

# KING & SPALDING

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December 19, 2000

## BY HAND DELIVERY

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

**Re: Docket Number 00N-1409 -- Physical Medicine Devices; Revision of the Identification of the Iontophoresis Device**

Dear Sir or Madam:

These comments are respectfully submitted on behalf of our client, Dynatronics Corporation.

### **I. Introduction**

On August 22, 2000, FDA published a proposed rule regarding iontophoresis devices. 65 Fed. Reg. 50949 (Aug. 22, 2000). In that proposed rule, FDA proposed to amend the physical medicine devices regulations to remove the class III (premarket approval) iontophoresis device identification. FDA stated:

In reviewing the iontophoresis classification as part of this process, FDA realized that it made an error in its identification of the class III iontophoresis device when the device was classified in 1983. Specifically, there were no preamendments devices that met the class III identification, because the definition had the unintended consequence of placing into class III all those iontophoresis devices intended for use with a drug whose labeling cannot bear adequate directions for the device's use with the drug (*i.e.*, a drug that had not been approved for iontophoretic delivery). Nevertheless, from 1977 to 1998, FDA cleared 41 510(k) submissions from 21 firms for devices that met the class III identification because they were not labeled for the diagnosis of cystic fibrosis or for use with a drug approved for iontophoretic delivery. . . .

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FDA is proposing to correct this error by revoking the class III identification. Any device that is not substantially equivalent to the class II device would be considered a postamendments device that is automatically classified in class III under section 513(f) of the act.

Id. at 50950.

The August 22 Federal Register Notice raises various factual, legal, and procedural issues. Some of these issues are highlighted below. By these comments, we respectfully seek -- among other things -- clarification from FDA regarding the issues raised.

## **II. Summary**

FDA's proposal in the Federal Register is confusing and inconsistent. The agency is proposing to take action that appears to be unsupported by the Federal Food, Drug, and Cosmetic Act and its implementing regulations, that will have a significant adverse impact on industry, and for which there are viable, legal alternatives. Among other things, we request that FDA, as required by its General Administrative Procedure regulations, respond fully to the issues raised in these comments and provide a thorough and comprehensive explanation of the reasons for any final rulemaking regarding iontophoresis devices.

## **III. Issues Raised By Federal Register Proposal**

### **A. The Proposed Rule is Confusing and Does Not Clearly Articulate the Basis for FDA's Proposal**

FDA's August 22, 2000 notice setting forth proposed agency action<sup>14</sup> is confusing and does not adequately explain what the proposal entails, the basis or rationale for the proposed action, FDA's authority to take the proposed action, or what the results of the proposed action would be.

According to FDA's General Administrative Procedure regulations, a proposed rule must include a summary "describing the substance of the document in easily understandable terms;" "[s]upplementary information about the notice in the form of a preamble that summarizes the proposal and the facts and policy underlying it . . .;" and "[e]ither the terms or substance of the proposed regulation or a description of the subjects and issues involved." 21 C.F.R. § 10.40(b) (2000); see 5 U.S.C.A. § 553 (2000). The current proposal does not describe the substance in easily understandable terms, nor does it provide an adequate description of or insights into the facts, policy, or issues involved; as a result, it is confusing and inadequate.

Based on our reading of the proposal, our own research, and conversations with various members of FDA's staff for clarification, we believe that the following is a correct understanding of the proposal:

