Section 207: Is Your Class III Designation Really Final?

Also known as "de novo," section 207 of FDAMA allows certain low-risk medical devices to be reclassified into Class I or Class II, thereby avoiding costly PMAs.

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ALMOST 98% OF MEDICAL DEVICES are cleared for marketing by the premarket notification or 510(k) process, making this an extremely important process for the medical device industry. According to the Medical Device Amendments of 1976, a device is cleared for marketing when it is rated "substantially equivalent" to a suitable predicate device and comparative data on the two devices is provided. The Safe Medical Devices Act of 1990 defines a *suitable predicate device* as one that is legally on the market without having been cleared via a premarket approval (PMA) review.

In general, CDRH has managed to make the substantial equivalence concept work quite well. Difficulties arise, however, when a simple, low-risk medical device submitted under a 510(k) has an unusual feature and CDRH is "unable to find" a predicate device. In this circumstance, the device is automatically declared to be Class III, requiring submission of a PMA application for market clearance. The problem with such a decision is that the preparation of a PMA application requires considerable capital, work, and other resources, including FDA resources. The cost of obtaining PMA for low-risk devices can become prohibitive because, unlike more-complex devices requiring such approval (e.g., a state-of-the-art pacemaker), the simple products are generally inexpensive.

The reclassification of the DOC Band (Cranial Technologies; Phoenix) into Class II is considered the first de novo action.

SECTION 207

FDA's concerns about the problems associated with classifying low-risk devices in Class III eventually led to section 207 of the FDA Modernization Act of 1997 (FDAMA), known as "Evaluation of Automatic Class III Designation." (The term *de novo* is also used to describe section 207; however, this usage is more common within the device industry than within FDA.) This section provides a new way for FDA to establish a Class I or Class II designation for low-risk devices, even though no predicate is available.

Section 207 is part of the risk-based regulation of medical devices propounded by CDRH director Bruce Burlington in his reengineering program.[1] According to an FDA backgrounder on the subject, the FDA Modernization Act of 1997 reinforces FDA's intent to focus its resources on medical devices that present the greatest risks to patients. Recognizing that it is not productive to require PMA for simple, low-risk devices, FDA has designated its compliance with section 207 as a priority[2] and published a guideline on the subject for the industry and CDRH staff on February 19, 1998.[3]

FDA GUIDANCE DOCUMENTS

An FDA overview of FDAMA states that an applicant who submits a premarket notification and then receives a not-substantially-equivalent (NSE) determination, placing the device into Class III, may request in writing (within 30 days) that FDA classify the product into Class I or Class II.[4] The request must include a description of the device, reasons for the recommended reclassification, and information to support the recommendation (see sidebar on page 120). Within 60 days from the date the request is submitted to FDA, the agency must classify the device by written order. A guidance document issued by CDRH is more specific, stating that "a signed order classifying the device should be sent to the requester by day sixty (60) following receipt of the request."[5] If FDA classifies the device into Class I or Class II, this device can be used as a predicate device for other 510(k)s. Within 30 days of notifying the applicant that the device has been classified into Class I or Class II, FDA will announce the final classification in the *Federal Register*. If FDA determines that the device will remain in Class III, the device cannot be distributed until the applicant has obtained approval of a PMA application or an investigational device exemption (IDE).

This law imposes a very tight timeline on FDA regarding section 207 submissions. It is unclear from the law whether a designation of Class III under this part of the act would also require a notice in the *Federal Register*. Presumably, if FDA decided the device should be left in Class III, this decision would be published in the *Federal Register* as well. The case study described below resulted in a Class II designation, so this question remains unresolved.

The CDRH guidance document covering section 207 further clarifies FDA's intent regarding the process: "While the process is new, its implementation is based on the types of information and data ordinarily submitted in 510(k)s and/or reclassification petitions."[5] The guidance further points out that the process limits its consideration to devices that have not been previously classified under the Federal Food, Drug, and Cosmetic Act and that have been relegated into Class III by written order. The guidance emphasizes that this process is available only to devices for which a request under section 513(f)(2) has been filed within 30 days after receipt of an NSE determination on a 510(k). FDA points out that an alternative to using section 207 is the filing of a reclassification petition in accordance with 21 CFR 860.134.

