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1149 30 EB-7 9352

3M

November 30, 1999

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

Re: Docket Number 97N-0023

To Whom It May Concern:

Please accept for filing the enclosed submission of the Pharmaceutical Division of Minnesota Mining & Manufacturing Company ("3M") regarding the FDA's proposed rule on Essential Use Determinations and the Use of Ozone-Depleting Substances, 64 Fed. Reg. 47719 (September 1, 1999). 3M is submitting two copies of its comments to Docket Number 97-0023; please date-stamp and return the additional copy in the postage-prepaid return envelope provided.

Thank you for your assistance.

Sincerely,

Maureen A. Convery kkw

Maureen A. Convery, Esq.
Office of General Counsel
Minnesota Mining & Manufacturing Company

cc: Florence Wong
Doug Patton

97N-0023

Minnesota Mining and
Manufacturing Company

3M Center, Building 220-11E-03
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C 9618

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

Re: Chlorofluorocarbon Propellants in Self-Pressurized Containers;
Determinations that Uses Are No Longer Essential; Docket No. 97N-0023

Dear Sir or Madam:

We respectfully submit these comments on behalf of the Pharmaceutical Division of Minnesota Mining & Manufacturing Company ("3M Pharmaceuticals" or "3M") of St. Paul, Minnesota, on the Food and Drug Administration's ("FDA") proposed rule for determining whether uses of chlorofluorocarbons ("CFCs") in self-pressurized containers are essential under the medical device exemption in the 1990 Clean Air Act ("CAA"), 42 U.S.C. § 7671c(d)(2).

3M recognizes FDA's difficult task in this proposed rulemaking to implement the requirements of a statutory mandate outside of and, in some respects, seemingly inconsistent with the agency's responsibilities under the Food, Drug, and Cosmetic Act ("FDCA"). 3M also recognizes the agency's difficult task in attempting to reconcile different and competing interests among the affected parties and different and competing public health concerns, especially those affecting patients.

3M is concerned, however, that this proposed rule goes beyond ensuring safe and

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3M recognizes FDA's difficult task in this proposed rulemaking to implement the requirements of a statutory mandate outside of and, in some respects, seemingly inconsistent with the agency's responsibilities under the Food, Drug, and Cosmetic Act ("FDCA"). 3M also recognizes the agency's difficult task in attempting to reconcile different and competing interests among the affected parties and different and competing public health concerns, especially those affecting patients.

3M is concerned, however, that this proposed rule goes beyond ensuring safe and

effective alternatives and attempts to add new burdens on companies already doing more than their fair share to develop new non-ODS technologies. In several areas, the proposed rule would impose requirements on the developers of new non-ODS technologies to solve problems that were never addressed by the manufacturers of the ODS products in the current marketplace. These additional requirements are not consistent with the CAA.

Moreover, the CAA does not condition transition from ODS products on a drug marketplace of non-ODS products that is optimal or is perfectly symmetrical with the ODS drug marketplace. It requires only that the marketplace preserve truly essential medications. 3M believes that FDA's proposed rule raises serious questions with regard to the mandate of the CAA. As described below, 3M believes important aspects of the rulemaking need to be clarified and that important mandates of the CAA need to be more closely adhered to in the final rule.

A. Essentiality Determinations for Currently Marketed Products.

1. Essential products vs. essential active moieties.

FDA proposes to make essentiality determinations for products currently on the market by identifying those active moieties for which the use of an ODS propellant is essential, and describing the exempted class of products as all products containing that particular active moiety.

This approach falls short of the requirement in the CAA that a product's essentiality be based on a determination by FDA that the "product" is essential, and that the determination be based on public notice and comment.

The CAA exempts ODS-containing products only where FDA determines that the product itself, as opposed to the product's active component, is essential and only where the public has had an opportunity for notice and comment. FDA's role is described in the CAA's

definition of "medical device":

The term "medical device" means any device (as defined in the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321)), diagnostic product, drug (as defined in the Federal Food, Drug, and Cosmetic Act), and drug delivery system –

(A) if such device, product, drug, or drug delivery system utilizes a class I or class II substance for which no safe and effective alternative has been developed, and where necessary, approved by the Commissioner; and

(B) if such device, product, drug, or drug delivery system, has, after notice and opportunity for public comment, been approved and determined to be essential by the Commissioner in consultation with the Administrator.

