

P.O. Box 12888  
Reading, PA 19612

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INTERNATIONAL

October 17, 2007

2400 Bernville Road  
Reading, PA 19605

(610) 378-0131

FAX: (610) 374-5360

Division of Dockets Management (HFA-305)  
Food & Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Subject:** Teleflex Medical comments on FDA Draft Guidance: *Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents* (dated July 19, 2007)

Dear Sir/Madam:

Please find attached Teleflex Medical's comments on FDA's Draft Guidance: *Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents* (dated July 19, 2007). Teleflex Medical markets various catheters with an antimicrobial treatment under the brand name Arrow International. If you have any questions regarding our comments, please contact me using the information provided below. Thank you.

Sincerely,



Chuck Morreale  
Director, Regulatory Affairs  
Teleflex Medical, Inc.  
Phone: 484.331.3660  
Fax: 610.478.3128  
E-mail: [chuck.morreale@teleflexmedical.com](mailto:chuck.morreale@teleflexmedical.com)

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**Teleflex Medical Comments on FDA Draft Guidance:**

***Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents***

(Dated July 19, 2007)

Listed in the table below is a summary of Teleflex Medical's comments regarding this proposed guidance document:

Co mment No.	Guidance Document Location	Comment / Question
1	Page 4, Line 20	We find the use of the word "Same" as being too restrictive. We recommend "similar" or "substantially equivalent" be used.
2	Page 4, Lines 24-26	How does the Applicant know the method of application and mechanism of release of a <u>predicate</u> device as it is usually proprietary and known only to the device manufacturer?
3	Page 7, Line 17	We recommend that the "target pathogens to the genus and species level" be removed form the "Indications for Use" and re-directed to another part of the Instructions for Use.
4	Page 8, Line 7	It may be impossible to ascertain the "method to apply the antimicrobial agent to the device" from the manufacturer of a <u>predicate</u> device. This information is usually proprietary to the manufacturer and not public information.
5	Page 8, Line 19	We recommend that "minimum effective concentration (MEC)" be removed. The determination of "minimum effective concentration (MEC)" may not be appropriate to an antimicrobial agent on a medical device. Antimicrobial activity can be demonstrated without determining a "minimum effective concentration (MEC)".
6	Page 9, Lines 1-2	We are unclear of the value of the antimicrobial system formulation prior to device treatment. For example, a constituent in an antimicrobial coating solution may not remain on the device after treatment. In this example, the antimicrobial coating solution concentration will likely exceed what remains on the device following treatment.
7	Page 9, Lines 4-7	We would ask for clarification of the total quantity of antimicrobial on a device. If this total quality of antimicrobial equates to antimicrobial concentration, how should this information be stated? It is unclear if concentration should be provided by weight, by length, by area or some other descriptive parameter.
8	Page 9, Lines 22-34	We would ask for further clarification of the demonstration of antimicrobicidal activity. Is it the intention to provide evidence of effectivity against all possible organisms or to the organisms a claim of effectivity is being made. Further, might it be more reasonable to choose the most common organisms and provide evidence of effectivity.
9	Page 9, Line 37	We would ask for further clarification on the characterization of the mechanism of release.

10	Page 10, Lines 14-20	Please see comment 5 above. We would ask that “Minimum Effective Concentration (MEC)” be removed and replaced with “Effective Device Concentration (EDC)”. Please see comment 7 above.
11	Page 10, Line 18-19	We would ask for further clarification for the statement, “Measure the MEC under conditions that are consistent with clinical use of the device?” In comments 5 and 7, we have concerns over the terms “Minimum Effective Concentration (MEC)” and how this concentration is to be measured.
12	Page 10, Lines 26-28	Identifying leaching residues/substances should be applied to all medical devices as it is not confined to antimicrobial material devices, but applied to all materials.
13	Page 12, Line 29	We would ask that clarification is provided for “preconditioning of the device with body fluid” It is unclear which body fluid and can it be simulated (if an applicable model is available).
14	Page 12, Line 30	We would ask that clarification is provided to the definition of “dynamic (rather than static) environment”.
15	Page 12, Lines 34-39	Clinical isolates are usually very poorly understood and possess variable stability in storage. Therefore, their susceptibility can be quite variable. We would ask that clarification be provided for why clinical isolates are necessary for this application.
16	Page 12, Line 37	Since clinical isolates can be unstable, it is prudent to use them for only a short period of time. The amount of testing required for a premarket notification submission may not be practical or possible under the short timeframe.
17	Page 13, Lines 18-21	Many animal infection models are not well controlled nor do they model the pathogenesis of human infections accurately. We appreciate the recommendation to contact FDA for further guidance on the use of animal studies. It may assist industry with a listing of animals studies or models that may be appropriate to allow for dialogue to begin with the Agency.
18	Page 14, Line 31-26	If the antimicrobial agent is not classified as a “drug,” we recommend this portion of the labeling be omitted.
19	General Comment	Does this guidance apply to “antimicrobial” technologies that are not drug/chemical based (e.g. UV light, electrical, modified surface topology or charge)? Some of these technologies affect microbial device colonization without killing the cells. Is it still antimicrobial?
20	General Comment	If it is necessary to perform a clinical study to claim “reduce or prevent device-related infections,” what is necessary to claim reduce or prevent bacterial adherence-- <i>In vitro</i> data, <i>In vivo</i> data? Please clarify.
21	General Comment	In addition to identifying the raw material of the microbial agent (e.g. page 8), we believe it is also necessary to specify identity, purity and strength of the antimicrobial agent(s) in its final processed form on the device.

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22	General Comment	We don't believe the method of application or mechanism of release is important, as long as the microbiological efficacy is equivalent (both duration and potency), and that the rate at which the agent is released is equivalent, whether there are other inert or active molecules released along with the antimicrobial agents, and that they be released with a breadth of coverage that is sufficient to equivalently protect the vulnerable surfaces of the device. The surfaces being protected thus need to be specified and the testing methodology needs to be able to demonstrate those surfaces are protected. There is no specification about the duration of protection--this may also be important.
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