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Request for Comment--Docket No. 01D-0262: Guidance for FDA Reviewers: Premarket Notification Submissions for Automated Testing Instruments Used in Blood Establishments

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

To Whom It May Concern:

Enclosed, please find comments for the above referenced docket number from Olympus America Inc. and Olympus Optical Co, Ltd. Tokyo, JAPAN for the proposed guidance document regarding premarket notification submissions for automated testing instruments used in blood establishments.

The Olympus organization is a manufacturer of automated instruments used in blood establishments. Since 1988, Olympus has manufactured automated instruments used in blood establishments for ABO/Rh and infectious disease screening. Currently, more than 90% of North America's blood supply is tested on Olympus analyzer systems.

These comments are provided in the hopes of improving the process for premarket notifications and the guidance documents that will pertain to those submissions.

Respectfully submitted,

Michael Campbell

Michael Campbell
Manager, Regulatory Affairs/Quality Assurance
Olympus America Inc.—Diagnostic Systems Group

Request for Comment--Docket No. 01D-0262: Guidance for FDA Reviewers: Premarket Notification Submissions for Automated Testing Instruments Used in Blood Establishments

Section II

1. The information listed in this guidance document is contrary to the stated purpose of a 510(k) premarket notification submission as presented in the background section. This section indicates that the purpose of a 510(k), as detailed in 21 CFR part 807 is to demonstrate substantial equivalence to a device that is already legally marketed.

2. This guidance document further exceeds the criteria that the FDA must use to determine substantial equivalence as defined in 21 CFR part 807.100(b). This section states that the FDA must use the information provided by a manufacturer, in that it requires more information than the evidence that a device is as safe and effective as a legally marketed device.

Section III

3. **Part A**-This part states that the information should include the software version number. The software version information is not a part of the information required in 21 CFR part 807.87(a) and should not be required if it is not normally referred to in the actual name of the device. Software versions are revised from time to time due to "bug" corrections that do not exceed the threshold of a subsequent 510(k) submission and as such, may not remain the same as the version number cited in the premarket notification, while still meeting the legal obligations of the premarket notification regulations.

4. **Part G**-The requirement for including a 510(k) statement or summary is codified in 21 CFR part 807.87(h) instead of 21 CFR part 807.92(a)(3).

Part J-

5. Item #1-The information separately required in this item is the same as the information included in section E item 4 that is sufficient to describe the devices operating characteristics, etc. This separate requirement of the same information in a differing format is a duplicitous requirement that is contrary to the Least Burdensome provisions of FDAMA.

6. Item #2-The requirement for a listing of all of the functions that are controlled by software represents an overly burdensome requirement when the fact that the topic of the submission is for an AUTOMATED SYSTEM. This full and detailed list exceeds the requirement that the agency's review focus on the information directly **relevant** to supporting the substantial equivalence (the determinant in a 510(k) submission) of the medical device. A more realistic and useful listing would be the items not controlled by the software.

7. Item #3-This item is too broad in its construction to provide any guidance on the actual information needed to fulfill the substantial equivalence determination. In addition, the detail required exceeds the information relevant to the determination of substantial equivalence. Based on the interpretation of this section, a control material selected by the operator of the system would be considered a limitation of the medical device. This information of the materials required but not provided is already required in the labeling of the device. In addition, proper selection of materials for control are the validation responsibility of the blood bank manufacturing process.

8. Item #5-This information is already required in the description of the operation of the instrument as it is relative to the substantial equivalence. Additionally, this information is conducted during the design phase risk analysis and validation as required by Quality System regulations. The requirement of this information in a 510(k) submission exceeds the information that is relevant to supporting the substantial equivalence of a medical device, which is the purpose of a 510(k) submission.

9. Item #6-The assembly of a matrix of cross references for all functional requirements to the appropriate design specifications is essentially an index of the entire design process and clearly represents information that, if required during the submission of a premarket notification, completely ignores the language and intent of the least burdensome regulation of FDAMA. The validation protocol and results of the validation activities (as submitted in the 510(k)) provides sufficient information to demonstrate the substantial equivalence as well as proper performance of the functional requirements.