42 U.S.C. § 7671(8).

Congress' clear intent that FDA's essentiality determination be focused on the product, as opposed to a component of the product, is clear from different language used on the two subsections of the medical device definition. Although in subsection (A) Congress focussed on the CFC component of the product (in requiring that the EPA assess whether there is a safe and effective alternative to the use of the ODS component of the product), in subsection (B) Congress required that the product itself be determined essential (by FDA rather than EPA and only after notice and comment).

This determination and, particularly, the requirement for notice and comment requires at a minimum that FDA identify the particular products that are determined to be essential and state the factual predicate for each product's essentiality. To address the CAA's requirement that products rather than active moieties be assessed and determined essential, FDA must amend its proposed regulation to identify the specific products that are deemed essential under the regulation and must provide in the record the factual predicate for each product's essentiality.

2. FDA's final (post-2005) criteria for removing ODS products.

After the year 2005, the proposed regulation acknowledges FDA's duty under the CAA to remove ODS products that are not shown to provide an "unavailable important public health benefit." 64 Fed. Reg. at 47741 (proposed § 2.125(g)(2), (f)(1)(ii)). This, FDA explains in the preamble to the proposed regulation, requires a "showing of special need and benefit." 64 Fed. Reg. at 47732. 3M supports this criterion because it is consistent with the agency's duty to determine that every ODS product is really "essential." 3M questions, however, certain criteria proposed by the agency for removing ODS products during the interim period prior to the year 2005, and the agency's commitment to apply the 2005 criteria in 2005.

3. FDA's interim (pre-2005) criteria for removing ODS products.

(a) Medical necessity vs. convenience, preference, and desirability.

Although it is appropriate for FDA to proceed cautiously in the initial phase of its implementation of the CAA, the agency cannot during this phase ignore the plain meaning of the CAA requirement that the ODS product be "essential." Congress' use of the term "essential" clearly requires that FDA determine that the product is necessary, as opposed to merely preferable or desirable. Thus, in making an essentiality determination for a product currently on the market, it is appropriate for the agency to consider whether patients will have a safe and effective alternative for their condition. This may involve an assessment of tolerability, patient compliance, and other problems that may leave a significant patient population without a truly safe and effective alternative. This assessment, however, cannot impose upon manufacturers of innovative non-ODS alternatives tolerability, compliance, or other requirements exceeding those imposed on the manufacturers of non-ODS products. The question under the CAA is not

whether the currently marketed ODS products are better (or cheaper) than non-ODS alternatives, but rather whether they are really “essential.”

The proposed rule fails in this regard with the proposed requirement that non-ODS products offer “comparable convenience” to the ODS products they replace. 64 Fed. Reg. at 47741 (proposed § 2.125(g)(1)). FDA’s use of the term “convenience” is potentially confusing and appears inconsistent with the mandate of the CAA that ODS products be “essential.” While it may be true that a product may be so inconvenient, in some sense of the word, that it cannot be used safely and effectively, the phrase “comparable convenience” suggests that the agency might consider elements of convenience having nothing to do with safe and effective use. FDA should not suggest to patients that they are entitled to expect no inconvenience from the transition to non-ODS products. FDA should revise its proposed regulation as follows:

Section 2.125(g):

FDA will use notice-and-comment rulemaking to remove the essential-use listing of a product in paragraph (e) of this section if the product meets any one of the following criteria . . .

