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May 31, 2001

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

RE: Docket No. OON-1625 – Proposed Rule on Rescission of Substantially Equivalent Decisions and Rescission Appeal Procedures

Dear Sir or Madam:

We request that you accept this filing as a comment on the proposed rule. On review of the docket we were surprised to find it was not included. However, we are unable to provide you any documentation of mailing.

Thank you for your consideration.

Sincerely,

Stephen L. Ferguson
Executive Vice President
Regulatory & Legislative Affairs
Cook Group Incorporated

Attachment: Letter dated 4/10/01

OON-1625

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April 10, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration, room 106 1
5630 Fishers Lane
Rockville, MD 20852

Re: Docket No. OON-1625 - Proposed Rule on Rescission of Substantially Equivalent Decisions and Rescission Appeal Procedures

Dear Sir or Madam:

The Cook Group, Inc. submits these comments on FDA's proposed rule on the rescission of substantially equivalent decisions and the procedures for challenging a notice of rescission. The proposed regulation was published in the Federal Register on January 16, 2001. Since 1963, Cook Group companies have participated in the development of numerous health care advances that have improved the lives of patients around the world. Cook has been at the forefront of medical research and 'product development for interventional radiology, interventional cardiology, urology, neuroradiology, vascular medicine, critical care and other evolving diagnostic and therapeutic practices. Led by Cook Incorporated, one of the largest privately held medical device manufacturing companies in the world, the Cook Group consists of numerous companies in North America, Europe, Asia and Australia which concentrate on diagnostic and therapeutic product development and manufacturing.

Our comments on the substance of the proposed regulation itself and its procedural shortcomings follow. In sum, Cook believes that rescission is not authorized by the Federal Food, Drug, and Cosmetic Act ("Act"), nor is it appropriate, except 'if there has been fraud (i.e., an untrue statement of material fact) in obtaining the clearance that is related to the substantial equivalence decision itself If FDA believes that there has been such fraud, it must be required to follow procedures by which that determination can be made while protecting the interests of all parties. Because of the seriousness of a fraud charge and the-number of parties that may be affected by a single rescission, the procedures should be formal and include a Part 12 hearing. All other parts of the proposed rule should be withdrawn.

Important to our comments is the difference between rescinding a 5 1 O(k) and withdrawing a PMA. FDA has clearly not taken this critical difference into account in

drafting its regulation. A rescission is unlike the withdrawal of a PMA because it affects not only the device at issue, but effectively results in the reclassification into class III of all of those devices substantially equivalent to it. As a result, each person who relied upon the rescinded 5 1 O(k) to establish substantial equivalence will lose the right to market their devices. The fact that rescission affects so many devices makes it an inappropriate remedy to deal with one problematic device. In addition, the fact that rescission in effect reclassifies devices makes it an illegal circumvention of the reclassification provisions of the Act.

Substantive Issues – Grounds for Rescission

The regulation sets forth six criteria for rescinding a premarket notification substantial equivalence order. All of the criteria, with the exception of the fraud criterion, appear to be excuses for reconsidering clearances based on a change in policy. A change in policy is not a sufficient reason to rescind a 5 10(k) clearance. See Concerned Citizens of Bridesburg v. EPA, 836 F.2d 777,786 (3d Cir. 1987) (an agency may not successfully characterize consistent decisions as inadvertent and be allowed to overturn them merely because of a change in policy). In addition, if there is a safety or effectiveness concern with a particular device, the agency has adequate enforcement tools to address that concern and need not resort to the drastic remedy of rescission. If the agency makes a substantial equivalence decision and others rely on it, FDA must use its enforcement discretion rather than an imperfect and, we believe, extralegal, tool like rescission that has numerous inappropriate repercussions. Although the agency may reconsider an order before it becomes final, clearly the proposed regulation exceeds this limit. Below, we point out a few specific flaws with each of the criteria.

Criterion One. The first proposed criterion for rescission is that the 5 1 O(k) does not satisfy the criteria under 21 C.F.R. § 807.100(b)(1) or (b)(2). The first question is how many bites of the apple does FDA get. In the substantial equivalence determination, the agency has already made the finding that the criteria under (b)(l) and (b)(2) for substantial equivalence were satisfied. Can it, or should it, review an already cleared device every few months to see if in the agency's opinion the device still meets the criteria?' Clearances should be based on the information, standards and analyses of the day, and not be subject to a constantly shifting universe of data, scientific knowledge and opinion. Otherwise, no one could rely on a clearance to make business decisions or for any other purpose. Moreover, since FDA does not have the time to consistently re-review 5 1 O(k)s, even when they are cited as predicates, FDA must be examining the clearance for some other reason, *e.g.*, a public health problem. If the device poses a risk to public health, there are other remedies that should be used to deal with that problem; merely because such remedies require the agency to meet a burden of proof is no reason to allow the FDA to avoid meeting its burden by taking the rescission route. Rescinding a device's classification is not the appropriate response to a public health problem anyway. Because other devices may not pose their predicate's health risks, it would be wholly inappropriate to vitiate their classifications and marketing status, and could threaten the public health by forcing good devices from the market.

