

Draft Guidance on Azacitidine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Azacitidine

Form/Route: Injectable/Intravenous; Subcutaneous

The proposed drug product should be qualitatively (Q1) and quantitatively (Q2) the same as the corresponding reference listed drug. Bioequivalence may be established based on comparative in vitro testing.

The three criteria to provide in vitro evidence that the test product, when reconstituted as a suspension for subcutaneous administration, demonstrates bioequivalence are:

1. **Physico-chemical Characteristics.** Evidence of equivalence that test and RLD products have the same final physico-chemical characteristics, such as viscosity, osmolality, and pH.
2. **Particle Morphology.** It is recommended that a suitable method for qualitative determination be used to allow observation of particles in the size range in which azacitidine particles are expected to fall. Representative micrographs should also be submitted. These data are supportive, and formal statistical testing is not applicable.
3. **Particle Diameter.** In addition, a suitable method should be used to determine particle diameter. The D_{10} , D_{50} , D_{90} and span (i.e., $D_{90}-D_{10}/D_{50}$) measurements can be analyzed by using the population bioequivalence (PBE) statistical approach.

The in vitro tests should be performed on ten samples from one lot of the test product and one lot of the reference listed drug.

Waiver request of in-vivo testing: Not applicable

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.

Additional Information:

For additional information regarding statistical analysis of in-vitro data, please refer to FDA Guidance for Industry: *Bioavailability and Bioequivalence Studies for Nasal*

Aerosols and Nasal Sprays for Local Action at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070111.pdf> and its companion document *Statistical Information from the June 1999 Guidance and Statistical Information for In-Vitro Bioequivalence Data* (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070118.pdf>).