DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

0855 '03 MAR -3 A11:30 February 13, 2003

Charles H. Kyper
Kyper & Associates LLC
103 Nolen Lane
Chapel Hill, NC 27516

Re: Docket No. 01P-0389

Dear Mr. Kyper,

This responds to your citizen petition dated August 31, 2001, and filed by the Food and Drug Administration (FDA) on September 5, 2001. FDA issued an interim response on March 6, 2002.

Your petition explained that the substantial equivalence order (510(k)) clearance for an endosseous implant device was held for several months pending an inspection of the manufacturing facilities for conformance with the Quality System (QS) Regulations current Good Manufacturing Practice (cGMP) requirements. The implant was found substantially equivalent in September of 2001. Your petition, in addition to addressing the specific circumstances of that 510(k), requested that FDA take general action with respect to all pre-clearance inspections for broad categories of medical devices. As discussed below, FDA is denying your petition in part and granting it in part.

Petition

First, you requested that FDA take administrative action to revoke Compliance Program 7383.003, providing for pre-clearance inspections of manufacturing facilities for Class III devices subject to premarket notification review under section 510(k) of the Act to determine compliance with the QS Regulation and cGMP requirements, and delete the reference to this Compliance Program on page 4 of the Compliance Program Guidance Manual: Inspection of Medical Devices; Final Guidance for Industry and FDA (CP 7382.845). Second, you requested that, pending completion of these actions, FDA take immediate administrative action to discontinue all further pre-clearance inspections for Class III pre-amendments devices undergoing premarket notification review.

You state that FDA should take these actions because FDA lacks the statutory authority to conduct these programs and because these inspections are nonproductive and wasteful of limited FDA inspection resources.

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Authority for Pre-clearance Inspection Program

The preclearance inspection program for Class III preamendments devices was established in 1993 pursuant to section 513(i) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360c(i)). In 1997, Congress enacted the Food and Drug Administration Modernization Act (FDAMA) FDAMA amended section 513. Currently, under section 513(f) (5) of the Act, 21 U.S.C. 360c (f) (5), FDA is not permitted to withhold an initial classification determination for failure to comply with a provision unrelated to a substantial equivalence (SE) decision, with one exception: FDA is permitted to withhold an initial classification if the agency determines that "there is a substantial likelihood that the failure to comply with {QS/GMP} regulations potentially presents a serous risk to human health." Thus, FDA has statutory authority to withhold a classification decision in the specific circumstances set forth in section 513(f) (5).

Other provisions of law also support pre-clearance inspection to determine compliance with the QS Regulation or cGMP requirements. Section 520(f) of the Act (21 U.S.C. 360j(f)) authorizes FDA to prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation, packing, storage, and installation of a device conform to cGMP requirements. The FDA regulations implementing this provision are codified in Part 820 of Title 21 of the Code of Federal Regulations (21 CFR Part 820), known as the Quality System (QS) Regulation. Furthermore, section 704 of the Act (21 U.S.C. 374) authorizes FDA to inspect establishments in which medical devices are manufactured, processed, packed, or held.

FDA is granting your request to revoke CP 7383.003 because the CP does not accurately reflect the authority given to FDA by section 513(f) (5) of the Act, as amended by FDAMA. FDA declines, however, to grant your request to discontinue all pre-clearance inspection for Class III pre-amendment devices undergoing premarket review under section 510(k) of the Act. As explained above, under section 513(f) (5) of the Act, FDA is authorized, in the limited circumstances described in that statutory provision, to withhold an initial classification decision (i.e., 510(k) clearance) for a product based on the sponsor's failure to comply with the QSR/GMP requirements. FDA also retains the statutory authority to enforce the QS Regulation and cGMP requirements by conducting inspection of manufacturing facilities under section 704 of the Act. These provisions provide the legal authority to FDA to conduct pre-clearance inspections for Class III pre-amendment devices undergoing premarket review under section 510(k).

Conclusion

1. FDA is granting your request that the agency take administrative action to revoke Compliance Program 7383.003 and delete the reference to this Compliance Program on page 4 of the Compliance Program Guidance Manual: Inspection of Medical Devices: Final Guidance for Industry and FDA (CP 7382.845).

2 FDA will continue to conduct inspections as authorized by sections 520(f) and 704 of the Act. FDA is entitled to conduct such an inspection regardless of the classification of the device. Some of these inspections may occur while a 510(k) submission is pending before FDA. Therefore, FDA is denying your request for immediate administrative action discontinuing pre-clearance inspection.

3. Consistent with the authority provided in section 513(f)(5), FDA is authorized to withhold a classification decision for a device, if FDA determines that there is a substantial likelihood that the failure to comply with the QS Regulation or cGMP requirements for the device potentially presents a serous risk to human health FDA will use this authority when it makes the requisite finding for a specific device.

If you have any questions about this response, please call Joseph M Shechan at (301) 827-2974.

Sincerely yours,

William K. Hubbard
Associate Commissioner for Policy
and Planning