Novartis Pharmaceuticals Corporation
Global Regulatory CMC
One Health Plaza
East Hanover, NJ 07936-1080

Tel 973 781 7500
Fax 973 781 6325

NOVARTIS

October 24, 2002

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

Subject: Response to Draft Guidance for Industry: "Inhalation Drug Products Packaged in Semipermeable Container Closure Systems, Federal Register, Friday, July 26, 2002, Docket No. 02D-0254

To whom it may concern:

Novartis is a world leader in the research and development of products to protect and improve health and well-being. As a global pharmaceutical corporation, Novartis is supportive of efforts to improve and to harmonize the technical requirements for registration of pharmaceutical products. After review of the above-cited guidance, we have the following comments:

General comment
Explanations of the scientific thought behind certain recommendations in the draft Guidance are valuable in promoting understanding of the FDA reasoning within the draft Guidance. However, some of these thoughts are open-ended. Focusing these ideas into more specific and measurable recommendations will improve the effectiveness of the Guidance, once finalized. As the document is made more specific, implementation of its recommendations by industry can be more uniform and regulatory review by FDA can be more consistent. Novartis' comments are made to draw clarity to these open points in the draft document.

Line-specific comments
Line specific comments are provided in tabular form below.

Line number	Comment
24	The term 'semipermeable' needs to be defined against a uniform standard. This information may be added in a Glossary at the end of the Guidance. Recommendations may include both materials of construction and test methodology (such as reference to standard USP tests) to assess permeability and loss of formulation components.
30, 38	As this draft Guidance addresses the sub-set of medications intended for pulmonary-compromised patients (asthma, COPD—reference line 46), systemic drugs intended for delivery by the pulmonary/nasal route should be specifically excluded from the scope of this Guidance, in the Introduction. Additionally, non-aqueous liquid inhalation products such as MDDPIs and DPIs should be excluded.
31	A regulatory mechanism needs to be proposed to qualify those products already approved and marketed in semi-permeable containers. Commercial materials may also be used in the development of new standards as noted earlier. The Agency should also consider alternative proposals to demonstrate that package concerns are not relevant to the clinical aspects of a particular marketed product (lines 77-87), should a sponsor wish to discuss them.
44, 57, 93, 127-132	Agency comments on volatile organic chemicals, potential contaminants in the local environment, identified and unidentified contaminants from secondary packaging and labeling adhesives, and the potential of formulation components to interact with these to form new impurities describe potential scenarios to introduce trace quantities of impurities into product formulations. To direct efforts in identification and quantification of impurities and reduce speculative studies, it would be useful to relate impurity quantification to known standards such as the ICH Guideline on Residual Solvents, a to-be-developed FDA list of suspect chemicals, or other scientific baseline.
141-144	Complete avoidance of paper labels on unit containers may prove impractical as multiple products become approved, and product identifiers become necessary to avoid misuse or errors in administration. Debossed or embossed molding on translucent or opaque white semipermeable containers may provide too little product differentiation. The Agency should consider establishment of standards or testing for direct-printing inks or label adhesives to qualify their use on liquid inhalation product container labels.

These comments are being provided in duplicate in written form and electronically as directed in the Federal Register Notice.

Thank you for the opportunity to comment. If you have any questions, please contact me at (973) 781-3379 or at e-mail: joan.materna@pharma.novartis.com

Sincerely,

(original signed)

Joan A. Materna
Senior Associate Director
Global Regulatory CMC