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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: **Docket No. 01D-0221**, Draft Guidance For Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components.

PDA is pleased to provide these comments on the Draft Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components. PDA is an international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical manufacturing and quality. Our comments were prepared by a committee of experts in this field.

The committee felt that the document would be more useful if it contained more guidance on situations where there is shared licensing and manufacturing. It was also felt that additional examples would help clarify the requirements.

If you have any questions regarding our comments, or how we may assist with further development of the Guidance, please contact me.

Sincerely,

Edmund M. Fry
President
fry@pda.org

Attachment: PDA comments on the FDA Draft Guidance for Industry, Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components.

01D-0221 C5

PDA Comments

Guidance for Industry: Biological Product Deviation Reporting of Licensed Manufacturers of Biological Products Other than Blood and Blood Components

Draft Guidance – August 2001

Docket No. 01D-0221, CBER 200036

Page Number of PDF Guidance Document	Section Title/Description	Comment/Recommendation for Revision
Page 2	II. Background 3rd paragraph	1) These bullet items are not directly stated in the referenced regulations.
Page 2	III. Guidance A) WHO MUST REPORT?	1) Definition of "control" does not specifically address the expectations for partners in a shared manufacturing arrangement for products other than blood and blood components. Specifically, if the deviation were to occur in the plant/process used by the manufacturer of the bulk product for further manufacturing use (and separately/partially licensed as such); it is not clear who is expected to be in "control" (and report as per 600.14) at this intermediate, yet partially licensed stage. It is recommended that the Guidance further define instances where one or both parties are required to report.
		2) This section should include examples that are more relevant to non-blood products, as per the title of the guidance. For example, a manufacturer that receives 2 or 3 components from another manufacturer that is partially licensed (under shared manufacturing; not as a final stage contractor) to manufacture the components through the bulk stage ("For Further Manufacturing Use") in partnership with another manufacturer who manufactures 1-2 additional critical components and formulates and fills all components into the final product (under final license). 3) SEE ALSO COMMENT ON PAGE 4 of this table (part IIIC of the Guidance – regarding timeframes for reporting in Shared Manufacturing Arrangements

PDA Comments

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Page 7	III.C. Flowchart Question 1: Was the event associated with the "manufacturing"?	1) The term manufacturing is defined on page 9, yet on page 17, Section IV.F., distribution of product prior to completion of review/approval of a supplement (PAS or CBE-30) under 21 CFR 601.12 is also cause for reporting of a BPDR. An actual deviation in manufacturing is not really the root cause for the reporting as per 21 600.14 in this case. Therefore, in this instance, one could answer "No" to the first question in the flow chart. There should also be a branch from question 1 (or question 1a) that leads to a question regarding the approval status of any supplement affecting the manufacture of the product.
Page 12	III.C. WHEN DO I REPORT?	1) Though contract manufacturers are addressed, the document does not address the time period for reporting under a "Shared Manufacturing" arrangement. If the license holder for the final product receives a partially licensed bulk component (licensed for "Further Manufacturing Use") under a Shared Manufacturing Arrangement, and there is a deviation identified in the manufacture of the bulk component after the affected final product is distributed; when does the time "clock" (45 days) for reporting of the deviation by the final license holder begin (if this is required)? It should be made clear in the Guidance that in a shared manufacturing arrangement, if the final license holder is required to report a deviation that occurs at the partial license holder, that the 45 day period begins when the final license holder is notified.

PDA Comments

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Page 14	IV.A. DO NOT REPORT:	1) First bullet: the statement "Material does not meet specifications and is rejected or not used in manufacturing" should read: "Material does not meet specifications and is rejected and is not used in manufacturing."
Page 14, 15 & 16	IV.B., C. & E.	1) Actual examples of non-reportable deviations and events should be included for PROCESS CONTROLS, TESTING and PRODUCT SPECIFICATIONS categories. 2) E. Product Specifications: The statement "Stability Testing failed during the labeled dating period" needs clarification. Does this apply to stability studies that may be conducted under any conditions (e.g. room temperature, freeze/thaw, etc.) or just to labeled temperature storage conditions?
Page 17	IV.F.	1) The abbreviations PAS and CBE should be defined. A distinction should be drawn between the CBE and CBE-30 and the term CBE-30 should replace CBE in the phrase "…less than 30 days after the submission of the CBE supplement" (3rd bullet). 2) "Outdated product" should be revised to read: "Product outdated at the time of distribution" (6th bullet).

General Comments Specific to Reporting of Biological Product Deviations

Page Number of PDF Guidance Document	Section Title/Description	Comment/Recommendation for Revision
NA	General Recommendations for BPDR General Instructions (Reporting Form FDA 3486)	1) It would be helpful if the FDA could list the registration numbers for licensed biological product manufacturers on the CBER Web Site (or make them otherwise readily available), as this number is required on the BPDR form and many manufacturers do not routinely use this number for regulatory submissions
		2) FDA should add a category that allows for reporting of instances when all affected product lots have been distributed and that none remain in the market (i.e. consumption tracking data projects that all doses would have been used by a certain date, and therefore are no longer on the market).
NA	General Recommendation for Electronic Submission	1) There is insufficient space in the electronic field to describe the deviation and root cause investigations. Additional characters should be allowed for these sections. The restriction to 999 characters prevents the inclusion of relevant supporting data and critical background information. Alternatively, the electronic format could allow for the attachment of an amendment or appendix for additional information.