FDA Issues Draft Guidance on Injectors

By Michael Gross, PhD, RAC

On 26 April 2009, the US Food and Drug Administration (FDA) released for comment, Draft Guidance for Industry and FDA Staff: Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products. The document—prepared by the Office of Combination Products in conjunction with the Center for Devices and Radiological Health, the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research—reflects FDA's current thinking on the development and registration of a variety of prefilled and unfilled injection devices including jet injectors, pen injectors, needle-free injectors, mechanically operated injectors and injectors with computerized or electronic elements. It also covers piston syringes.

The draft guidance pertains to injectors intended for standalone, general use, as well as prefilled and unfilled single-use and multi-use injectors that may be used with a class of drugs or biologics and those intended for use with a specific drug or biologic. It also pertains to injectors that are constituent parts of single-use, kit or cross-labeled combination products. In addition, the draft guidance addresses safety accessories associated with the use of these injectors.

Injectors may be subject to different regulatory provisions depending upon their intended use, technological characteristics, proposed labeling and packaging. Many are intended for use with a variety of drugs and biologics and are marketed as standalone, general-purpose devices. Often, these are marketed under a premarket notification clearance (i.e., a 510(k)) but occasionally an injector may require a Premarket Approval Application (PMA). Other injectors may be intended for use with a specific drug or biologic and may be prefilled or co-packaged with a drug or biological product, or separately provided with mutually conforming labeling. These are combination products according to 21 CFR 3.2(e). A single marketing application (i.e., New Drug Application (NDA) or Biologic License Application (BLA)) may be sufficient for these products, but under certain circumstances two applications may be submitted (i.e., an NDA or a BLA and a device submission, usually a 510(k)). The draft guidance explains how NDAs and BLAs that follow the Common Technical Document (CTD) format may include device information within a single application. It also discusses the utility of including device product codes in NDAs and BLAs. With respect to standalone injectors cleared under a 510(k), the draft guidance discusses various 510(k) application options that may be used for premarket notification and notification of device modifications.

Detailed guidance is included on the format and content of marketing applications and how they may be structured. It suggests that the device information contained in an NDA or BLA should follow the content in a 510(k) application, although in this context this information is not used to establish substantial equivalence. The draft guidance suggests that in order to include information in an NDA or BLA application about an injector that has been previously cleared under a 510(k), a letter of authorization to reference information in the 510(k) application may be needed. The draft guidance also recommends that labeling be developed with the user in mind. A long list of elements that may be included in the content of injector labeling is outlined.

Scientific and technical advice on injector development, including preclinical, clinical and human factors testing, and studies of biocompatibility, leachables-extractables, shelf life, functionality, suitability, container closure integrity testing and sterility assurance, is provided. The draft guidance points out the importance of considering human factors in design control

and risk management activities conducted during device development. Regardless of whether a device is developed as a stand-alone injector or intended for use with a specific drug or biological product, the draft guidance notes that, depending upon the intended use population or environmental conditions, the injector design may need to consider human factors that would affect its safety or effectiveness.

The draft guidance addresses the important issue of how to conduct stability studies on injectors containing drug or biological products. It also recommends specific injector performance testing data that should be included in applications and how such studies should be conducted when injectors are prefilled. The draft guidance provides advice on cross-contamination testing of multi-use nozzle jet injectors, which have the potential to transmit disease when blood contamination of the fluid path or injectable product occurs during a previous injection. It recommends against developing injectors that require between-use cleaning of any component in or around the fluid path.

FDA is now accepting comments on the draft guidance. To ensure comments are considered before the draft is finalized, they should be submitted no later than 27 July 2009. Comments should be submitted in writing to the Division of Dockets Management (HFA305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852 or electronically to www.regulations.gov.

Author
Michael Gross, PhD, RAC, is a senior consultant with the Biologics Consulting Group (www.bcg-usa.com), specializing in quality, regulatory and technical issues for combination products. Over his 30-year career, he has worked for FDA and for drug, biological product and medical device manufacturers. Gross has spent more than 20 years working on combination product problems. He can be reached at mgross@bcg-usa.com.