(3) For individual active moieties marketed as ODS products and represented by one new drug application (NDA) and one strength:

(i) At least one non-ODS product with the same active moiety is marketed with the same route of administration, *and* for the same indication, as the ODS product containing that active moiety *and provides a level of convenience that will not significantly impair safe and effective use.*

(b) Post-approval data

FDA proposes to consider the first year's marketing experience with a non-ODS product in assessing whether a similar ODS product is essential and may remain on the market. It is, of course, appropriate for FDA to consider any available marketing experience with the non-ODS product in determining whether the ODS product remains essential. It is not appropriate, however, for FDA to presume that an ODS product is essential, and delay transition to the non-ODS product, until a certain quality and quantity of marketing data are generated for the non-ODS product.

It is troubling that FDA suggests that it will expect postmarketing data regarding, inter alia, effectiveness in broader patient populations. 64 Fed. Reg. at 47723. It is unclear how postmarketing data can demonstrate effectiveness, and FDA should clarify that such a demonstration is not a requirement. Where there is no evidence that the non-ODS product poses a unique safety or efficacy issue for a significant patient subpopulation, it is inappropriate to impose data requirements over and above those required to determine safety and effectiveness for the product's labeled uses.

It is particularly inappropriate for FDA to impose a requirement for a new clinical investigation to assess comparative safety or efficacy. When this issue was discussed at the meeting of the Pulmonary-Allergy Drugs Advisory Committee ("PADAC") on November 22, 1999, the committee members generally expressed reservations about the agency's requiring post-approval clinical studies after determining that the non-ODS product was in fact safe and effective for the same indications for use.

The committee members thought such studies might be too large, too expensive, and

might not yield useful “real world” data. Committee members also expressed concerns over whether FDA would require manufacturers of non-ODS products to answer questions and solve problems that have not been solved with regard to currently marketed ODS products. One committee member noted specifically that there will always be subpopulation questions for these types of products and that serious questions remain regarding safety and effectiveness of currently marketed ODS products for certain patient subpopulations.

FDA should retract its suggestion that new data and, possibly, new clinical studies may be required to ensure an additional level of proof of safety and effectiveness in all subpopulations.

FDA should also delete from the proposed rule the requirement of one-year’s post-marketing experience in the United States. Although the agency questions whether foreign marketing experience is as valuable as experience in the United States, there is no basis in the rulemaking for presuming that extensive foreign experience has no value that might offset the agency’s desire for one year’s domestic experience.

(c) Manufacturing Capacity

FDA proposes to consider whether the non-ODS product is, in fact, available for patients. 64 Fed. Reg. at 47722. While it may be appropriate for the agency to consider known manufacturing or supply difficulties that could preclude availability of the medication, it is not appropriate for the agency to impose specific manufacturing requirements, such as a requirement for multiple manufacturing sites, that have never been imposed on manufacturers of existing products. Moreover, there is no basis in the record for a finding by the agency that the current use of two manufacturing sites by the manufacturer of an ODS product means that the

manufacturer of a non-ODS product cannot supply the market with one manufacturing site.

(d) Cost

The agency has proposed to consider cost in the context of product availability. 64 Fed. Reg. at 47723. In this regard, FDA uses the term “affordability.” FDA has no authority under the FDCA or under the CAA to regulate drug pricing or the economics of the marketplace, and FDA cannot base an essentiality determination on this criterion. Moreover, in the PADAC meeting on November 22, 1999, the committee members were virtually unanimous that cost should not be a factor in determining whether a product is essential and that it would be unreasonable to expect the new non-ODS technologies to compete with the pricing structure of currently-marketed ODS products, especially where ODS products are marketed as generic drugs.

The only concern expressed by committee members related to the possibility that an unusually steep increase in cost might make the non-ODS product so inaccessible to certain patients that it would result in increased mortality. Despite FDA’s posing a question to the PADAC about the basis for this concern, there is no evidence in the record or elsewhere to suggest that non-ODS replacement products will be inaccessible due to prohibitively high pricing. Indeed, as FDA notes in the preamble to the proposed rule, all available evidence suggests that the non-ODS replacement products will not be priced significantly higher than similar, branded ODS products. 64 Fed. Reg. at 47729, 47739.

FDA should not create a false and unreasonable expectation on the part of patients using ODS products that the CAA mandates comparably priced non-ODS products. FDA should retract references to product “affordability” and focus instead on whether a product is medically

essential.

