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

May 23, 2001

Comments regarding Docket No. 01D-0177
Immunotoxicology Evaluation of Investigational New Drugs Draft Guidance Document

Dear Regulator,

I would like to compliment your organization for drafting a concise, thorough document. As a member of the Society of Toxicology's Immunotoxicology Specialty Section, I have been keenly interested in seeing immunotoxicology added to the list of important areas for pharmaceutical evaluation. Although the document covers many important topics, there are two issues I would like to see further addressed.

1] **Cancer therapies.** More clarification of the language for antitumor drug requirements would be appreciated. In Section IV, immunosuppression, a statement for solid tumor adverse effects *versus* hematologic malignancy is given. Additionally, Section IX discusses myelotoxicity with prophylactic measures. However, no distinction is made for cytotoxic *versus* non-cytotoxic agents. Bone marrow suppression is an anticipated frequent adverse event due to cytotoxic agent therapy for solid tumors. Because the effects are general in nature, and not targeting a particular bone marrow subpopulation, would findings from immunotoxicology analyses add value to the standard toxicology studies? I am unsure of the answer to this, but perhaps some consideration should be given to the type of agent being tested. Also, if the compound is not first in its class and information from clinical trials has been gained with similar compounds, could this information be used *in lieu* of new animal studies? Perhaps some language could be added to the document to distinguish cytotoxic from non-cytotoxic agents as well as broader information as to follow-up for flowchart.

01D-0177 C1

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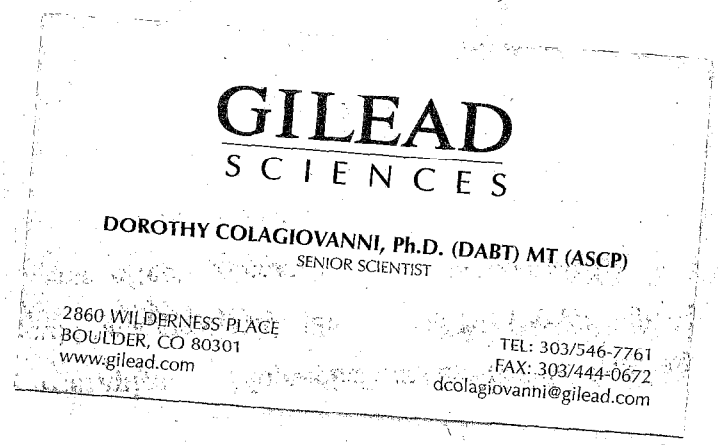
2] **Liposomal agents.** There is no mention of liposomal agents in the document. In Section III there is language referring to evaluation of macrophages if distribution is to the reticuloendothelial system, but, no specifics are given. Liposomal agents preferentially distribute to the RES and are found in the highest concentrations frequently in the spleen and liver. They also concentrate readily in macrophages. Specific guidance as to how to deal with this type of drug formulation would be extremely helpful to those of use that work with liposomes. For example, if we know that a drug concentrates in the RES and we do not see any immunotoxicity, can the fact that it is a liposomal formulation negate the additional studies suggested in Section III? I would appreciate clarification of this topic.

Thank-you for review of my comments and if you require further clarification, please do not hesitate to contact me.

Sincerely,

DBColagiovanni

Dorothy B. Colagiovanni, Ph.D. (DABT)
Senior Scientist



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