Admittedly, the process outlined in section 207 (Figure 1) only applies to devices for which a 510(k) has just been judged NSE, as opposed to the wider applicability of a standard reclassification petition. However, a strong argument for using the section 207 process if it applies is that it imposes a very tight time restraint on FDA. Historically, reclassification petitions are not given high priority because FDA prefers to expend its resources on activities that have obvious deadlines.

A CASE IN POINT

The authors have had firsthand experience with section 207 of FDAMA. The following case is of special interest because it was the first section 207 action completed by CDRH. The device involved was a cranial orthosis, called the DOC Band, manufactured by Cranial Technologies Inc. (Phoenix). The DOC Band was developed as an alternative to surgery for the treatment of a condition known as positional plagiocephaly, meaning deformation of the head caused by persistent positioning in one orientation. Until recently, this deformity was confused with a similar condition known as craniosynostosis, which is a premature fusion of one or more sutures of the skull. Incidences of positional plagiocephaly have been increasing steadily since 1992, when the American Academy of Pediatrics recommended that infants sleep on their backs to reduce the risk of sudden infant death syndrome (SIDS).[6] Whereas true craniosynostosis requires surgical intervention, surgery is rarely required for positional plagiocephaly. However, because of the lack of alternatives, cranial vault remodeling surgery was often performed on children who had positional plagiocephaly.

In order to manufacture the cranial orthosis, the manufacturer obtains a model of the infant's cranium by taking a cast of the head and then filling this negative mold with plaster of paris. The device is then formed around this model once certain refinements are made. The device works by applying a mild dynamic pressure to the prominent aspects of the infant's head, restricting growth in those directions while encouraging growth in adjacent, flattened areas.[7] In a sense, the head is being persuaded to grow into a more symmetrical shape.

The 510(k) Submission. In the original submission of a

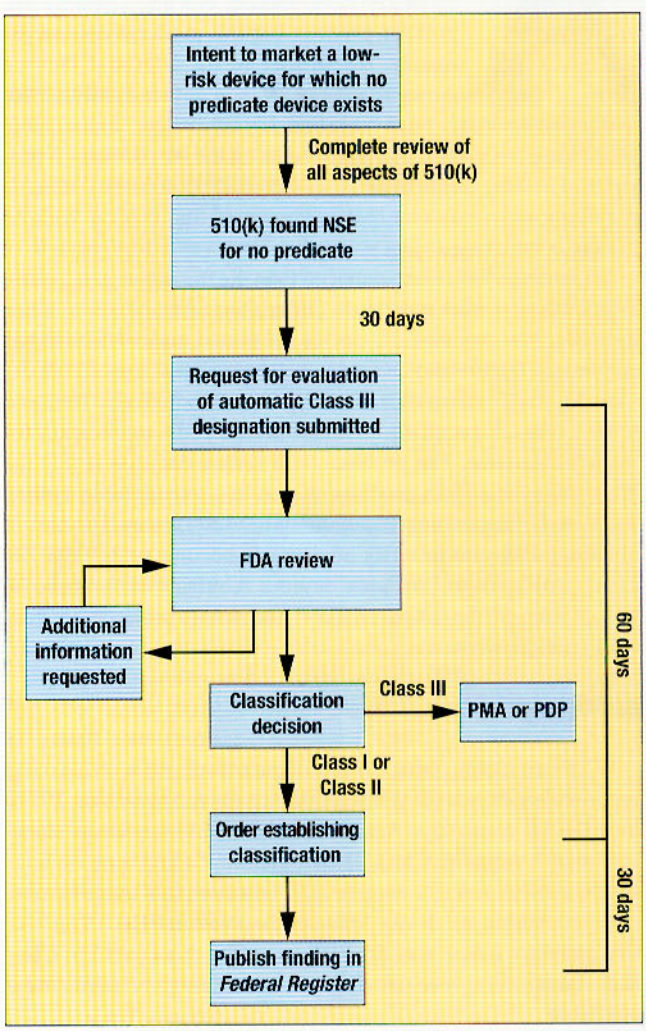

Figure 1. Flowchart titled Evaluation of Automatic Class III Designation Process.[5]