(e) Multiple NDAs

Closely related to the issue of cost is the requirement in the proposed rule that, where there are two NDAs for ODS products with the same active moiety, FDA will deem the ODS products essential until there are at least two NDAs for non-ODS products with the same active moiety. 64 Fed. Reg. at 47741 (proposed § 2.125(g)(4)). The agency offers no policy rationale for this requirement, nor any explanation whatsoever other than an oblique reference to the agency's desire to consider costs of non-ODS products in determining essentiality. 64 Fed. Reg. at 47733.

FDA has no authority to impose this sort of market symmetry to ensure comparable product pricing. The CAA requires a determination that the ODS product is essential to patient care, not that it is essential to preserving a symmetrical marketplace. Moreover, even if FDA were authorized to police drug pricing, the agency provides no basis in the record for concluding that two non-ODS NDAs are required for "affordability" in a market replacing two non-ODS NDA products, but not in a market replacing one non-ODS NDA product. While FDA may for its own reasons want to see two non-ODS NDAs replacing two ODS NDAs, there is no basis in the record or in logic for the requirement, and certainly no basis in the CAA requirement that the ODS products be replaced unless they are demonstrably essential. Thus, the agency should change the proposed rule as follows:

Section 2.125(g):

(3) ~~For individual active moieties marketed as ODS products and represented by one new drug application (NDA) and one strength:~~

(i) At least one non-ODS product with the same active moiety is marketed with the same route of administration, for the same indication, for the same strengths, and with approximately the same level of convenience of use as the ODS product containing that active moiety;

(ii) Supplies and production capacity for the non-ODS product(s) exist or will exist at levels sufficient to meet patient need;

(iii) At least 1 year of ~~U.S.~~ postmarketing use data is available for the non-ODS product(s); and

(iv) Patients who medically required the ODS product are adequately served by the non-ODS product(s) containing that active moiety and other available products; or

~~(4) For individual active moieties marketed as ODS products and represented by two or more NDA's or marketed in multiple distinct strengths;~~

~~(i) At least two non-ODS products that contain the same active moiety are being marketed with the same route of delivery for the same route of delivery, for the same indication, and with approximately the same level of convenience of use as the ODS products; and~~

~~(ii) The requirements of paragraphs (g)(3)(ii), (g)(3)(iii), and (g)(3)(iv) of this section are met.~~

Should FDA retain the requirement in the proposed regulation that two non-ODS NDAs replace two ODS NDAs, the agency should clarify that where the ODS products are significantly different, e.g., one is for asthma only and the other is for COPD only, a single non-ODS product might replace a single ODS product. For example, where the two ODS products are for entirely different indications, a non-ODS replacement product for one of the indications might make the ODS product for that indication nonessential, while the ODS product for the different indication might remain essential. This could be done as follows:

Section 2.125(g)(4):

For individual active moieties marketed as ODS products and represented by two or more NDA's or marketed in multiple distinct strengths;

(i) At least two non-ODS products that contain the same active moiety are being marketed and at least one of the non-ODS products is marketed with the

same route of delivery for the same route of delivery, for the same indication, and with approximately the same level of convenience of use as the particular ODS products; and

(f) Unapproved uses.

FDA proposes to consider in determining essentiality whether a non-ODS product meets the needs of patients who use the product for unapproved uses. 64 Fed. Reg. at 47723. This would place the manufacturer of a new non-ODS product in a precarious position because current agency policy precludes manufacturers of new products from promoting their products for off-label uses. Moreover, the agency applies this policy with intense scrutiny during the launch campaigns of new products. If the agency expects the non-ODS manufacturer to establish patient acceptance of the new non-ODS product for off-label use comparable to that of an ODS product that has developed an off-label market over many years, the agency must accompany its rule with a new policy that will allow promotion of off-label uses by the new manufacturer.

