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BY HAND DELIVERY

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1062 (HFA-505)
Rockville, MD 20852

Re: Additional Comments of Ethicon, Inc. in Response to Reopening of Comment Period for the Proposed Reclassification and Draft Special Controls Guidance for Absorbable Hemostats (Dockets 2006N-0362 and 2006D-0363)

The following comments, on behalf of Ethicon, Inc. ("Ethicon"), are intended to supplement our client's previous, more comprehensive comments dated January 29, 2007. Ethicon remains opposed to the reclassification of absorbable hemostats as currently described by FDA in its notice of proposed rulemaking and draft special controls guidance. Ethicon also continues to question the legal sufficiency of the notice given in FDA's proposed rulemaking documents, as well as the adequacy of the administrative record. While helpful, this thirty-day reopening of the comment period is not, in Ethicon's view, sufficient to alleviate these concerns because it did not correct the deficiencies in the administrative record or administrative file.

I. FDA Has Not Corrected Or Addressed The Deficiencies In The Docket

The agency's May 8th Federal Register notice announcing the reopening of the comment period (72 Fed. Reg. 26011) states that the decision to reopen was made in response to two requests for extension of the comment period. These extension requests were submitted more than four months ago – in December of last year, and Ethicon was one of the requesting parties. Ethicon's purpose in seeking an extension was to ensure that interested parties had sufficient opportunity to identify and address information that had been omitted from the docket, and to encourage FDA to correct the deficiencies by adding the omitted documents. FDA has not corrected these deficiencies.

2006D-0363

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In its extension request dated December 21, 2006, Ethicon identified the following omissions from the docket and from the discussion in FDA's proposal:

- Briefing materials provided to the General and Plastic Surgery Devices Panel in preparation for the 2002 and 2003 meetings, and/or prepared by FDA in connection with such meetings.
- Documentation describing and explaining the deviations in FDA's proposed draft guidance from the special control elements presented to and relied on by the Panel in recommending reclassification.
- A report discussing or a list identifying the published literature and Medical Device Reports on which FDA relied in its presentation to the 2003 Panel, as well as any analysis of published literature and MDR data generated since the 2003 Panel meeting.
- Information discussing the relevance of two post-2003 PMA approvals for absorbable hemostatic devices, one composed of an entirely new material than the products considered by the Panel in 2003.

Ethicon's January 29 comments noted the following additional omissions from the docket:

- An April 2, 2004 FDA-issued Public Health Notice concerning the risk of paralysis from use of absorbable hemostatic agents in or near bony and neural spaces.
- The November 23, 2005 letter submitted by Ethicon providing new information about the types of risks that concern surgeon-users of absorbable hemostat devices.

Besides bringing these omissions to FDA's attention in the context of the rulemaking proceeding, Ethicon through counsel also submitted a Freedom of Information Act (FOIA) request on January 3. This request asked for documents comprising the 21 C.F.R. §10.70 "administrative file," which FDA was required to compile documenting the discussions and process leading to its decision to seek reclassification of absorbable hemostatic devices. Ultimately, FDA did provide some of the missing documents in a response to the FOIA request— i.e., certain briefing materials provided to the 2002 and 2003 Panels. The agency's incomplete response to the FOIA request, however, coupled with the gaps in the administrative docket, suggests a more fundamental issue – whether FDA has even considered the relevant post-Panel information. In any event, the administrative record is still incomplete, and the

administrative file does not comply with FDA's own regulations.¹ Thus, while Ethicon appreciates FDA's providing this additional opportunity to comment, the value of this additional period is undercut by the failure to complete the record. Once again, therefore, Ethicon urges FDA to correct these deficiencies before proceeding further with the proposal to reclassify absorbable hemostatic devices.

II. The Composition Of The 2002 And 2003 Panels Was Inadequate

Ethicon's January 29 comments explained how the composition of the 2002 and 2003 Panels consulted by FDA was too narrow given the scope of surgical applications in which absorbable hemostats are routinely used. Neither Panel, for example, included any experts in specialties such as cardiovascular, neurological, ENT, trauma, transplant, orthopedic or urological surgery. The use of absorbable hemostats poses materially different risks for these specialties than the risks familiar to the Panel members in their own practices.

Publicly available procedure data and Ethicon's own research, for example, indicates that absorbable hemostatic devices are used in more than 90 percent of the approximately 800,000 laminectomy, craniotomy and spinal/cervical fusion procedures performed annually in the US; more than half of the approximately 350,000 coronary artery bypass graft and valve procedures; and approximately 80% of the approximately 250,000 vascular procedures including carotid endarterectomies, abdominal aortic aneurism graft, and femoro-popliteal arterial graft surgeries. These products are also used extensively in orthopedic, ENT, transplant and trauma surgeries, which combined account for several hundred thousand uses of these products annually in the US. These important specialty areas were not represented at the Panel meetings. The knowledge and expertise of the 2002 and 2003 Panels did not adequately encompass or reflect the experience and risks inherent with these widespread uses of absorbable hemostats.

Furthermore, as Ethicon previously stated, the Draft Special Controls differ in some significant respects from the general principles that the Panel endorsed. Therefore we believe that FDA should, in accordance with the Federal Advisory Committee Act, consult with members of the 2003 Panel to obtain feedback regarding these discrepancies. There is nothing to indicate that the Panel members who voted to recommend reclassification would have endorsed the actual Draft Special Controls Guidance that ultimately was issued.

¹ In addition to the gaps previously noted, the worksheet from the 2003 Panel is not in the record.

III. Combination Absorbable Hemostat Products Containing Thrombin Pose Additional Concerns Not Considered Or Discussed In The Proposal

Ethicon has already provided comments objecting to FDA's proposal to include hemostats containing licensed thrombin within the category of products to be reclassified, and to review all such products via the 510(k) process. There is, however, an additional concern that warrants comment. Under the proposal, FDA apparently would allow the addition of licensed thrombin to absorbable hemostatic devices without regard to the specific indications for which the thrombin product is licensed. These indications, however, may not align with the proposed indications for the hemostat component. For example, Thrombin, JMI is currently indicated "as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and venules is accessible," and at least 2 additional thrombin biological license applications (BLAs) – one a human thrombin and one recombinant-based product – are known to be currently under review by FDA. Additionally, Baxter has an approved BLA for thrombin "for further manufacturing" in relation to its FloSeal PMA, which might be subject to the proposed reclassification order. If so, the indications for this thrombin could be governed solely under the 510(k) process. This complexity is yet another reason why FDA should clarify that hemostat combination products, including those containing thrombin, will be evaluated and reviewed on a case-by-case basis according to the procedures codified in FDA's Final Rule defining the "primary mode of action" of a combination product (70 Fed. Reg. 49,848 (Aug. 25, 2005)). There should be nothing "automatic" about the classification and review pathway for absorbable hemostat combination products.

IV. Conclusion

Ethicon appreciates the additional opportunity to comment afforded by FDA's reopening of the comment period. For the reasons set forth above and in the Company's January 29, 2007 comments, Ethicon continues to believe that the proposed regulatory definition and special controls for absorbable hemostatic devices are inadequate to provide the required "reasonable assurance of safety and effectiveness" for these significant risk devices. In addition, Ethicon would again urge the agency to correct the procedural and substantive deficiencies, and reissue the proposal before proceeding further with this reclassification effort.

Respectfully submitted,



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