SOP # S-0105-01-069Y | STANDARD OPERATING PROCEDURES |

SAMPLING AND TESTING THE PIVOTAL BATCH TABLET AND CAPSULE DOSAGE FORMS

1. PURPOSE

The purpose of this Standard Operating Procedure is to describe the sampling and the testing plan and sampling points required for each pivotal batch (or pilot plant scale) manufactured.

2. RESPONSIBILITY

① Symbol indicates Protocol for sampling and Testing of the Pivotal Batch prepared by Project and Process Development Managers. Sampling and Testing Protocols are approved by the R&D and QA.
② Symbol indicates sampling performed by validation team.
③ Symbol indicates sampling performed by plant QA Technicians.
④ Symbol indicates In-process physical testing performed by the plant QA Technicians.
⑤ Symbol indicates Batch Release Testing performed by the plant QC Analytical Laboratory.
⑥ Symbol indicates testing performed by the R&D Analytical Laboratory.
⑦ Symbol indicates analysis and evaluation of the test data generated, performed by the R&D Validation Team and approved by the R&D Quality Assurance.

3. FREQUENCY

Performed with each pivotal or pilot plant batch.

4. PROCEDURE

4.1. SAMPLING AND TESTING PLANS FOR IN-PROCESS MATERIALS

◊ **On Milled Granulate**

Sampling Plan - Physical Tests

One sample (about 100g) from each storage container will be collected ②.
A second sample will be collected and retained for retesting, if so required ②.

Physical Tests Required

- Sieve Analysis⑥
- Bulk and tapped density⑥
- Moisture (if required by in-process manufacturing specifications) ⑥

◊ **On Final Blend**

Sampling Plan - Physical Testing:

Three samples (~100g) will be collected ② from the top, middle and bottom of each storage container.
A maximum of three additional samples will be collected according to the same procedure and retained for retesting, if required.

SAMPLING AND TESTING THE PIVOTAL BATCH TABLET AND CAPSULE DOSAGE FORMS

Sampling Plan - Chemical Testing of granulate:
Ten (10) samples, each sample equivalent to the stated sampling weight per unit dose, will be collected from the Y-Cone (left and right arms and cone leg).
Where flow bins double as mixer containers, the samples are collected ② from the top, middle and bottom.
20 samples will be collected in the same procedure mentioned below for retesting, if so needed.

Sampling Plan ② for Chemical Testing of tablet or capsule:
Ten (10) samples, each equivalent to the following tablet core or capsule fill weights of the final dosage unit:-

⇒ sample one dosage unit for unit weights greater than 400 mg

⇒ sample two dosage unit for unit weights greater than 200 mg and LT 400.

⇒ sample three dosage unit for unit weights greater than 100 mg and LT 200.

⇒ sample four dosage unit for unit weights less than 100 mg.

Sample the beginning (10), middle (10) and end (10) of the off-loading process.
When a flow-bin is used as a mixer device **and** as a storage container, no re-sampling is needed.
20 samples will be collected ② in the same procedure mentioned above for re-tests, if retesting is required.

Sampling method: unless specified in the specific protocol, the samples will be collected② using a dedicated thief sampler equipped with an appropriate die.

Chemical Testing Plan
The samples will be assayed ⑥ for full monograph requirements, on one set of 10 samples.
Two other sample sets will be retained for retesting, - if required.

Physical Testing Plan
Each sample will be tested for:
- Sieve analysis⑥
- Bulk and tapped density⑥

SAMPLING AND TESTING THE PIVOTAL BATCH TABLET AND CAPSULE DOSAGE FORMS

4.2 COMPRESSED TABLETS - (FINISHED DOSAGE FORM)

Hardness **R**ange **V**erification **S**tudy (HRVS)

Sampling Plan - (for tablets and tablet *cores* only).

Samples should be collected as they are compressed at the upper and lower limits of hardness specification. These limits are specially set during the compression run (about 10% of the batch run per extreme hardness limit) for the purpose of the HRVS, as shown.

10% HRVS (**lower**)——————Target Range[1]_80%——————10% HRVS (**upper**)————

Samples at the ***target*** hardness should be collected ② directly as they exit the press, at a minimum of 3 intervals, representing the beginning, middle and end of the tabletting compression run (collect a minimum of 100 000 units net[1]).

Testing Plan - (HRVS)

Tablets compressed at each limit (**upper** and **lower**) shall be tested as follows:

- 20 tablets for weight determination ⑥ ❶
- 20 tablets for thickness determination ⑥ ❶
- 20 tablets for hardness determination ⑥ ❶
- Friability test: ⑥ Tablets less than 650 mg; Test 6.0 - 6.5 g of tablets, but not less than 20 tablets. Tablets more than 650 mg; Test 10 tablets only.
- 12 tablets for dissolution profile - at *each* hardness limit.⑥ ❷

[1]OGD rules - not less than 100 000 units net in this target range

IN-PROCESS TESTING DURING TABLET COMPRESSION OR CAPSULE FILLING.

Sampling Plan Testing Plan for compressed tablets or filled capsules at normal target settings of which a minimum of 100 000 net must be compressed.

Each sample will be tested as follows:-

- 20 tablets or *capsules* for weight④ ❶
- 20 tablets for thickness ④ ❶
- 20 tablets for hardness ④ ❶
- Tablet friability for tablets less than 650 mg; Test 6.0 - 6.5 g of tablets, but not less than 20 tablets.④ Tablet friability for tablets more than 650 mg; Test 10 tablets only.④
- 6 tablets / *capsules* for dissolution ⑥ ❷
- Assay on each sample according to specific monograph. ⑥

SAMPLING AND TESTING THE PIVOTAL BATCH TABLET AND CAPSULE DOSAGE FORMS

❶ Will be performed on the same tablets in the stated order.
❷ For tablet cores to be coated, dissolution profile shall be performed on tablets collected from each interval - total of 12.

NOTE: for tablet cores that will be coated, any other test required by the specifications must be performed on the representative sample only.

4.3 Coated Tablets
If more than one load (sub-lot) is processed in the coating machine, dissolution test⑥ as per finished product specifications will be performed on 6 coated tablets from *each* load (sub-lot).

4.4 Release and Stability for Finished Product
Each drug product strength is tested for release ⑤ (by plant QC unit) and initial stability interval ⑥ (by R&D Lab Unit).
Comparative Dissolution Profiles (CDP):-
Comparative dissolution profile ⑥ (for Generic vs. Innovative) will be checked on **12** tablets sampled from the package configuration sent to the bioequivalent study.

4.5 Evaluation of Test Parameters
The physical and chemical parameters tested are evaluated ⑦ to confirm the uniformity of the batch and where applicable to comply with the written product specifications.

5.0 Limits/Limitations - none

6.0 Corrective Action - none

7. 0 Documentation

A manufacturing flowchart will be added to all protocols.

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