4. Timely initiation of transition under the final (post-2005) criteria.

The proposed regulation leaves open the possibility that the interim criteria for removing products from the market will, in effect, govern transition to non-ODS products well beyond the year 2005. FDA does not commit in the proposed rule to the timing of commencement of transition under the 2005 criteria. The 2005 criteria are meaningless unless they are applied, and the 2005 date is meaningless unless the criteria are applied on that date.

FDA should be committed and prepared to enforce the 2005 requirements when they take effect. FDA's notice-and-comment process under the 2005 criteria could take months or years, and should commence immediately on the 2005 effective date. The final regulation should commit FDA to this timely initiation of transition, at least with regard to ODS products

containing active moieties that are also contained in non-ODS products. The final regulation should also clarify that the 2005 criteria are not limited in application to products “not available without an ODS.” This could be accomplished by amending the regulation as follows:

Section 2.125(g)(2):

After January 1, 2005, ~~the product is not available without an ODS and~~ FDA determines that the product no longer meets the criteria in paragraph (f) of this section after consultation with a relevant advisory committee(s) and after an open public meeting (prior to January 1, 2005, FDA shall publish a notice providing a schedule for advisory committee consultation and a public meeting regarding essentiality for all ODS products that contain an active moiety that is also contained in a non-ODS product); or

B. Determinations for Discontinued Products Essentiality.

For discontinued products, FDA proposes that all such products be deemed non-essential. 64 Fed. Reg. 47741 (proposed § 2.125(g)(1)). 3M agrees that discontinued products cannot be determined to be essential because no patients are relying on the product and the removal of the product from the market evidences that there is no medical need for the product.

C. Essentiality Determinations for New Products.

For new products (products approved after promulgation of the final rule), the proposed regulation would apparently deem such products essential based solely on whether they fall within a class of essential products defined in the regulation. As discussed above, these classes would be defined based solely on the active moiety in the product. FDA would not consider any other fact about the product or its use, and would not consider whether there was any significant patient population in need of the new product. The proposed rule would, thus, deem future unidentified products “essential” in situations where there are no patients depending on the product and where there is no population of patients identified as needing the new product.

Moreover, the new product would be deemed essential without any opportunity for notice-and-comment on whether the new product serves any patient need. This outcome cannot be squared with the mandate of the CAA.

1. Determining essentiality based solely on active moiety.

As discussed above, the CAA exempts ODS containing products only where FDA determines that the product itself, as opposed to product's active component, is essential and only where the public has had an opportunity for notice and comment.¹ The identity of the active moiety in a newly approved ODS product cannot, by itself, establish essentiality for the new product.

FDA concedes this point in other parts of the proposed rule. This is most clearly demonstrated in the agency's proposal to deem a discontinued product non-essential regardless of whether the product's active moiety falls within one of the regulation's "essential use" designations. 64 Fed. Reg. 47741 (proposed § 2.125(g)(1)).²

Moreover, FDA appears to agree that a newly-approved product, upon which patients do not rely and which offers no significant therapeutic benefit over other products in the marketplace, cannot be deemed medically necessary or essential based solely on its active

1 As discussed above, although subsection (A) of the CAA medical device definition focuses on the ODS component of the product (in requiring the EPA assess whether there is a safe and effective alternative to the use of the ODS component of the product), subsection (B) requires that the product itself be determined essential after notice and comment.

2 FDA concedes the significance of many factors other than active moiety in the provisions for amending the regulation to remove essential use designations:
A non-CFC product simply having the same active moiety as a CFC product is only one factor to be considered. Other factors, such as whether the non-CFC product has the same route of administration, the same indication, and can be used with approximately the same level of convenience are important considerations.

64 Fed. Reg. at 47735. See also id. at 47741 (proposed § 2.125(g)(3)(i)).

moiety. This is evidenced in the proposed regulation's requirement for determining essentiality for a newly-approved product that does not fall within one of the moiety classes identified in the rule. In this circumstance, FDA would not look merely at the product's active moiety but would rather require a showing that, inter alia, the "product will provide an unavailable important public health benefit." 64 Fed. Reg. 47741 (proposed § 2.125(f)(1)(ii)) (emphasis added).

