3.13 Packaged Investigational Medicinal Product (Packaged IMP)

A formulated product which has undergone all stages of production including packaging in its final container.

3.14 Pivotal Bioequivalence Study

A study conducted to demonstrate bio-equivalence between the clinical trial formulation on which substantial evidence of safety and effectiveness has been generated and the proposed sales formulation to support an NDA/MAA.

3.15 Reference sample (Reserve sample)

A sample of a batch of API, excipients, packaging material, or bulk or packaged IMP which is stored for the purpose of being analyzed should the need arise during the shelf life of the batch concerned. The reference sample shall be stored in the same container closure system in which the product is packaged or shipped, or in one that has essentially the same characteristics, (i.e. mimics the container-closure system). The IMP reference sample may be taken after manufacturing or after primary or secondary packaging.

3.16 Reference standard for BE Studies

The drug product against which the test article is being tested. This is either, (1) the drug product that was used in the clinical studies demonstrating substantial evidence of safety and effectiveness for the test article's claimed indication, or (2) the marketed product in the case where the test article is being compared to the originator/reference product to establish bio-equivalence.

3.17 Retention sample

A sample of a unit from a batch of packaged IMP. It is typically trial specific and stored for visual identification purposes should the need arise during the shelf life of the batch concerned. This sample can be a physical specimen or an electronic file or photograph based on local legislative and regulatory requirements, and may only be required once per trial.

3.18 Test Article for BE Studies

The drug product for which a company is seeking NDA/MAA approval or supplemental application, e.g. the proposed sales formulation.

4 Responsibilities

It is the responsibility of each site to have procedures in place which comply with this guideline and with local legislative or regulatory requirements where they are different.

The responsibility for the retention of all reference samples lies with the site

6 Appendices

6.1 Appendix A Reference Samples

Sample	Quantity	Retention Period
Raw Materials	N/A	N/A
Intermediates	N/A	N/A
API	2X quantity to perform release testing (excluding sterility/pyrogen testing where 1X is required)	11 years after release
Excipients	2X quantity to perform release testing (excluding sterility and/or microbial tests where 1X is required)	5 years after release
Primary Packaging and Printed Packaging Components	At least one sample	5 years after release
Bulk IMP including manipulated comparators and diluents	2X quantity to perform release testing (excluding sterility/pyrogen testing where 1X is required)	10 years after release
Packaged IMP	2X quantity to perform release testing (excluding sterility/pyrogen testing where 1X is required)	10 years after release
Comparators	N/A	N/A
Drug Delivery Systems	50 (for multiple dose delivery systems)	2 years after end of trial or 7 years maximum
Packaged Product (BA/BE)	5X quantity to perform release testing for drug product (test article) and reference standard	5 years after approval of NDA or 5 years after completion of study if NDA is withdrawn or not approved

