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Draft Guidance on Degarelix Acetate

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This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on generic degarelix acetate.

Active Ingredient:	Degarelix acetate
Dosage Form; Route:	Powder; subcutaneous
Strengths:	EQ 80 mg base/vial and EQ 120 mg base/vial
Recommended Study:	In vitro study

In vitro study:
The proposed test product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] (Q1/Q2) the same as the Reference Listed Drug (RLD).

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference product.
[2] Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ±5% of those used in the reference product.

Active pharmaceutical ingredient (API) sameness between the test product and the RLD is demonstrated by characterizing the following properties: primary sequence, secondary sequence and aggregation states. The API sameness study should be performed on at least three exhibit batches of the test product and three batches of the RLD (as available) that are reconstituted following the RLD label instruction.

Bioequivalence may be established based on comparative in vitro testing of three exhibit batches of both strengths of the test[3] and Reference Standard (RS) products including:

i. Physicochemical characteristics. Evidence that the freshly reconstituted test and RS products have comparable physicochemical properties including reconstitution time, acetic acid content, appearance, optical density, viscosity, and pH. The reconstitution should be done following the label instruction.

ii. Gelling kinetics. Sponsors should provide justification for the experimental condition(s) employed for inducing gels of the test and RS products. Gels of the test and the RS products should be induced under the same experimental condition(s) (including appropriate physical conditions, in a suitable salt solution and/or biological medium). The gelling kinetics can be determined by monitoring the change in viscoelastic properties (e.g., storage modulus, loss modulus, Tan δ) and optical density over time.

iii. In vitro drug release. Acceptable comparative in vitro drug release of degarelix from the test and RS products. Detailed information on development and validation of a proposed in vitro drug release testing method should be provided.

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[3] The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.