Indeed, this must be the standard for determining essentiality for any new product, whether or not the product has the same moiety as a product already marketed and designated essential in the final regulation. As discussed above, the CAA requires that FDA make essentiality determinations for products rather than for product components. In the case of a new product, there is no basis in the rulemaking record or in logic for making an essentiality determination based solely on the active moiety in the product.

Moreover, even if the CAA provided FDA with latitude to make prospective essentiality determinations based solely on active moiety, FDA could not support its proposed rule. FDA has advanced no policy justification for a proliferation of new ODS products that offer no therapeutic advance over existing products and are deemed essential solely because they have the same active moieties as other products on the market.

2. Notice and an opportunity for comment on a new product's essentiality.

Congress made clear in the section 601(8)(B) of the CAA not only that FDA must make essentiality determinations for individual products as opposed to product components, but also that the public be provided notice and an opportunity for comment regarding each product's essentiality. FDA's proposed rule would circumvent this requirement. The public cannot be deemed to have had proper notice and an opportunity to comment on a product's essentiality

when the product and its characteristics have not been identified for the public, and the product may not even exist until some time in the future. Moreover, as FDA's rulemaking makes clear, a product's essentiality depends in part on an assessment of patient needs and alternative products, which may change significantly by the time the new product is developed and proposed for the marketplace. FDA's proposed rule provides notice and comment only for new active moieties, whereas the CAA requires notice and comment for new products.

Thus, as discussed above, FDA must amend its proposed regulation to identify the specific products that are deemed essential under the regulation and limit the essentiality determination to those products. The proposed regulation should also be amended to clarify that an amendment to the regulation is required for new products as opposed to new active moieties. This should be done as follows:

Section 2.125(f):

Any person may file a petition under part 10 of this chapter to amend paragraph (e) of this section to add or remove an essential ~~use~~ product.

D. FDA's Finding of Adulteration and Misbranding.

FDA proposes to remove from the current regulation the agency's finding that a non-essential drug product is adulterated and misbranded under the Federal Food, Drug, and Cosmetic Act ("FDCA"). 64 Fed. Reg. at 47720. The agency acknowledges that this finding is still valid under the statute. *Id.* Removal of the finding from the regulation might require an additional burden of proof for the agency should the agency have to demonstrate in court that a non-essential product is adulterated or misbranded under the statute. The agency offers no cogent reason for placing this additional burden upon itself and should not abrogate its lawful

authority under the FDCA over non-essential products. The agency should retain this express finding in the new regulation.

E. Restricting Labeling for Non-Essential Uses.

FDA declines to consider indications for use in making essentiality determinations, arguing that it must take the product as is and must find it essential if any approved use is essential. 64 Fed. Reg. at 47741 (proposed § 2.125(g)(1)). In this regard, FDA ignores the mandate of the CAA. It is well established that a product, and its safety and effectiveness, cannot be divorced from its labeling. Accordingly, a product's essentiality cannot be considered without regard to the product's labeling. A product labeled for one safe and effective use and nine unsafe or ineffective uses is not, as labeled, safe and effective. Similarly, a product labeled for one essential use and nine non-essential uses is not, as labeled, essential. Such a product would have to be relabeled for only its essential use. Any other interpretation of the CAA would undermine the purpose of the statute, which FDA acknowledges is the "phaseout of CFC use."

64 Fed. Reg. at 47736.

FDA should revise its proposed regulation in this regard as follows:

Section 2.125(g):

FDA will use notice-and-comment rulemaking to remove the essential-use listing of a product in paragraph (e) of this section if the product meets any one of the following criteria . . .

(3) For individual active moieties marketed as ODS products and represented by one new drug application (NDA) and one strength:

(i) At least one non-ODS product with the same active moiety is marketed with the same route of administration, ~~for the same indication~~ one or more of the ODS product indications, and with approximately the same level of convenience of use as the ODS product containing that active moiety; . . .

This would require the manufacturer of the ODS product with some but not all of the indications of the non-ODS product to revise the labeling of the ODS product to remove the indications covered by the non-ODS product.