- Over a period of 21 years, FDA cleared 41 premarket notifications ("510(k)s") from 21 firms for devices that met the class III identification for iontophoresis devices;
- FDA now says that it made an "error" in its identification of the class III iontophoresis device category;
- FDA believes that there were no drugs, prior to May 28, 1976, that were approved (i.e., labeled) for use with iontophoresis devices;
- Because there were presumably no drugs labeled for use with iontophoresis devices prior to 1976, FDA contends that there can be no preamendments devices that meet the class III designation;
- Because FDA believes that no drugs were labeled specifically for use with iontophoresis devices prior to 1976, the class III classification for these devices should never have existed;
- Accordingly, FDA is proposing to revoke the class III designation;
- In order for an iontophoresis device (other than one intended for use with pilocarpine) to be legally marketed, a company must have an approved new drug application ("NDA") that is device-specific (i.e., the drug must be approved specifically for use with that company's device);
- There currently is one company that manufactures an iontophoresis device that has an approved NDA for use with its particular device;
- NDAs for iontophoretic use (device-specific or otherwise) are not required for pilocarpine;
- Iontophoresis devices used with pilocarpine will only need to change their labeling in order to stay on the market; and
- On the effective date of a final rule based on this proposed rule, FDA intends to rescind all of the 510(k)s for devices intended to be used with drugs, other than pilocarpine, if there is not a device-specific NDA approval for a drug to be used with that particular 510(k)-cleared device.

Please verify whether the above understanding of FDA's proposed rule is correct. The following discussion is based on this understanding of the proposal.

#### **B. FDA's Proposal Is Based on an Incorrect Premise**

FDA's proposal is premised on the assumption that there could not have been any class III preamendments iontophoresis device uses because there were no drugs labeled for iontophoretic use prior to May 28, 1976. FDA does not provide a basis for this premise. We are not aware of anything in the law or otherwise to suggest that a device is no longer a preamendments device simply because the drug or drugs with which the device was used prior to 1976 were not specifically labeled for use with that device.

In order to demonstrate that a manufacturer's device was in commercial distribution prior to May 28, 1976, and thus a preamendments device, the manufacturer must show four things:

1. The device was displayed, advertised, or otherwise offered for sale before May 28, 1976, for a specific intended purpose or purposes, with no limitations (e.g., no limitation to research or investigational use);
2. the manufacturer had, before May 28, 1976, accepted, or been prepared to accept, at least one order to purchase the device that resulted, or would have resulted, in a contract of sale for the device in the United States, generally with delivery to occur immediately or at a promised future date;
3. the device was not being offered or accepted only for research or investigational use; and
4. the manufacturer of the device can provide adequate documentation establishing (1) through (3) above to the satisfaction of the Food and Drug Administration.

Compliance Policy Guide 7124.19 (September 24, 1987), at 1.

These criteria in no way suggest that a drug used with a device prior to 1976 must be labeled for use with the device, nor that such drug labeling would, in any way, impact the status of the *device* which was "displayed, advertised, or otherwise offered for sale before May 28, 1976." Moreover, it is our understanding that, prior to May 1976, drugs may not have been generally labeled for use with devices. Similarly, prior to May 1976, the inverse was probably true -- that devices were not generally labeled for use with particular drugs.

Please explain FDA's basis and authority for determining that a device on the market prior to May 28, 1976 cannot be considered a preamendments device if the drugs with which it was used pre-1976 were not specifically labeled for use with the device. Please also explain whether FDA believes that this same theory is applicable to any other devices used with drugs prior to May 1976.

**C. There is No Basis for Treating Pilocarpine Differently From Other Drugs Used with Iontophoresis Devices.**

Wescor, Inc.'s submission to this docket, dated October 25, 2000, indicates that pilocarpine was not labeled for use with iontophoresis devices prior to May 28, 1976 ("[I]t is the belief of the undersigned that no drug in commercial distribution prior to 28 May 1976 or at present is explicitly labeled for cystic fibrosis diagnosis through delivery by iontophoresis." Letter from Wayne K. Barlow, President/CEO, Wescor Inc., to Dockets Management Branch, Food and Drug Administration 1 (October 25, 2000)). If this is the case, then, per FDA's logic, the use of pilocarpine with an iontophoresis device would be a class III use and 510(k)s for all of these devices would be rescinded since there do not appear to be NDAs for pilocarpine use with iontophoresis devices. Despite this, according to conversations with the agency, FDA is suggesting that iontophoresis devices for use with pilocarpine can continue to be sold, even if

this proposed rule were promulgated, so long as such manufacturers change their labeling. As a result, the agency is treating pilocarpine and manufacturers of devices designed for use with pilocarpine, differently from other drugs and other manufacturers of iontophoresis devices.