Section K

10. Item #2-Providing a full description of all hardware components, their performance characteristics, and specifications is an overly burdensome requirement that exceeds the intended purpose of a 510(k) review for determination of substantial equivalence. Additionally, this contradicts the requirement that the Secretary "**shall** consider whether data required for approval of an application can be reduced through

postmarket controls" (FDAMA section 205(C)). The Quality System regulation requirements of maintaining Device Master records (21 CFR part 820.181) is an adequate postmarket control to fully define the hardware of a system.

11. Item #5-Given the expected life of an automated instrument and the specific listing of required information presented in this section (as applicable), a sequential numbering process for every page printed over the life of the instrument can serve no useful purpose in demonstrating for reviewers the substantial equivalence of a device. In addition, this sequential number would serve no purpose for operators given the presentation of actual identifying information relevant to the printout being created.

12. Item #5-The requirement for a run valid/invalid determination to be generated on printed pages does not consider the method for printing. Prints that are not generated in a batch process (i.e.; generated as a data point is read or interpreted) cannot be assessed as valid until all appropriate pre and post operation controls and safeguards are performed. Also, the determination of the validity of test results is based on multiple factors that cannot be assessed until after operation is complete and the operator has reviewed the printouts and compared the results with the visual evaluation of the samples.

13. Item #5-Requiring all of the information on each page of a printout does not consider that the test method for some instruments is more of a modular process in that some pages contain the control information for the test run and some pages contain the actual test information for the samples. All of the pages together comprise the test run and each page, when considered independently from the total set of printouts for the run, is meaningless.

14. Item #6-The instrument is used in the manufacturing process of the blood facility that operates it. As such, modifications of the instrument and or test run methodology are a portion of the manufacturing process for the operating facility and outside the control of the instrument manufacturer. As such, the audit trail for tracking these changes should be considered as a portion of the manufacturing activity and appropriately documented in the operator's change control system. Given this system to control the changes to the instrument or test methodology, this requirement in a 510(k) submission violates the requirement that the Secretary "**shall** consider whether data required for approval of an application can be reduced through postmarket controls" (FDAMA section 205(C)). In addition, the process for tracking the changes to the instrument or methodology exceeds the information necessary to determine the substantial equivalence of a medical device.

15. Item #8 a-The description of all the software components including the operating systems and databases exceeds the regulatory requirements of FDAMA section 205 (D) in that the Secretary "**shall only** request information that is necessary in making the determination of substantial equivalence" and that the Secretary "**shall** consider the least burdensome means of demonstrating substantial equivalence." The general description of the operating process of an automated medical device will include information related to the higher level software components, but the full listing of all components is neither least burdensome, nor necessary for substantial equivalence determinations.

16. Item #8 b-As written, this item requires the submission of the entire engineering schematic for the instrument to demonstrate the interfaces between the multiple printed circuit boards that make up an automated instrument. All of these interfaces are tested during the validation of the design of the instrument and are not necessary to demonstrate the substantial equivalence of a medical device. In addition, the requirement for this amount of detail exceeds the least burdensome provisions of the FDA Modernization Act.

    A more realistic and useful subset of information would be of the greatest use for reviewers. The subset of interfaces between the instrument, and accessory components, and a host system (as applicable) would provide information useful in assisting the reviewer understand the configuration of the instrument.

Section L

17. Entire Section-While there is no argument that performing an adequate Hazard Analysis is essential in the design and development process for any medical device, the requirement that this information be presented in the 510(k) submission for a medical device exceeds the information required in 21 CFR part 807 for the content of a 510(k) submission. In addition, the post market, and in fact, premarket control, of Design Control as required in 21 CFR part 820 (Quality System Regulations) serves as an adequate method to reduce the amount of information required in premarket notifications pursuant to the requirements of FDAMA section 205 (C).

18. Item #3 c-When the standard operating procedures and national or international standards used in the design and development process are outlined and referenced in the previous section, the additional requirement for providing definitions of terms is a duplicitous requirement. If a manufacturer is conducting operations inline with applicable standards, the definitions used by that manufacturer would be the same as the definitions present in the applicable standard.