F. Expedited Review.

FDA suggests that it will not provide expedited review to non-ODS products deigned to replace ODS products. 64 Fed. Reg. at 47732. FDA should state unequivocally that it will provide expedited review for such non-ODS replacement products. FDA's obligations here flow from the clear intent of Congress in the CAA that FDA play in important role in implementing transition to non-ODS products and removing CFCs from the environment.

G. Determining Essentiality Prior to Promulgation of a New Regulation.

FDA must promulgate a final regulation on essentiality determinations as soon as possible because, as is evident from the above discussion, FDA's current regulation cannot satisfy the requirements of the 1990 CAA. The current regulation contains exemptions for broad categories of products such as adrenergic bronchodilators. These exemptions were neither promulgated under the CAA nor intended to be permanent. They are, moreover, inconsistent with the mandate of the CAA that FDA determine, for any product proposed for introduction onto the market, that the product itself be determined essential and that the determination be based on notice and opportunity for public comment.

The current section 2.125 does not address individual products and cannot satisfy the requirement for notice and comment. The public was never provided with notice and an opportunity for comment on the ODS products now in the marketplace. Moreover, the CAA

clearly does not contemplate determinations based on notice-and-comment proceedings that took place before the CAA even existed.

Even if the CAA allowed for drug class evaluations of essentiality that predated the CAA, FDA's essentiality determinations in section 2.125 could not pass muster because they were based on an assessment of technologies and products on the market more than twenty years ago. FDA made clear in the original promulgation of section 2.125 that the broad exemptions in the regulation were never intended to be permanent but were rather meant to be updated constantly in light of new technologies, drugs, and other circumstances. The agency states in the 1978 preamble to the regulation that it will assess the need to amend the regulation upon the mere "submission" of any "data in support of a reformulated product that does not include a chlorofluorocarbon." 42 Fed. Reg. at 24,538.

The 1978 findings upon which the exemption for adrenergic bronchodilators, corticosteroids and other CFC MDIs was based are now out of date and clearly erroneous.³ Application of the current regulation, thus, violates both the CAA and the Administrative Procedure Act (APA), 5 U.S.C. § 706(2)(A). See Detsel by Detsel v. Sullivan, 895 F.2d 58, 64 (2d Cir. 1990); American Civil Liberties Union v. FCC, 823 F.2d 1554, 1565 (D.C. Cir. 1987),

³ FDA stated the scientific justifications it originally relied upon in exempting the use of CFC's in adrenergic bronchodilator MDIs:

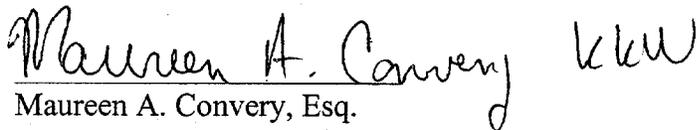
The first fact was that, unlike other commercially available propellants, the chlorofluorocarbons maintain a constant internal canister pressure throughout the shelf life of the product. As a result, a self-pressurized container containing a chlorofluorocarbon can deliver a potent therapeutic drug in precisely metered doses, with the last dose containing the same quantity of drug as the first dose. Further, these drugs, because of their chlorofluorocarbon propellant, provide a uniform distribution of the therapeutic agent in small particle size to hard-to-reach mucous membranes.

42 C.F.R. §22029. FDA's approval of an MDI with a non-CFC propellant negates these findings.

cert. denied sub nom. Connecticut v. FCC, 485 U.S. 959 (1988); Natural Resources Defense Council v. Herrington, 768 F.2d 1355, 1408-09 (D.C. Cir. 1985).

FDA should make a clear public statement acknowledging that the current regulation (section 2.125) cannot be relied on to deem new ODS products essential. FDA must subject any newly approved ODS product to notice and comment and must determine its essentiality based on medical need for the specific product in the current environment.

Respectfully submitted,



Maureen A. Convery, Esq.

Office of the General Counsel

Minnesota Mining & Manufacturing Company

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