FDA has provided no basis for its dissimilar treatment of pilocarpine and devices that use pilocarpine in the proposed rule. See United States v. Diapulse Corp., 748 F.2d 56, 62 (2d Cir. 1984) (“However, we must insist that the FDA apply its scientific conclusions evenhandedly and that it not ‘grant one person the right to do that which it denies to another similarly situated . . .’”, quoting Marco Sales Co. v. Federal Trade Comm’n, 453 F.2d 1, 7 (2d Cir. 1971)); United States v. Undetermined Quantities of . . . “Exachol”, 716 F. Supp. 787, 795 (S.D.N.Y. 1989) (“In every context, the overriding principle of fairness is always the same: the government must govern with an even hand.”).

Please explain how FDA’s proposal with regard to pilocarpine use is consistent with the rationale articulated in FDA’s proposal, (i.e., that devices can continue to be marketed only if there is an NDA specific to that device or where the drug, pre-1976, was specifically labeled for use with iontophoresis devices) and/or how FDA can permissibly treat such drugs/devices in a manner different from other products that would be subject to the proposal.

#### **D. FDA Has Not Articulated Any Scientific Basis for Requiring an NDA for Every Brand of Iontophoresis Device**

Iontophoresis treatment requires the following elements: the iontophoretic applicator; the delivery and dispersive electrodes; the drug to be administered; the protocol; the clinician; and the patient.

It is our understanding that all iontophoresis devices work in essentially the same way: (1) the appropriate treatment polarity is set; (2) the desired current dose is set; (3) the current is set equal to the patient’s comfort level or electrode current density rating; (4) delivery time is calculated based on current and dose; and (5) an electrical current drives the medication through the skin and into the underlying tissues.

Based on medical device reports (“MDRs”) and other information, it appears that the primary complications associated with iontophoresis device use are: (1) allergic skin reaction to the drug, the electrical current or electrode adhesive; or (2) skin irritation or burns resulting from skin sensitivity to current, under-saturation or drying of electrodes, the use of currents higher than recommended for electrode size, or failure to inspect delivery site for areas that can cause high resistance (hotspots), such as moles, scars, new wounds, newly shaved or abraded skin, dry skin conditions, or very thin skin as seen in young children and geriatric patients.

It is our understanding that drugs used with devices are not typically approved for use with a particular brand of device but are, rather, approved generally and thus can be marketed for use with any device of that type. This is consistent with FDA’s “Intercenter Agreement Between The Center for Drug Evaluation and Research and The Center for Devices and Radiological

Health” (October 31, 1991) (“Intercenter Agreement”). In that Agreement, FDA categorizes iontophoresis devices as “[d]evice[s] with [the] primary purpose of delivering or aiding in the delivery of a drug that [are] distributed without a drug (i.e., unfilled).” Intercenter Agreement at 3. FDA goes on to say:

For a device intended for use with a category of drugs that are on the market, CDRH will be the lead center for regulation of the device under the device authorities. The effects of the device use on drug stability must be addressed in the device submission, when relevant. An additional showing of clinical effectiveness of the drug when delivered by the specific device will generally not be required. The device and drug labeling must be mutually conforming with respect to indications, general mode of delivery (e.g., topical, I.V.), and drug dosage/schedule equivalents.

Intercenter Agreement at 4. This statement, placing CDRH as the lead center and noting that a showing of clinical effectiveness of the drug when delivered “by the specific device” will “generally not be required” and that information on drug stability must be addressed only “when relevant” does not suggest a significant concern by FDA about drug stability/effectiveness in specific iontophoresis devices or, in any case, that there is a need for device-specific NDAs.

FDA has not provided any information or evidence in its proposal to suggest that there are valid reasons (e.g., drug-related safety or efficacy concerns associated with different iontophoresis devices) why NDA approvals should be device-specific.<sup>1</sup> Nor, for that matter, has FDA explained why the use of pilocarpine with more than one brand of iontophoresis device is different, from a technical standpoint, from the use of other drugs.