REQUEST FOR EVALUATION OF AUTOMATIC CLASS III DESIGNATION[5]

In order to facilitate review, the request for Evaluation of Automatic Class III Designation should include the following information:

- A coversheet clearly identifying the submission as "Request for Evaluation of Automatic Class III Designation" under 513(f)(2).
- The 510(k) number under which the device was found to be not substantially equivalent.
- A statement of cross-reference to the information contained in the 510(k).
- The classification being recommended under section 513 of the act.
- A discussion of the potential benefits of the device compared to the potential or anticipated risks when the device is used as intended.
- A complete discussion of the proposed general and/or special controls to ensure reasonable assurance of the safety and effectiveness of the device, including whether the product should be exempt from premarket review under section 510(k), whether design controls should be applicable, and what special controls would allow the agency to conclude the device was reasonably likely to be safe and effective for its intended use.
- Any clinical or preclinical data not included in the 510(k) that is relevant to the request.

premarket notification for this device on December 16, 1996, Cranial Technologies carefully tried to draw substantial equivalence to the Boston Body Jacket, a device that is used in much the same way to correct scoliosis. Although the jacket is used on the chest, the technology is the same: the manufacturer forms a cast and then creates an orthosis from the cast to encourage the body toward a more symmetrical shape. The materials used in the two devices are also the same. Because the DOC Band was a cranial orthosis, the company also drew equivalence to the halo systems used in traction and for stabilizing badly damaged vertebrae in the neck. Use of the halo is more severe because metallic pins are set into the skull so that the head can be held rigidly in one position to protect the spinal cord from further damage. Also, the halo system is commonly used with adults or older children as opposed to infants. Despite these differences, the parallel seemed fairly apparent. However, FDA disagreed that the Boston Body Jacket and the halo system were predicate devices, and on March 13, 1997, the agency rated the DOC Band as NSE. As a result, the cranial orthosis was placed in Class III requiring a premarket approval "because there was no predicate device."

Cranial Technologies requested a meeting with Office of Device Evaluation (ODE) officials to establish the agency's concerns, which ODE had not specified when releasing the NSE rating. The request for a meeting was not granted, but telephone conversations were held with an ODE supervisory reviewer, who described his concerns about the DOC Band, and with an FDA legal specialist, who concurred that an appeal of the NSE determination was permissible and reasonable.

On June 26, 1997, the company submitted an appeal of the NSE decision. CDRH acknowledged receipt of the submission on August 1, 1997, and agreed to reopen the premarket notification submission. Additionally, CDRH informed the company that they were having the submitted preamendment status information evaluated by the Office of Compliance. CDRH further stated that they would be contacting the company for additional information. On September 26, 1997, in the hope of fostering a favorable resolution of the appeal, the company decided to submit extensive, recently obtained information on the subject. This submission was followed by a few telephone discussions early in 1998.

ODE's concerns about this device were transmitted to the company in a letter dated March 12, 1998. The letter reiterated the NSE determination but showed some flexibility: "[ODE] recognize[s] that there were cranial helmets, indicated for use as protective post-surgical headgear, legally on the market before enactment of the Medical Device Amendments." Thus, FDA accepted the existence of a predicate, which was a major step forward. The letter continued that the DOC Band had been reviewed in comparison with this protective helmet, but after careful consideration, ODE had decided that the DOC Band was not substantially equivalent to devices marketed prior to May 28, 1976. According to the letter, the DOC Band "had a new indication for use that alters the therapeutic effect in comparison to [protective] cranial helmets, impacting safety and effectiveness, and is therefore considered a new intended use."

The March 12 letter provided a detailed list of FDA's concerns regarding the impact of this device on infant brain development:

- The short-term and long-term effects on the child's growth and development.
- The acute neurologic and dermatologic effects from treatment.
- The risks associated with mechanical failure of the device.
- The increased risk for head and neck trauma resulting from routine or sudden infant movements.

The letter indicated that Cranial Technologies had a right to file a submission for classification, but in view of the above concerns, "general controls would be inadequate and special controls difficult to develop." Despite FDA's response, the company decided to proceed with the request under section 207 since the alternative—a PMA application—was highly unappealing.