19. Item #5-The presentation of the methods of controls used to eliminate or mitigate hazards in this section has been previously required in section J5 of this guidance document.

20. Item #6-A full trace of the control methods to the design specifications, as well as the items of the design verification, validation, and testing, is an excessive matrix document that serves no purpose in the determination of substantial equivalence determinations, which are the legal focus of the premarket notification review. This information and linkage is present in the Design History File of a medical device. Additionally, it is reviewed during the Design Review process and the legal responsibility for creating and maintaining this information is a sufficient control pursuant to section 205 (C) of the FDA Modernization Act.

21. Example Hazard Analysis Table-See comment # 20 concerning column heading "Trace".

Section M

22. Opening Statement for this Section-This statement is absolutely correct in that the purpose of the validation information submitted during the premarket notification review is to substantiate the labeling claims for the instrument.

23. Items 1-3-The information required in these items is not part of the information needed to substantiate the labeling claims of the instrument. This Test Plan, Populated Decision Tables and Alpha testing in the developer's environment, is used to conduct and complete the design validation activities required in 21 CFR part 820.30. The Design Control requirements for this information is a sufficient control as indicated in section 205 (C) of FDAMA and requiring the inclusion of this data in a premarket notification violates that regulatory requirement as well as the least burdensome methods for demonstrating substantial equivalence.

24. Items 1-3-Presentation of this information does not satisfy the requirements for demonstrating substantial equivalence to a legally marketed device, as such it fails to comply with the legal requirements of the FDA Modernization Act. Also, information that is not directly necessary in the determination of substantial equivalence is not required in premarket notification submissions as specified in 21 CFR part 807. The information listed in items 4 and 5 of this section is the information critical to the demonstration of substantial equivalence and should comprise the extent of the validation information required in the premarket notification for medical devices.

Section N

25. The information regarding configuration management and change control that is required in this section fails to comply with the regulations for the content of a 510(k) submission as found in 21 CFR part 807. This information is not shown as a requirement of a 510(k) in the applicable federal regulations, thus CBER has no legal standing to list this information as a requirement of a 510(k) premarket notification in this guidance document. In addition, this information is irrelevant to the information that will be necessary to determine substantial equivalence pursuant to the requirements of FDAMA section 205 (D). Furthermore, the postmarket controls of Design Change (21 CFR part 820.30 (i)), Document Controls (21 CFR part 820.40), Device Master Records (21 CFR part 820.181), and Device History Records (21 CFR part 184) are more than sufficient postmarket controls that the Secretary **must** consider in the reduction of information required in premarket notification submissions (FDAMA section 205(C)).

General Comments on the Entire Guidance Document

26. The information that CBER has proposed requiring during the review of 510(k) submissions goes beyond the legal responsibility that CBER has in regards to review of medical device 510(k) submissions. This information clearly exceeds the legal requirements of reviewing data solely for the purpose of arriving at a determination of substantial equivalence between a proposed medical device and a device that is already legally marketed. The information listed in this guidance document is clearly focused on requiring a medical device manufacturer to prove that a medical device is safe and effective instead of substantially equivalent. This is contrary to the purpose of a 510(k) as well as the intended purpose of the guidance document created.

27. By planning to require the level and degree of information proposed in this guidance document, it appears that CBER is attempting to modify the regulations for medical devices as they apply to medical devices used in blood bank establishments via promulgation of a guidance document rather than following the legal requirements for modifying federal regulations. The requirements proposed in this guidance are seeking to apply the requirements of a BLA or PMA to a medical device simply because of the operation and location of the device without any legal justification.

28. The guidance document itself serves as an ongoing example of CBER's avoidance of the implementation of the Least Burdensome provisions for the medical devices within the division's area of review. If the information listed within this guidance document is implemented, the review process for medical devices within CBER will take a dramatic step backwards in terms of review time, as well as alignment with the

device review policies implemented within CDRH. In addition, CBER, by implementing requirements for data that clearly exceed not only the least burdensome provision of FDAMA, also fail to align themselves with the substantial initiatives that CDRH has undertaken in implementing the Least Burdensome provisions of FDAMA in terms of the Interagency Collaboration portion of the FDAMA (section 414(c)).

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