Please explain the scientific basis for the agency’s belief that iontophoresis devices (other than those that use pilocarpine) should be 510(k)-cleared only if there is a drug that is specifically approved for use with that particular device and why these same arguments do not apply equally to pilocarpine.

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<sup>1</sup> In this context, please note that FDA’s regulations require that every significant FDA decision must have a file that contains: “(1) Appropriate documentation of the basis for the decision, including relevant evaluations, reviews, memoranda, letters, opinions of consultants, minutes of meetings, and other pertinent written documents; and (2) The recommendations and decisions of individual employees, including supervisory personnel, responsible for handling the matter.” 21 C.F.R. § 10.70(b).

**E. The Approach Taken in the Proposed Rulemaking Is at Odds with the Statutory Requirements and Established FDA Procedure Regarding How to Address Class III Preamendments Devices**

The Safe Medical Devices Act of 1990 added certain provisions to section 515 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C.A. § 321, et seq. Section 515(i) states:

- (2) After the [Secretary orders manufacturers of devices introduced into interstate commerce before May 28, 1976 to submit a summary of information respecting their devices] but before December 1, 1995, the Secretary shall publish a regulation in the Federal Register for each device --
- (A) which the Secretary has classified as a class III device, and
  - (B) for which no final regulation has been promulgated under section 515(b), revising the classification of the device so that the device is classified into class I or class II, unless the regulation requires the device to remain in class III.

21 U.S.C.A. § 360e(i)(2).

Consistent with this is a 1994 memo from the Acting Director of the Office of Device Evaluation (“ODE”) to ODE Division Directors which says that:

The Safe Medical Devices Act of 1990’s (SMDA’s) new section 515(i) requires FDA to order industry submission of a summary of and a citation to any information known or otherwise available to the manufacturer, including adverse safety and effectiveness information, for preamendments class III devices not yet subject to a 515(b) final order and to reconsider their classification in light of redefinition of class II. The Safe Medical Devices Act of 1990 (SMDA) revised the definition of class II to include devices for which ‘general controls’ by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish “special controls,” rather than to establish “performance standards” as had been required by the 1976 Act. SMDA also directs FDA to revise the classification of such preamendments class III devices into class I or class II or require the device to remain in class III, and directs FDA to issue a schedule for 515(b) rulemaking within 12 months of publication of a regulation retaining a device in class III. However, SMDA does not prevent the FDA from proceeding immediately to section 515(b) rulemaking on specific devices, in the interest of public health, independent of the 515(i) process.

Memo from Susan Alpert, M.D., Ph.D., Acting Director, Office of Device Evaluation to ODE Division Directors at 1 (April 19, 1994) (“Alpert Memo”).

As a result of the SMDA mandate, FDA classified devices into three groups:

Group 1 devices are devices that FDA believes raise significant questions of safety and/or effectiveness, but are no longer used or are very limited in use. Group 2 devices are devices that FDA believes have a high potential for being reclassified into class II. Group 3 devices are devices that FDA believes are currently in commercial distribution and are not likely candidates for reclassification.

62 Fed. Reg. 32352, 32353 (June 13, 1997). Iontophoresis devices were categorized as “high priority Group 3 devices,” for which FDA was to initiate a rulemaking in 1996. Alpert Memo, Appendix A.

Agencies are obligated to follow their statutory mandate. See Federal Trade Commission v. National Lead Co., 352 U.S. 419, 428 (1957) (an agency can only carry out powers granted to it by Congress). Nevertheless, the proposed regulation follows neither the statutorily mandated procedures nor FDA’s proposed action plan.<sup>2</sup> Instead, FDA’s proposed rulemaking simply drops the class III classification and substitutes a plan whereby the one company that currently holds an NDA can market its product, other companies (who have devices that use pilocarpine) can be considered class II devices that can stay on the market if they provide revised labeling to the agency, and all other iontophoresis devices will have their 510(k)s rescinded. Such changes must have a basis in the statute and regulations and must reflect permissible and relevant factors. Robbins v. Reagan, 780 F.2d 37, 48 (D.C. Cir. 1985) (a “change in direction from a previously announced intention” is scrutinized closely by the courts and must be based on permissible and relevant factors.)

