PDA Headquarters
Bethesda Towers
4350 East West Highway
Suite 150
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-0296
www.pda.org

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Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Reference: Draft Guidance for Industry and Food and Drug Administration Staff: *Technical Considerations for Pen, Jet, and Related Injectors Intended for Use With Drugs and Biological Products*; Federal Dockets Management System Docket FDA-2009-D-0179

Dear Sir/Madam:

PDA is pleased to offer comments on the document titled "Draft Guidance for Industry and Food and Drug Administration Staff: Technical Considerations for Pen, Jet, and Related Injectors Intended for Use With Drugs and Biological Products". PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments were prepared by a committee of experts with experience in injector and combination product issues, including members representing our Combination Products Interest Group and our Biotechnology Advisory Board and Regulatory Affairs and Quality Committee. PDA appreciates the opportunity to offer comments on this Draft Guidance and wishes to thank FDA for the opportunity to do so.

PDA embraces this document as a significant step forward in addressing industry questions and concerns associated with Injectors and assuring these products are safe and effective. PDA applauds this interagency effort which seeks to clarify the requirements associated with development of regulatory submissions associated with various injector types and the unique challenges associated with these products. PDA is willing to offer any possible assistance to FDA and indeed to any of the agencies involved in this effort in furthering these important concepts and recommendations.

With regard to the draft guidance document, we have provided detailed comments identified by line number and have included a supporting rationale in the accompanying table. In addition to the comments provided in the attached document, the following comments represent overall points noted throughout the Guidance that PDA believes are important to address in order to strengthen this guidance document and improve the ability of manufacturers to comply with its recommendations:

- The scope of the Guidance appears to be quite broad and comprehensive. However, the guidance offered on the various topics does not clearly identify the appropriate scope or situations in which these recommendations are applicable. For example:

    - Lines 239-272 regarding the section titled "Comparison to an Existing Delivery Method," include a broad and extensive list of attributes to include in this comparison, but do not clarify that some of the attributes would not be applicable to certain Injector types. We believe that the current content and format may cause confusion in interpretation by manufacturers and recommend that FDA generate a table or matrix that clearly identifies the various Injector types and the attributes that apply to each Injector type.

    - Line 610 regarding the section titled "Dose Accuracy" indicates that multi-dose injectors should confirm that subsequent doses are same as initial dose, but does not acknowledge that ISO 11608 requirements should apply for dose accuracy associated with Pen Injectors. We recommend that the ISO 11608 standard and associated scope of its usage be included in other sections of the Guidance, such as line 443.

    - Line 104-230, regarding the section titled "Injector Description" does not clearly identify which Injector types or situations would be associated with the recommendations of this section. We again recommend that FDA generate a table or matrix to clarify the recommendations as they apply to the unique Injector types, taking into consideration the Injector types in recognized consensus standards. We also recommend explaining how the terms "product class" and "product line" apply to these Injector types.

- As an overall comment, PDA believes that the current Guidance document is not formatted or written in a manner in which the manufacturer can clearly identify which recommendations apply to their specific situation and recommends that FDA consider further clarification throughout the Guidance. We further recommend that language be added to the scope that, in situations in which ISO 11608 standard requirements do not align with this Guidance, the standard will take precedence over this Guidance.

- During our review the PDA committee also noticed that the standards identified in lines 771 and elsewhere are not the versions currently listed as FDA recognized standards. To prevent confusion it would be beneficial to link the guidance document to the current revisions while also taking under consideration the addition of other applicable standards associated with sterilization and packaging or performance such as ISO 17665, ISO 10993, and ISO 11137.

Again, PDA appreciates the opportunity to comment on this draft Guidance document and provides these recommendations for your consideration. PDA believes that these comments will clarify and strengthen the Guidance document to better serve the needs of both regulators and industry.

We would be pleased to offer our expertise in a public discussion and/or meeting with FDA to provide clarification of our comments. Should you wish to pursue that opportunity, or if there are any other questions, please do not hesitate to contact me.