The De Novo Process. On March 26, 1998, Cranial Technologies submitted a section 207 de novo request for classification of the DOC Band, recommending that the device be placed in Class II. The submission closely followed the guidance document issued by CDRH on this process.[5] The company provided extensive data backing its position and suggested several possible special controls to provide for safe and effective use of the device and to perhaps mitigate some of CDRH's concerns.

While CDRH's handling of the 510(k) (K964992) review and subsequent appeal had consumed 15 months, its response to the section 207 submission was prompt and highly interactive. James Dillard, deputy director, Division of General and Restorative Devices, was placed in charge of the section 207 process actions. Dillard established a working group headed by an expert

reviewer from the General and Restorative Devices Division. The group also included an expert from the Division of Dental, Infection Control, and General Hospital Devices. Ensuing interactions involved many phone calls and faxes between Dillard's office and company officials and consultants. Both sides invested strenuous efforts to meet the section 207 deadlines.

The expert reviewer acknowledged receipt of the section 207 request on April 7. She also called and faxed Cranial Technologies on April 10, requesting that the company better define the device's indications for use on positional plagiocephaly, rule out related problems, and clarify other treatment options to be tried before starting orthotic treatment. In addition, she requested that the company provide, by April 17, outcome data from major clinical trials as well as the trials' protocols, summary data, discussions, and conclusions.

Although these materials were submitted on time, the expert reviewer and an ODE specialist phoned the company on April 21 requesting further information. The company faxed additional information to the expert reviewer; however, the information was not what ODE wanted. On April 27, the expert reviewer clarified what materials were wanted, and on April 30, the specified information was supplied to ODE. On May 14, the expert reviewer phoned the company requesting a new description of the device, including all variations; a refinement of treatment ages; and a revision of labeling, which had been provided earlier. The company responded on May 15 and interactions continued until May 29.

On May 29, Cranial Technologies received an order classifying the DOC Band into a new Class II device category. This new type of device was identified as a "neurology device under 21 CFR 882.5970," and described as "a cranial orthosis, which is a device intended for medical purposes to apply pressure to prominent regions of an infant's cranium in order to improve cranial symmetry and/or shape." Most orthoses are classified as physical medicine devices in Class I and are exempt from 510(k) requirements. The authors believe that the device was placed in Class II because CDRH was concerned about the sensitive nature of an infant's rapidly growing skull and developing brain. The order further stated that, although some Class II devices are 510(k) exempt (section 510(m)), premarket notification was necessary for a cranial orthosis to provide reasonable assurance of the safety and effectiveness of the device. As a result, the device is not exempt from premarket notification requirements, and companies who intend to market such a device must submit a premarket notification to FDA prior to marketing the device.

CONCLUSION

The first section 207 action was completed on July 30, 1998, when the above classification of cranial orthosis devices was published in the *Federal Register*.[8] This action paralleled that described in the May 29 letter from ODE. Although the publication in the *Federal Register* occurred about 60 days after the notification letter was received (instead of the 30 days prescribed by section 207), the company viewed the date of the notification letter as the vital date and later publication in the *Federal Register* as ratification of the ODE action.

The authors believe that the extensive scientific and clinical data provided might have been sufficient to arrive at the same result under regular classification procedures. However, experience indicates that CDRH, especially when it has safety and effectiveness concerns, rarely down-classifies a device. The outcome of a traditional classification process would have been doubtful, and certainly would have been time-consuming.

In this first de novo action, ODE established many precedents and effectively accomplished its goals. Other de novo actions have since been initiated resulting in one device being reclassified to Class II and other devices being forced to remain in Class III. The second device reclassified to Class II was the Perio 2000 system, a generic type of device that FDA identified as an "in vivo sulfide detection device" (21 CFR 872.1870). The effective operation of section 207 also indicates that CDRH's risk-based regulation of devices is becoming a reality. Not only was the final outcome favorable for the manufacturer and the patients who needed the device, but it also enabled FDA to make its decision after establishing special controls to ensure safe and effective use of the device.

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