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February 20, 2002

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Rm. 1061  
Rockville, Maryland 20857

Re: **Docket Number 01-30491**

Subject: **3M Drug Delivery Systems' Comments to Draft Guidance for Industry – *Integration of Dose-Counting Mechanisms into MDI Drug Products***

Dear Sir/Madam,

Enclosed please find 3M Drug Delivery Systems' comments on FDA's Draft Guidance for Industry – *Integration of Dose-Counting Mechanisms into MDI Drug Products*. These comments are provided in reference to Docket Number 01-30491.

3M Drug Delivery Systems supports the initiative by the Division of Pulmonary and Allergy Drug Products (DPADP) to develop guidance on, and encourage industry to incorporate, dose counting mechanisms into MDI drug products. 3M looks forward to further dialogue with DPADP to integrate reliable dose counting or actuation monitoring devices into MDI products.

***3M's Comments:***

**Section II. BACKGROUND**

The first paragraph states that, "...an MDI labeled to deliver 120 metered-actuations may expel 20 to 30 additional actuations (depending on the specific fill target for that product). However, the amount of drug per spray in those additional 20 to 30 actuations will be inconsistent and will eventually become negligible." 3M believes that this incorrectly characterizes the actuations after the labeled number for all products. In fact, for some products, the majority of actuations after the labeled number will offer consistent dose delivery. We suggest that the message be modified to note that for some products consistent delivery may be achieved, however, this can vary from one product to another and the patient can not rely on every MDI to offer a therapeutic dose after the labeled number of actuations.

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In the third paragraph of this section, the final sentence states, “Technological advances have made it possible for manufacturers to incorporate into their devices economical, reliable, integrated dose-counters to reflect how many actuations remain in a canister.” As a generalization this may be correct, however, the technological advances may yet to be realized for all MDI devices. Economical and reliable dose counting devices for MDIs have not been approved for use yet and it is difficult to state that a successful applicant will have economically incorporated a dose counting mechanism. Also, the term “integrated” as used in some technical circles may be used to distinguish a “top mounted” counter affixed to the canister from a counter that may be incorporated into the actuator/mouthpiece (integrated). We suggest that the intent of the paragraph is maintained with this last sentence deleted.

**Section III. INTEGRATION OF DOSE-COUNTING MECHANISMS  
INTO MDI DRUG PRODUCTS UNDER DEVELOPMENT**

**B. Reliability Issues**

The guidance notes that clinical use studies should be conducted. Additional guidance on these studies would be beneficial, i.e., can these be accomplished with a “focus panel” of patients to assess patient acceptance and ability to use the device (making the distinction between traditional clinical trials with clinical metrics). Consideration should be given to special populations, e.g., elderly patients or pediatric patients who may be challenged by manipulating an MDI which incorporates a dose counting device versus the product they may currently be using.

Also, we are aware of a specific comment to the guidance made by the European Pharmaceutical Aerosol Group (EPAG) which suggests that if a dose indicator is to be used with a product, it should be incorporated into the program no later than Phase III clinical trials. While we recognize that any delivery device change introduced after Phase III trials are conducted make interpretation of the clinical results more difficult, incorporating a dose indicator into blinded trials may interfere with control of bias, particularly when an active comparator is used as a control. Use of the product with a dose indicator in Phase III studies should not be a specific requirement when information on the technical function and the perceived utility are addressed by alternate studies.

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Thank for the opportunity to provide comments to the draft guidance. Should you have any questions regarding the comments, please don't hesitate to call me (651 736-5015).

Respectfully,

A handwritten signature in cursive script that reads "D.M. Markoe, Jr." with a small flourish at the end.

David M. Markoe, Jr.  
Senior Regulatory Specialist  
3M Drug Delivery Systems



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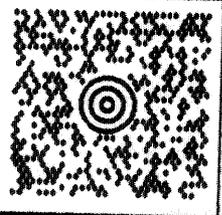
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