Sincerely,

Richard V. Levy, Ph. D.
Senior Vice President, Scientific and Regulatory Affairs, PDA

Enc: Pen Ink Injector Guidance Commentary

cc: Robert L. Dana, PDA
Lisa Hornback; Hornback Consulting

PDA Comments: Draft Guidance for Industry and Food and Drug Administration Staff: Technical Considerations for Pen, Jet, and Related Injectors Intended for Use With Drugs and Biological Products

Line Number	Comment/Rationale	Suggested Revision
25 - 27	It is unclear whether this guidance document supersedes the document titled *"Guidance on the Content of Premarket Notification [510(k)] Submissions for Piston Syringes."* The remainder of this guidance does not appear to specifically address piston syringes.	Guidance should indicate that this document does not apply to unfilled piston syringes, which are covered under existing document titled "Content of Premarket Notification [510(k)] Submissions for Piston Syringes."
120	The patient population is part of the description of the medicinal product	Delete this requirement and refer to the medicinal product labeling instead
174 - 179	Injectors which are designed according to ISO 11608-1 have no direct contact to the medicinal product. Therefore compatibility of the injector materials with the medicinal product is not applicable. See lines 664 et al. for appropriate testing of container closure systems.	Precede to 174-179: "The following items need to be fulfilled for any direct product contact materials"
239	The guidance suggests including information on comparison to existing devices. This should only be required for 510(k) injectors. It asks for a detailed and comprehensive comparison table. This is not consistent with the least burdensome statement at the beginning of the document.	Add clarification regarding types of submissions in which this comparison table is required. Recommend that this requirement only be extended to 510(k).
282	PDA does not believe all changes to injector are necessarily major changes. The level of detail in B.2 is too detailed for this document and should be addressed in separate combination products guidance document on the subject.	Remove section B.2 or provide a general guidance document on combination products which indicates whether 510(k) guidance is applicable to combination products. Add reference to the document titled "Deciding When to Submit a 510(k) for a Change to an Existing Device."
334 - 347	There are two types of graduation marks: - graduation marks for the dose setting - graduation marks as indicators for information only It is recommended to base the validation requirements on the type of graduation mark	Recommendation to align the definitions with ISO 11608-1: "3.10: Indicator: means by which the amount of preset dose is shown. 3.11 Residual scale: graduated scale which indicates the remainder on medicinal product in the cartridge" The submission should include validation of the accuracy of the dose setting markings (preset dose).

Line Number	Comment/Rationale	Suggested Revision
406	The level of detail requested about the materials is overly burdensome for all materials of construction – a material change to an external part would not be expected to have a substantial impact on the device performance. Likewise, some materials are well characterized and might be easily interchangeable even in parts of the device that drive dose accuracy and therefore could be changed without notification, given use of design control systems. The level of detail should be commensurate with outcome of the risk analysis process, i.e., parts identified to have a high potential to create a hazardous situation should be more tightly controlled and potentially included in the submission. Again the CDRH guidance documents should be used to assist in evaluating when such a material change should be considered significant particularly when the information is in the drug NDA.	Suggest modify line 410 to read "Specifically for critical components, the submission should provide the..." Also recommend that "brand name" be removed from Line 411.
417 - 441	Injectors which are designed according to ISO 11608-1 have no direct contact to the medicinal product. Therefore testing of interactions of the injector materials with the medicinal product is not applicable. See lines 664 et al. for appropriate testing of container closure systems.	Clarification regarding for which type of injector this requirement is applicable is recommended.
508 - 539	Stability studies for combination products are typically conducted with final assembled product (injector with the drug/biological product). The rationale for stability testing of the injector alone is not clear. Functional testing with the injector alone is not possible.	Remove "For stability and expiration dating, the testing should consider the injector alone and the injector with the drug/biological product. For the injector alone, the data should demonstrate that the injector can be reliably and reproducibly used for the labeled number of injections." Add: “For stability and expiration dating, the testing should consider the injector with the drug biological product.”