Please explain the authority under which FDA deviated from the SMDA’s section 515(i) requirements and its own articulated strategy, and the reasons for doing so.

#### **F. There Is No Statutory or Regulatory Mechanism to Drop a Class III Designation**

There does not appear to be either a statutory or regulatory mechanism set forth in the Food, Drug, and Cosmetic Act (“FDCA”) or supporting regulations for revoking a device

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<sup>2</sup> It bears noting that even FDA’s 510(k)-clearance letters to iontophoresis manufacturers noted this process: “An iontophoresis device that is intended to use a direct current to introduce ions of soluble salts or other drugs into the body for medical purposes other than those specified for class II devices is classified into class III (21 C.F.R. § 890.5525). We published our strategy for calling for premarket approval (PMA) applications in the enclosed Federal Register, dated May 6, 1994, and the enclosed memorandum dated April 19, 1994.” Letter from Celia M. Witten, Director, Division of General and Restorative Devices, Office of Device Evaluation, Center for Devices and Radiological Health, to Carolyn M. Steele Husten, EMPI, Inc., December 28, 1998.

classification. Please explain the statutory/regulatory mechanism under which the agency is proposing such a revocation.

#### **G. FDA Does Not Have the Authority to Rescind 510(k)s for Iontophoresis Devices**

FDA has stated that it will rescind 510(k)s that have been cleared for uses other than cystic fibrosis diagnosis unless there are drugs approved for use with those specific iontophoresis devices. We do not believe that FDA has such authority.

We are unaware of any provision in the FDCA authorizing FDA to withdraw or rescind a premarket notification filed pursuant to section 510(k) of the Act. In contrast, the FDCA contains explicit provisions for withdrawal of approval in many other sections of the statute where FDA has the authority to authorize marketing of a product. See, e.g., § 410(i) (expressly authorizing repeal of a food additive regulation); § 505(e) (expressly authorizing withdrawal of approval of a new drug application); § 512(e) (expressly authorizing withdrawal of approval of a new animal drug application); § 515(e)(1) (expressly authorizing withdrawal of approval of premarket approval application); § 520(g)(5) (expressly authorizing withdrawal of approval of an investigational device exemption); and § 721(d) (expressly authorizing procedure for repeal of a color additive regulation).

FDA's regulations contain procedures that require notice to the applicant holder of an opportunity for a hearing on a proposal to withdraw product approval, in order to implement these other statutory authorities governing the withdrawal of product approvals. See, e.g., 21 C.F.R. § 814.46 (withdrawal of approval of premarket approval application ("PMA")); 21 C.F.R. §§ 314.150, 314.151 (withdrawal of approval of a new drug application and abbreviated new drug application); 21 C.F.R. § 514.115 (withdrawal of a new animal drug application); and 21 C.F.R. § 71.30 (procedure for filing objections to and hearings for repeal of color additive regulations). We are aware of no such procedures for a proposal to withdraw 510(k) clearance.

In contrast to the statute's express identification of situations where FDA has the authority to withdraw its approval of a marketing application, there are many statutory provisions requiring the submission of information to FDA which do not contain any provision -- either express or implied -- to withdraw or rescind such submission. See, e.g., § 510(c) (registration of drug and device manufacturing establishments) and § 510(j) (drug and device listing). To our knowledge, FDA has never suggested that it has the authority to withdraw or rescind an establishment registration or a drug or device listing. Nor could it rescind such a submission. The premarket notification provision is, in this regard, the same as the registration and listing requirements. For this reason, premarket notification was included in the same section of the FDCA as registration and listing. Indeed, FDA routinely reminds manufacturers that a premarket notification finding of substantial equivalence is not an approval.

