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Vice President
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PhRMA

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June 1, 2006

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20857

Re: Docket No. 2006N-0105
PhRMA Comments on Food and Drug Administration Notice appearing in Federal Register ; Vol. 71, No. 60 Wednesday, March 29, 2006; Agency Information Collection Activities: Proposed Collection; Comment Request; Environmental Impact Considerations

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA companies are leading the way in the search for new cures. PhRMA members alone invested and estimated $39.4 billion in 2005 in discovering and developing new medicines. Industry-wide research and investment reached a record $51.3 billion in 2005.

PhRMA supports the current FDA approach to assessing potential environmental impact under the National Environmental Policy Act (NEPA). There does, however, appear to be an opportunity to eliminate unnecessary work related to requests for categorical exclusions for actions on Investigational New Drugs (INDs). Specifically, PhRMA is responding to the invitation to comment on page 15754 of the subject Federal Register notice. For reference, items (1) and (4) state:

(1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility

(4) Ways to minimize the burden of the collection of information...

Regarding 21 CFR Part 25.15 (a), (d): Categorical exclusion criteria 21 CFR Part 25.31 (e) action on an IND. PhRMA recommends that this exclusion criterion be changed to read as follows:

21 CFR Part 25.31 (e) Action on INDs where the drug or biologic product is derived from wild plants or animals. Action on other types of INDs do not require a claim for a categorical exclusion.

2006N-0105 C1

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PhRMA proposes this change for the following reasons:

A. The document published in 1998 by FDA titled "Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications" states (on page 8 in Section III C3bii) that: "INDs generally involve relatively small quantities of a drug or biologic product and treatment of a limited number of patients. Many INDs never result in the filing of an NDA or application for marketing approval of a biologic product, which would allow for the wide-spread commercial sale of the product. CDER and CBER will evaluate INDs on a case-by-case basis where the drug or biologic product is derived from wild plants or animals to determine whether the extraordinary circumstance provision in 21 CFR 25.21 is invoked."

B. PhRMA member companies have been providing claims for categorical exclusions for action on an IND since the early 1990's for active pharmaceutical ingredients (API) in all therapeutic classes. PhRMA companies have no indication of FDA having used this extensive number of claims for a categorical exclusion as the basis for denials pertinent to potential environmental impact as described under NEPA. This history indicates these claims for categorical exclusion have little "practical utility" and that changing the requirement so that no claims are required for categorical exclusion actions on an IND, as recommended above, represents an excellent way to "minimize the burden of the collection of information."

C. Usage of an API under an IND is site limited and time bounded, indicating that the potential for patient excretion of an API to the environment is extremely limited. The API usage scenario under an IND indicates these claims for categorical exclusion have little "practical utility" and that changing the requirement as recommended by PhRMA so that no claim is required represents an excellent way to "minimize the burden of the collection of information."

D. In recent years it has been established by consensus of a range of stakeholders [see, for example, *Human Pharmaceuticals: Assessing the Impacts on Aquatic Ecosystems*. RT Williams, Editor. 2005. Society of Environmental Toxicology and Chemistry] that potential risk from pharmaceuticals in the environment pertains to long-term, chronic exposure. Consequently, usage of an API under an IND will not result in the type of exposure widely accepted as being of potential environmental concern. Furthermore, prior to marketing approval of an API, the FDA will have the opportunity to review potential environmental impact through its Environmental Assessment requirements under NEPA. This logic also demonstrates that claims for categorical exclusion for INDs have little "practical utility." Changing the requirement so that no claims are required for IND categorical exclusions, as described above, represents an excellent way to "minimize the burden of the collection of information."

E. If claims for categorical exclusion were not required as proposed by PhRMA, and using the data in the subject notice from FDA, it would have eliminated work on up to

1933 categorical exclusions (15464 hrs) for INDs in 2005 that ultimately had no "practical utility."

In summary, the historical experience of PhRMA companies, the FDA Guidance for Industry and good science all support that categorical exclusions should be automatically granted for actions on INDs where the drug or biologic products are not derived from wild plants or animals. The burden of collecting information and submission of claims for categorical exclusions for actions on these INDs has no "practical utility."

PhRMA appreciates the opportunity to evaluate and comment upon the subject Notice. On behalf of our members we urge your consideration of the approach outlined in these comments. If you or your colleagues need additional information, please feel free to contact Thomas. X. White, PhRMA Technical Consultant at (202) 835-3546, or email to txwhite@phrma.org.

Sincerely,

Alice E. Till

Alice E. Till, PhD.