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Incorporating Medical Device Information in to CTD/eCTD Module 3 for a Drug-Device Combination Product

In September 2016 CDER and CBER released a revised eCTD Technical Conformance Guide (http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM465411.pdf) containing technical recommendations on eCTD applications. As was the case for the previous version, the Guide does not establish FDA policy rather it explains FDA's current thinking about the format of eCTD applications.

The Guide generally recommends that for a drug delivery device or pre-filled drug delivery system, device constituent part product information and related engineering and manufacturing information should be located in the same eCTD sections that would provide similar information for the drug or biological product alone.

As the result of pharmaceutical industry push-back funneled through the Office of Combination Products, the previously stated recommendation of not using eCTD section 3.2.R for device constituent part information has changed to now allow supportive information for device constituent parts for functional container closure systems (e.g., drug delivery device) to be located in section 3.2.R. For other types of combination products, information about device constituent parts which would not have a logical location within section 3.2.P should also be placed in section 3.2.R.

Quality system compliance information for the combination product as a whole should be located in 3.2.P (with appropriate hyperlinks to section 3.2.R). For drug delivery devices and prefilled systems, the Guide recommends describing how compliance with the Management Responsibility, Design Controls, Purchasing Controls and CAPA requirements of 21CFR820 is achieved. 3.2.P.7 can continue to be used for devices that serve as primary or secondary container closure. This section may link to section 3.2.R as appropriate for device constituent testing. Section 3.2.R Regional Information. 3.2.R may be used for device engineering design documentation are not otherwise provided in Section 3.2.P.7, such as design Inputs, design outputs, design verification plan and summary report and supporting data, the risk management file and the traceability matrix. For a drug delivery device or prefilled drug delivery system certain 3.2.P elements may repeat for the drug product and the entire combination product.

A reviewer's guide should be provided in section 1.2 following the application cover letter. It should provide a high-level overview (with reference links) of the submission's content and should list the location of information in the eCTD. It should identify the location of information that cannot be further identified by the standard eCTD titles and numbering.

The industry was unsuccessful in convincing FDA to change the its recommendation on the location of human factors information. The Guide currently recommends that combination product human factors validation study results be located section 5.3.5.4, with links from Module 3. This is not a desirable outcome since some concern exists in industry that by classifying human factors studies as clinical studies for the purpose of formatting an eCTD, in the future such studies could become subject to user fees and GCP requirements. But keep in mind that this is only a recommendation and not policy; deviation from this recommendation should be worked out with the reviewing CDER or CBER division.

Other recommendations in the revised Guide regarding combination products are as follows:

Adhere to eCTD headings as defined in the FDA technical specification C*omprehensive Table of Contents Headings and Hierarchy*. Adhere to ICH and FDA eCTD heading specifications. Numbered eCTD/CTD titles should not change. “Node extensions" should not be used to create new elements. In 3.2.R, new leaf titles should also not be used. Instead, identify device information should be identified with the prefix, DEVICE.

Form 356h should identify all facilities involved in the manufacture and testing of the combination product and its constituent parts. Section 3.2.P.3 should include device constituent part information pertaining to manufacturing and/or assembly of the finished combination product, as a whole. This section may hyperlink to device constituent manufacturing information in 3.2.R.

3.2.P.3.1 should identify the type of manufacturing and testing activities that occur at each facility. For each facility subject to 21 CFR part 4, identity if it follows a combination product streamlined quality system approach and identify the quality system platform upon which the streamlined system is based (i.e., cGMP or QSR).