

## **CPC Injector Systems Working Group**

### **Questions Outlining Goals and Top Issues**

#### **Introduction**

The purpose of the meeting is to discuss key regulatory and technical issues with respect to pre-filled injector systems, including autoinjectors and other advanced injection technologies (“injectors”). Industry believes that any regulatory guidance and review policies applicable to injectors should be developed with input and agreement from all relevant parties within FDA -- including the Centers to ensure consistent expectation and application of requirements during the regulatory review process. Additionally, existing guidance applicable to injectors should be applied consistently across Centers in their current form or should be updated, if necessary, to ensure all Centers are in agreement with the current available guidelines.

FDA feedback on key issues has sometimes been inconsistent over time and across CDER divisions, and sometimes appears not to include CDRH participation and/or input at the appropriate times during development or during the review process. In addition, device development concepts and terminology are not always communicated with clarity in FDA feedback. As an example, CDER has sometimes requested “ease of use” testing be performed on injectors. Although this “ease of use” testing is commonly understood to be a form of human factors testing, this terminology may not convey FDA expectations clearly since it is not used in the current draft human factors and usability engineering guidance or by CDRH. Further, the value of “ease of use” studies is not clear when considering that the objective of human factor studies is to ultimately test the device under realistic conditions to demonstrate the risk of user error has been appropriately mitigated by the design of the device. Therefore, greater clarity in FDA requirements and feedback that would distinguish or define particular “ease of use” testing, “use experience” in clinical trials, and formal human factors studies, is desired.

While we envision the majority of applicable current and future guidance to be driven by OCP, as new guidance applicable to injectors is developed, input and sign-off should be sought from all of the Centers to ensure consistent application. Additionally, the CPC proposes that the relevant Centers to work with OCP to promulgate a glossary of terms, testing and study expectations that would be common to all drug/biologic products, and the available regulatory pathways for most injector products to ensure consistent policy, terminology, and feedback across Centers. This guidance could be made publicly available on OCP’s FAQs webpage or as written draft guidance.

Below are key issues that CPC proposes for discussion at the June 21, 2012 meeting. We recognize that FDA will not be able to address all of these issues now without internal, inter-center deliberation, but we hope that initial feedback and dialog on some of them will be fruitful. Some of these topics (e.g., clinical study requirements) have been more comprehensively addressed in our prior CPC Clinical Trial Q&A document of May 14, 2012, (attached) and we have included some of these topics below for consideration of any early feedback that FDA may be able to provide at this time, specifically as it relates to injectors.

## Key Issues

- Bridging Strategies for presentation switches
  - Applicable data requirements
  - Application requirements
- Human Factors Studies
  - When are they required
  - Use in supporting promotional claims
- Coordination between centers
  - Timing with respect to submission review, specifically, timing of labeling review by non-primary Centers
  - Guidance development
- Submission requirements
  - Post-approval changes to combination products
  - Evaluation of submission types for generic drugs marketed in an injector (e.g., 505(b)(1) vs. 505(b)(2) vs. ANDA)
- Consistency between FDA’s Technical Guidance for Injectors and ISO standards including the 11608 series
- Analytical release testing requirements for the combination product (e.g., functional testing requirements)
- Consistent application of FDA and ICH guidance allowing fulfillment of chemical/drug stability requirements of “bare” container closure when injector/device does not provide additional protection.

## Sample Questions

### **A. Data Requirements (These items are with reference to the CPC Clinical Trial Q&A document)**

1. After reviewing the CPC Clinical Trial Q&A document, can FDA now share, more specifically, its current thinking on the kinds of bridging strategies that it expects to see to support the safety and efficacy of a follow-on injector presentation to an injector that was previously developed as a pre-filled syringe presentation?
2. What are the basic principles companies need to address when switching presentations (i.e., from a prefilled syringe to an injector, or between injectors)?
  - i. Should industry analyze clinical, technical and other requirements differently (full studies versus bridging studies) if the product in development represents a switch in presentations?
  - ii. If so, how should these different requirements should be analyzed?
3. What are the medical/scientific concerns that have led FDA to conclude that a bioequivalence study or PK comparability study must be performed when:
  - i. there is a change in the delivery presentation without a change in route of administration (e.g., from a pre-filled syringe to auto-injector both with subcutaneous routes of administration; from a vial and syringe to auto-injector both with intramuscular routes of administration and the needle gage and length are unchanged)

*or*

- ii. A different drug constituent part is used with an established delivery system (e.g., approved combination product of drug 1 in injector “X” to and NDA/BLA-approved drug 2 in auto-injector “X”)?
- iii. Are there data (other than results from a bioequivalence or PK study) that could be presented to FDA to address these concerns?

## **B. Submission Requirements**

1. Can OCP provide an update on the status of its efforts to develop a guidance on post approval changes to combination products or comment specifically with respect to injectors, when a change occurs in the constituent part with a secondary mode of action?
  - i. In the context of minor modifications to an injector’s design that may or may not be encompassed in the NDA/BLA text, are 510(k)-analogous approaches appropriate?
  - ii. Does FDA have consistent interpretations of the change supplement regulations (e.g., CBE, CBE 30, AR, PAS) that would generally apply to injector modifications based on historical supplement reviews and typical injector change categories?
2. Are there any circumstances when a presentation switch (approved injector to a new injector) should be submitted as an original NDA or BLA as opposed to an sNDA or sBLA?

## **C. Human factors**

1. When is human factors testing of an injector not required for marketing approval?
  - i. If the injector is approved and in commercial use with a similar drug in a similar user population, is it possible to leverage existing human factor data?
2. Is a risk analysis/justification as suggested in human factors guidance an appropriate approach to address the regulatory risk that minor differences in an injector studied in design validation, in clinical trials (as the future marketed product), or in various stages of human factors iterative studies, would not be accepted as a “representative product” where the differences are not likely to, or only theoretically could, impact usability, and/or would not be apparent to the user?
3. When is it permissible to include usability statements obtained from human factors testing in promotional claims?
4. Does FDA agree that simulated use studies where the activities are not “interventional” (participants do not inject a drug or insert a needle into their skin) are non-clinical research and development (R&D) studies of the device function and NOT clinical studies of the device or drug under the current regulatory schemes (not subject to Parts 812 or 312)?