each manufacturer, including contractors and each proposed production site or facility involved in manufacturing and testing:

| **Name and address**  **(include block(s)/unit(s))** | **Responsibility** |
| --- | --- |
|  |  |
|  |  |
|  |  |
|  |  |

***2.3.P.3.2 Batch Formula***

Largest intended commercial batch size:

Other intended commercial batch sizes:

<information on all intended commercial batch sizes should be in the QIS>

(a) List of all components of the FPP to be used in the manufacturing process and their amounts on a per batch basis (including components of mixtures prepared in-house (e.g. coatings) and overages, if any):

| **Strength (label claim)** |  |  |  |
| --- | --- | --- | --- |
| **Master production document**  **reference number and/or version** |  |  |  |
| **Proposed commercial batch size(s) (e.g. number of dosage units)** |  |  |  |
| **Component and quality standard**  **(and grade, if applicable)** | **Quantity per batch (e.g. kg/batch)** | **Quantity per batch (e.g. kg/batch)** | **Quantity per batch (e.g. kg/batch)** |
| <complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection> | | | |
|  |  |  |  |
|  |  |  |  |
| Subtotal 1 |  |  |  |
| <complete with appropriate title e.g. Film-coating > | | | |
|  |  |  |  |
|  |  |  |  |
| Subtotal 2 |  |  |  |
| Total |  |  |  |

***2.3.P.3.3 Description of Manufacturing Process and Process Controls***

(a) Flow diagram of the manufacturing process:

1. Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:

***2.3.P.3.4 Controls of Critical Steps and Intermediates***

(a) Summary of controls performed at the critical steps of the manufacturing process and on isolated intermediates:

| **Step**  **(e.g. granulation, compression, coating)** | **Controls (parameters/limits/frequency of testing)** |
| --- | --- |
|  |  |
|  |  |
|  |  |
|  |  |

Proposed/validated holding periods for intermediates (including bulk product):

***2.3.P.3.5 Process Validation and/or Evaluation***

(a) Summary of the process validation and/or evaluation studies conducted and/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):

Document code(s) for the process validation protocol(s) and/or report(s) (including reference number/version/date):

**2.3.P.5 Control of FPP**

***2.3.P.5.1 Specification(s)***

(a) Specification(s) for the FPP:

| **Standard (e.g. Ph.Int., BP, USP, in-house)** | | |  |
| --- | --- | --- | --- |
| **Specification reference number and version** | | |  |
| **Test** | **Acceptance criteria**  **(release)** | **Acceptance criteria**  **(shelf-life)** | **Analytical procedure**  **(type/source/version)** |
| Description |  |  |  |
| Identification |  |  |  |
| Impurities |  |  |  |
| Assay |  |  |  |
| etc. |  |  |  |
|  |  |  |  |
|  |  |  |  |

**2.3.P.7 Container Closure System**

1. Description of the container closure systems, including unit count or fill size, container size or volume:

|  |  |  |  |
| --- | --- | --- | --- |
| **Description**  **(including materials of construction)** | **Strength** | **Unit count or fill size**  **(e.g. 60s, 100s etc.)** | **Container size**  **(e.g. 5 ml, 100 ml etc.)** |
|  |  |  |  |
|  |  |  |
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|  |  |  |
|  |  |  |

**2.3.P.8 Stability**

***2.3.P.8.1 Stability Summary and Conclusions***

(c) Proposed storage statement and shelf-life (and in-use storage conditions and in-use period, if applicable):

|  |  |  |
| --- | --- | --- |
| **Container closure system** | **Storage statement** | **Shelf-life** |
|  |  |  |
|  |  |  |

***2.3.P.8.2 Post-approval Stability Protocol and Stability Commitment***

1. Stability protocol for *Primary stability batches* (e.g. storage conditions (including tolerances), batch numbers and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s):

| **Parameter** | **Details** | |
| --- | --- | --- |
| Storage condition(s) (◦C, % RH) |  | |
| Batch number(s) / batch size(s) | <*primary batches*> | |
| Tests and acceptance criteria | Description |  |
| Moisture |  |
| Impurities |  |
| Assay |  |
| etc. |  |
|  |  |
| Testing frequency |  | |
| Container closure system(s) |  | |
|  |  | |

(b) Stability protocol for *Commitment batches* (e.g. storage conditions (including tolerances), batch numbers (if known) and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s):

| **Parameter** | **Details** | |
| --- | --- | --- |
| Storage condition(s) (◦C, % RH) |  | |
| Batch number(s) / batch size(s) | *<not less than three production batches in each container closure system>* | |
| Tests and acceptance criteria | Description |  |
| Moisture |  |
| Impurities |  |
| Assay |  |
| etc. |  |
| Testing Frequency |  | |
| Container Closure System(s) |  | |
|  |  | |

(c) Stability protocol for *Ongoing Batches* (e.g. storage conditions (including tolerances), number of batches per strength and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s):

| **Parameter** | **Details** | |
| --- | --- | --- |
| Storage condition(s) (◦C, % RH) |  | |
| Batch size(s), annual allocation | *<at least one production batch per year (unless none is produced that year)* *in each container closure system >* | |
| Tests and acceptance criteria | Description |  |
| Moisture |  |
| Impurities |  |
| Assay |  |
| etc. |  |
| Testing frequency |  | |
| Container closure system(s) |  | |
|  |  | |

***2.3.P.8.3 Stability Data***

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

**Change History**

**Date of preparation of original QIS:**

|  |  |  |
| --- | --- | --- |
| **Date of revised version** | **Section (e.g. S.2.1)** | **Revision** |
|  |  |  |
|  |  |  |
|  |  |  |