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SEP 22 1999

September 21, 1999

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

RE: **Docket No. 99D-1738**  
Draft Guidance for Industry on Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action

Dear Administrator:

Kos Pharmaceuticals, Inc. (Kos), and Aeropharm Technology, Inc. (ATI), a wholly owned subsidiary of Kos, is submitting comments to FDA in response to the request published in the June 24, 1999 Federal Register regarding the *Draft Guidance for Industry, on Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action*, Docket No. 99D-1738. Our General comments to the guidance document are attached.

Kos/ATI is a member of the IPACT-1 Consortium and also supports this group's position concerning the development of Nasal Aerosols and Nasal Sprays guidances. Kos/ATI believes that the comments to be submitted by this group should play a central role in the continued development of this guidance for industry.

Kos/ATI greatly appreciates and supports FDA's efforts to develop a guidance for Industry for Nasal Aerosols and Nasal Sprays products. If you have any questions concerning our comments, please call me at (305) 512-7039. Thank you for the opportunity to provide FDA with our comments and suggestions.

Sincerely,

JoAnn H. Smith  
Regulatory Affairs, Associate

99D-1738

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## **SECTION V - Bioavailability and Bioequivalence: In Vitro Studies**

### Section V (B) – Test and Metrics

The guidance recommends the use of automated actuation stations for all comparative BE *in-vitro* tests to decrease variability in drug delivery due to operator factors. From this point on, the guidance reads as though this is a requirement, not a recommendation. Also, the guidance does not provide any information for use of a non-automated testing mechanism. Consideration should be given and specified within the guidance document for use of non-automated testing systems.

### Section V (B) (2)(b) – Instrumental Methods

#### Laser Diffraction

Laser diffraction may not be a viable method for measuring particle size distribution in all cases. Kos suggests that particle size distribution data from the plume be included as a requirement and that appropriate test methods be specified within the guidance.

#### Multistage Cascade Impaction (CI) or Multistage Liquid Impinger (MSLI)

The guidance states that the deposition of the drug should be reported for all Group I accessories and the upper stage, i.e., valve stem, actuator, inlet port. Does this mean drug mass only? Is particle size required?

### Section V (B) (3) – Instrumental Methods

#### Spray Pattern

In this section the guidance specifies that spray pattern measurements should be taken at three appropriate distances from the actuator. However, the CMC guidance for Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products states only that measurements should be taken “at different distances (e.g., two).” Consistency between both guidance documents is needed.

### Section V (B) (4) – Instrumental Methods

#### Plume Geometry

The guidance requires two views for plume geometry. Kos suggests that one view is sufficient to collect the data specified within this section of the guidance.

## **CONCLUSION**

Kos strongly supports the development of a guidance document for Industry on Nasal Aerosols and Nasal Spray Drug Products and appreciates the Agency's efforts in developing the current draft guidance. Given the variety and complexity of formulations and devices in this drug delivery technology area, Kos recognizes the difficulties and challenges present in the development of a single guidance document that adequately covers this range of diverse products. Kos also recognizes the value to industry of a guidance of this type, and believes it is important that this guidance be written in a way that recognizes and incorporates the diversity of products represented by this class of pharmaceuticals.

Kos believes this will clarify for industry what aspects of pharmaceutical performance and quality the Agency considers important to control. In addition, a general guidance document will help industry understand the reasoning behind the Agency's views and the Agency's expectations for new products. Further, when product attributes and technical issues dictate alternate approaches, developers can easily focus their interactions with the Agency on those specific issues.

We hope our comments will be of value to the Agency and we look forward to the ultimate publication of a final guidance that will effectively serve the current and future needs of the Nasal Aerosol and Nasal Spray products industries.



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5847 '99 SEP 27 10:00

September 24, 1999

Attention: Mr. John Gomez  
Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

RE: **Revised Binder Label for Docket No. 99D-1738**

Draft Guidance for Industry on Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action

Dear Mr. Gomez:

Per our telephone conversation on September 24, 1999, attached are revised labels for the binders containing our comments to the Draft Guidance for Industry on Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action, Docket Number 99D-1738. Please place the revised labels over the existing binder labels.

Thank you for your assistance in this matter. Should you require additional assistance concerning this submission, please contact me at 305-512-7039.

Sincerely,

A handwritten signature in black ink, appearing to read 'JoAnn H. Smith'. The signature is fluid and cursive, with the first letters of each word being capitalized and prominent.

JoAnn H. Smith  
Associate, Regulatory Affairs

**LEFEX**

**Federal Expre**

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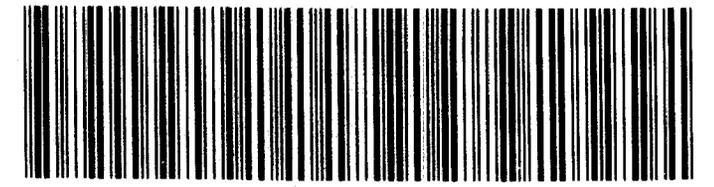
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