In this regard, while the Safe Medical Devices Act ("SMDA") did attempt, in section 513(i), to codify FDA's existing practice regarding 510(k) clearances and even added a provision for FDA issuance of an "order" finding substantial equivalence, the amendments did not amend

section 510(k), change the “premarket notification” reference in section 510(k), nor add a mechanism by which that order could be revoked, repealed, withdrawn, or rescinded. Without such authority, FDA cannot rescind a 510(k) since a government agency may exercise only the powers granted it by the statutes enacted by Congress. See National Lead Co., 352 U.S. at 428. See also Civil Aeronautics Bd. v. Delta Air Lines, Inc., 367 U.S. 316, 322 (1961) (“[T]he determinative question is not what [an agency] thinks it should do but what Congress has said it can do.”).

There are other remedies available to FDA to address a situation where FDA believes a product that has entered the marketplace under the 510(k) process is either unsafe or ineffective. These remedies are set forth in the misbranding and the adulteration provisions of the FDCA. Moreover, FDA has civil penalty authority for products shipped in violation of the FDCA and authority to require a recall of a product where it presents a risk of serious adverse health consequences.

FDA itself has argued that it has the authority to rescind cleared 510(k)s only in cases involving: (1) a serious adverse risk to public health and safety; (2) data integrity or fraud on the agency; or (3) other compelling circumstances. Letter from Joseph A. Levitt, Deputy Director for Regulations and Policy, Center for Device and Radiological Health, to Nancy Singer and Marlene K. Tandy (September 11, 1995). FDA’s August 22 Federal Register Notice, however, did not suggest that there are any serious adverse risks to public health and safety associated with iontophoresis devices or that there are data integrity issues or fraud associated with the cleared iontophoresis 510(k)s. Nor has FDA identified any “compelling circumstances” for the potential rescission of these 510(k)s.

Please explain the authority and basis for the agency’s proposal to rescind cleared 510(k)s for all iontophoresis devices (other than those designed for use with pilocarpine) for which there is not a device-specific NDA approval.

#### **H. FDA’s Proposed Rule Will Have a Dramatic Negative Impact on Industry But Will Not Reduce Off Label Use of These Devices**

If FDA’s proposed rule becomes final, only one company’s iontophoresis device and one drug approved and labeled for use with that particular iontophoresis device can, at this point in time, be legally marketed, outside of the context of cystic fibrosis diagnosis. All other iontophoresis devices will be taken off the market unless NDAs are approved for use with those particular devices. The process of obtaining NDA approval is very long and expensive. Many device manufacturers do not have the resources to pursue such approval and, as a result, will simply go out of business. Indeed, it is our understanding that one manufacturer sold its iontophoresis devices business to a larger company believing that it could not stay in the business if device-specific NDAs were required.

If one thought here is that off-label use of iontophoresis devices would be reduced if this proposed rule becomes final, this is not the case. Rather, the result of this rule would simply be

that fewer companies will be able to market their devices. These marketed devices, however, can -- and will -- still be used with the same variety of drugs and for the same off-label purposes as they are currently, *i.e.*, the one device that can be marketed, if FDA's proposed rule becomes final, can be used not only with the one drug approved for use with that device but with *any* drug on the market.

#### **I. FDA Has Other Appropriate Means of Addressing Iontophoresis Issues**

Under the SMDA, FDA may change the classification of a device from class III to class II if the agency determines that special controls would provide reasonable assurance of the safety and effectiveness of the device. 21 U.S.C.A. § 360c(e)(2)(A). Rather than explicitly requiring a showing that a device is safe and effective to determine its classification, Congress focused on whether special controls would provide a reasonable assurance of safety and effectiveness of the device. The legislative history of the SMDA describes the type of evidence required to meet the new reclassification standards: "adequate evidence that the application of special controls will provide reasonable assurance of the reclassified device's safety and effectiveness." H.R. Rep. No. 101-808, 101<sup>st</sup> Cong., 2d Sess., at 28. Congress thus focused on evidence relating to the adequacy of general and special controls to assure the safety and effectiveness of a medical device. As to the specific findings required by FDA to support reclassification, Congress provided that FDA find that "such classification is appropriate and will provide adequate assurance of the device's safety and effectiveness." *Id.* Iontophoresis devices may well fit these criteria for reclassification.

