

GDUFA Regulatory Science Priorities for Fiscal Year 2018

FDA prepares a yearly list of regulatory science initiatives for generic drugs as part of a commitment made in the Generic Drug User Fee Amendments (GDUFA) of 2012. This commitment continues in the Generic Drug User Fee Amendments of 2017 (GDUFA II). These initiatives are chosen based on input from FDA, industry and other stakeholders.

GDUFA II regulatory science supports fulfilment of submission review and pre-ANDA commitments. The regulatory science program enables the conduct of research to investigate scientific issues that are encountered during review of regulatory submissions. In addition, research is important for the development of guidances and recommendations that can guide generic product development and the pre-ANDA phase. The GDUFA II pre-ANDA commitments provide a new program designed to accelerate access to generic versions of complex products. The pre-ANDA program allows FDA to engage with applicants in pre-ANDA meetings that propose new or alternative development strategies for generic drug products. Elements of this new program, including the development of product-specific guidances and pre-ANDA meetings, require FDA to constantly build on a strong scientific foundation related to complex generic drug products. FDA depends on this scientific foundation to develop new guidances that describe new, more efficient equivalence methods.

FDA held a [public workshop](#) on May 3, 2017, and proposed 15 scientific initiatives to accelerate access to generic drug products. FDA considered comments raised in the workshop discussions and submitted to the docket and have established the following FY 2018 GDUFA regulatory science initiatives. FDA will track and report against these initiatives for the next five years of GDUFA II. In each year of GDUFA II, FDA may revise the list and indicate when initiatives are complete.

The initiatives are organized according to the categories of complex products described in the [GDUFA II Commitment Letter](#) and the need to develop efficient and modern generic drug review tools:

Complex active ingredients, formulations, or dosage forms

- Improve advanced analytics for characterization of chemical compositions, molecular structures and distributions in complex active ingredients
- Improve particle size, shape and surface characterization to support demonstration of therapeutic equivalence of suspended and colloidal drug products

- Establish predictive in silico, in vitro and animal studies to evaluate immunogenicity risk of formulation or impurity differences in generic products
- Develop predictive in vitro bioequivalence (BE) methods for long-acting injectables
- Develop better methods for evaluating abuse deterrence of generic solid oral opioid products, including in vitro alternatives to in vivo nasal studies

Complex routes of delivery

- Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)
- Expand characterization-based bioequivalence (BE) methods across all topical dermatological products
- Expand characterization-based BE methods across all ophthalmic products
- Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) clinical endpoint BE studies for inhaled corticosteroids
- Develop alternatives to clinical endpoint BE studies for locally-acting nasal products

Complex drug-device combinations

- Evaluate the impact of identified differences in the user-interface on the substitutability of generic drug-device combination products

Tools and methodologies for BE and substitutability evaluation

- Improve quantitative pharmacology and bioequivalence trial simulation to optimize design of BE studies for complex generic drug products
- Integrate predictive dissolution, PBPK and PK/Pharmacodynamic (PD) models for decision making about generic drug bioequivalence standards
- Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System of Class 3 bio-waivers to non-Q2 (quantitatively inequivalent) formulations
- Develop methods that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution and utilization patterns and drug safety and quality data) for decisions related to generic drug approval and post-market surveillance of generic drug substitution