In addition, subsection 807.100(b)(2) departs from the statute'by requiring "data" establishing substantial equivalence instead of "information." The regulation states that FDA will find substantial equivalence if the device has the same intended use and differing technological characteristics if:

> (B) The data submitted establishes that the device is substantially equivalent to the predicate device and contains information, including clinical data if deemed necessary by the Commissioner, that demonstrates that the device is as safe and as effective as a legally marketed device; and
>
> (C) Does not raise different questions of safety and effectiveness than the predicate device.

21 C.F.R. § 807.100(b)(2)(ii)(B), (C) (emphasis added). In contrast, the statute makes clear that data may not be necessary to establish substantial equivalence when device technologies differ. Act § 513(i)(1)(A)(ii)(I). It states that substantial equivalence is present in the case of the same intended use and differing technological characteristics if

> the information submitted that the device is substantially equivalent to the predicate device contains information, including appropriate clinical or scientific data if deemed necessary by the Secretary or a person accredited under section 523, that demonstrates that the device is as safe and effective as a legally marketed device, and
>
> (II) does not raise different questions of safety and effectiveness than the predicate device.

Act § 513(i)(1)(A)(ii)(I) and (II) (emphasis added). Thus, the proposed regulation compounds the error made in the earlier regulation by again misstating the law. It exceeds FDA's statutory authority in allowing FDA to require data in a 5 10(k) by providing it the authority to rescind a 5 10(k) if information in the submission establishes substantial equivalence but there is no data in the submission that did so. This criterion should be stricken. If this criterion becomes final, it should reflect the statute and not § 807.100, which departs from the law in a substantive way.

Criterion Two. The second proposed criterion for rescinding a 5 1 O(k) is that "based on new safety or effectiveness information, the device is not substantially equivalent to a legally marketed device." Proposed § 807.103(a)(2). Again, one question is how many bites of the apple does FDA get. FDA should make its determination based on the information available at the time; if the information is inadequate, the FDA's remedy is to find the device not substantially equivalent. If a problem subsequently crops up with a device, which must be the only reason FDA would consider using rescission, FDA has adequate enforcement remedies to use to protect the public health. Changing the classification of a device and perhaps a whole category of devices must be done in the way that tracks the Act's reclassification procedure for preamendment and substantially equivalent devices, *i.e.*, notice and comment rulemaking, and should not be done under a newly invented rescission authority. This criterion should be stricken.

Criterion Three. The third proposed ground for rescinding a substantially equivalent order is that:

> (i) FDA or the 5 1 O(k) holder has removed from the market, for safety and effectiveness reasons, one or more legally marketed device(s) on which the substantial equivalence determination was based, or
>
> (ii) a court has issued a judicial order determining the legally marketed device(s) on which the substantial equivalence determination was based to be misbranded or adulterated.

Proposed 21 C.F.R. § 807.103(a)(3). Again, FDA is ignoring the fact that a rescission is a revocation of a device's classification, and this criterion has nothing to do with a device's classification. In such cases, devices that claimed the removed predicate may still be substantially equivalent to other legally marketed devices. Similarly, the device removed from the market may have been removed because of a feature that the subject device does not have or because of faulty manufacturing. The removed device and the subject device are not identical, nor are they necessarily manufactured in the same manner; they are merely substantially equivalent. Further, the predicate that was used, may have been found to be misbranded because of a labeling issue that does not exist with the device at issue. If there is a threat to the public health, FDA has other authorities available to it that are more than adequate, and does not need a rescission remedy. This criterion should be stricken. If, however, FDA decides to keep this criterion, it should modify it in the following way. Because of the threat to public health of taking devices off the market, FDA should make it possible for 5 1 O(k) holders, when there is no immediate danger to the public health, to try to establish substantial equivalence to predicates that have not been removed from the market or found by a court to be adulterated or misbranded, or to otherwise distinguish the device that has had the problem. Additionally, assuming no predicates, the agency should review the track record of the devices found equivalent to the problematic predicate and automatically do a risk based classification under section 5 13(f)(2). Moreover, the reason a device was removed from the market must be limited to characteristics that would affect the later device's classification before rescission of the subsequent device would be appropriate.

Criterion Four. The fourth criterion, rescission because the 5 1 O(k) contained or was accompanied by an untrue statement of material fact, is the only justifiable criterion (assuming FDA has rescission authority), but should be modified. First, the untrue statement must be tied to the substantial equivalence determination, or else rescission is merely a punitive measure. Moreover, because of the seriousness of a charge of fraud, and because of the potential reliance of others on the substantial equivalence determination, a formal 21 C.F.R. Part 12 hearing should be provided to ensure that the determination of fraud is made with adequate due process and that all parties who have a stake are heard.