Alternatively, FDA can (if iontophoresis devices do not meet the class II criteria) retain the class III classification for iontophoresis devices, but provide for a grace period to allow manufacturers of iontophoresis devices to stay on the market while they compile, file, and await approval of their PMAs, including use of any drugs approved for use with iontophoresis devices. Allowing a grace period under these circumstances would put the companies on a more equal footing and would be consistent with statements made by FDA during the course of the reclassification process for other devices -- that preamendments devices that were required to remain in class III would have a grace period in order to obtain PMA approval and that the agency would not endeavor to pull longstanding devices from the market.

The FDCA gives FDA the discretion to allow for such a grace period, providing that: "Nothing in this Act shall be construed as requiring the Secretary to report for prosecution, or for the institution of libel or injunction proceedings, minor violations of this Act whenever he believes that the public interest will be adequately served by a suitable written notice or warning." 21 U.S.C.A. § 336. Here, where these drug-device combination products have been on the market for over 20 years, do not appear to have significant safety or efficacy issues, where FDA's action would have a drastic impact on industry, and where FDA has not previously suggested that it would attempt to immediately remove long-time products from the market if a class III determination were made, the public interest would be well served by allowing for a grace period until appropriate approved applications are in place.

#### **IV. The Preamble to FDA's Final Rule Must Explain FDA's Decisionmaking**

FDA's General Administrative Procedure regulations require that a final rule published in the Federal Register must have a preamble, including supplementary information about the regulation, that contains references to prior notices relating to the same matter and a summary of each type of comment submitted in the proposal and the Commissioner's conclusions with respect to each. 21 C.F.R. § 10.40(c)(3). The regulations further note that the preamble is to contain a thorough and comprehensive explanation of the reasons for FDA's decision on each issue. Id.

Accordingly, any final rule published with regard to iontophoresis devices must, at a minimum, address each of the issues identified above and contain a "thorough and comprehensive explanation" of FDA's reasoning, consistent with 21 C.F.R. § 10.40(c)(3).

#### **V. Request**

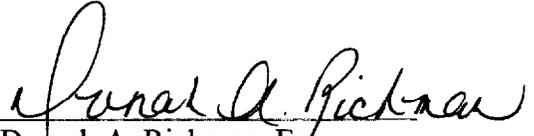
Based on the above, we respectfully request that FDA:

- (1) Reclassify all iontophoresis uses to class II. Allow all current 510(k)-holders to maintain their device clearances and continue to market their iontophoresis devices. For new devices coming on the market, one special control could be that the device must be labeled for use with a drug approved for use with *any* specific iontophoresis device, or a drug approved (in the future) for broader categories of iontophoresis devices, and that these new 510(k)s demonstrate substantial equivalence, consistent with the above-quoted language in the Intercenter Agreement, to other iontophoresis devices that have been cleared for use with an approved drug; **or**
- (2) If FDA determines, pursuant to statutory criteria, that a class III designation is appropriate, that it follow the statutorily mandated requirements for maintaining this classification, and provide a grace period for devices to remain on the market while obtaining PMA approval including use of any drugs approved for iontophoretic delivery; **or**
- (3) Assuming that FDA's final rule contains some or all of the same elements contained in the proposed rule, that the agency provide a full explanation of its rationale, consistent with the regulatory requirements set forth at 21 C.F.R. § 10.40(c)(3), demonstrating that the current proposal is based in law and fact, has appropriate and supportable scientific justification, and is not internally inconsistent.

\* \* \* \* \*

Thank you for the opportunity to provide these comments.

Sincerely,

  
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