Criterion Five. The fifth ground for rescission seems more punitive than related to whether a device is substantially equivalent or not. The fifth ground is that

> the premarket notification included or should have included information about clinical studies and these clinical studies failed to comply with applicable institutional review board regulations (part 56 of this chapter) or informed consent regulations (part 50 of this chapter) in a way that the rights or safety of human subjects were not adequately protected

Proposed 21 C.F.R. § 807.103(a)(5). While we agree wholeheartedly with the importance of compliance with the institutional review board and informed consent requirements, we do not think that failure to comply with these requirements is a legitimate reason for rescinding a premarket notification clearance. Despite the presence of these deficiencies, the data may nevertheless be legitimate and the classification may nevertheless be appropriate. Rescission is not an appropriate remedy. In addition, the "should have included" language is very troubling, as it suggests that FDA is determining after the fact that clinical data should have been included in the 5 1 O(k). This is simply not a lawful way for a regulatory agency to do business. This criterion should be stricken.

Criterion Six. The sixth ground for rescission is also too broadly stated and not linked closely enough with a 5 1 O(k) substantial equivalence determination. The sixth. ground is that:

> the premarket notification contained clinical data submitted by a clinical investigator who has been disqualified under § 812.119 of this chapter.

Proposed 21 C.F.R. § 807.103(a)(6). Even if this were a legitimate reason for rescission, this proposal is stated too broadly. First, there may be other data or information in the 5 1 O(k) that supports substantial equivalence,, so that the clinical data submitted by the disqualified investigator is not necessary to the -finding. Even the clinical investigator disqualification regulation incorporates this concept. See 21 C.F.R. § 812.119(e). In addition, this ground for rescission does not require that the data itself be tainted. That should be a requirement, or the 5 10(k) holder should at least be able to establish the contrary. Finally, the 5 1 O(k) holder may have a lot more information and data on the device that will support its substantial equivalence, and such holders should be able to use this information to prevent rescission from occurring. We urge FDA to strike this criterion. Alternatively, we urge the agency to limit the criterion to proof that the disqualified investigator's data was fraudulent.

Procedural Issues -- FDA's Analysis of Impacts

Based on the paucity of information in the proposal's preamble, it appears that FDA's analysis of impacts was not done properly. FDA completely ignored the domino effect of rescission. Rescission is not like withdrawing approval of a PMA. In the case of a PMA, only the single device that is the subject of the PMA is affected. Since a substantial equivalence determination is a classification determination and others may use the cleared device as a predicate, a single rescission can affect a large number of devices.

FDA in the preamble refers to Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601 – 612) (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1999 (Public Law 104–121)), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). While we do not believe that FDA's analysis satisfied any of these, our focus is on the agency's failings in the area of the Regulatory Flexibility Act.

The Regulatory Flexibility Act. In the preamble to the proposal, the FDA states that it need not analyze regulatory options that would minimize any significant impact of a rule on small entities, since the rule would not have a significant impact on a substantial number of small entities. It bases this conclusion on the fact that FDA has only proposed five rescissions from 1997 through 1999 and one rescission through May 2000. It states, "FDA does not believe that this level of activity represents a significant impact on a substantial number of small entities." 66 Fed. Reg. 3523, 3525 (2001). There are two flaws with this - FDA does not acknowledge that any rescission may have domino effects, to the extent other clearances are based on the rescinded 510(k), and the number of rescissions FDA identifies is artificially low.

FDA cannot conveniently ignore the potential repercussions of each potential rescission, even if it claims the rescissions to date have not had such repercussions (which itself is not clear). There may be numerous premarket notification clearances based on a product whose substantial equivalence determination is rescinded, and additional clearances may be based on those clearances. The legal marketing of all of these products will be affected by a single rescission.

In addition, the six rescissions acknowledged by the agency may not accurately reflect what one could expect in the future for a couple of reasons. First, the numbers may be low because FDA may have been reticent to use a controversial authority, which could be successfully challenged; if the regulation is finalized it will have no such qualms, and in fact may be emboldened. Second, the time periods chosen seem odd'and FDA should explain what happened in the latter half of 2000 and prior to 1997, and why the rescissions from those time periods were not mentioned. In the past, FDA has acknowledged many more rescissions than it acknowledges in the preamble to this proposal.

In sum, a substantial number of small entities may very well be significantly affected to a degree that FDA is in violation of the Regulatory Flexibility Act. FDA should have done the analysis required under the Regulatory Flexibility Act, since it cannot estimate how high the number of rescissions will be based on the past number, and because it ignored the domino effect of a single rescission.

Conclusion

For the foregoing reasons, we urge FDA to withdraw its entire proposal, or, in the alternative, conduct the appropriate analyses under the Regulatory Flexibility Act, the Unfunded Mandates Reform Act of 1995 and Executive Order 12866, and revise the regulation so that the only ground for rescission is fraud directly related to substantial

equivalence determinations. Moreover, Part 12 formal hearing procedures should be used because of the substantial significance of a rescission.

Sincerely,

Stephen L. Ferguson