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December 18, 2008

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

Re: FDA-2008-D-0525: Draft Guidance for Industry on New Contrast Imaging Indication Considerations for Devices and Approved Drug and Biological Products

Dear Sir or Madam:

The Academy of Molecular Imaging (AMI) and the Institute for Molecular Technologies (IMT) are pleased to submit comments to the Food and Drug Administration regarding its Draft Guidance for Industry on New Contrast Imaging Indication Considerations for Devices and Approved Drug and Biological Products ("Draft Guidance"), which was published in the Federal Register (Vol. 73, No. 195) on October 7, 2008.

AMI is composed of academicians, researchers and nuclear medicine providers utilizing molecular imaging technologies, including positron emission tomography (PET) and PET with computed tomography (PET/CT). AMI supports molecular imaging education, training, research and clinical practice through its annual scientific meeting, its educational programs, and its journal, *Molecular Imaging & Biology.*

IMT is a not-for-profit organization and an official Council of the Academy of Molecular Imaging whose mission is to advance the development, approval, appropriate use and reimbursement of molecular imaging technologies. To further its mission, IMT educates medical and science professionals, patients, Congress, government agencies and the public about molecular imaging, and promotes cooperation between organizations with similar missions. The IMT membership comprises representatives of scientific, industrial, manufacturing, product and service companies and service providers.

We appreciate the Food and Drug Administration's efforts to provide guidance for manufacturers, sponsors, and holders of marketing applications for medical imaging device, drug, or biological products that provide image contrast enhancement with respect to new contrast imaging indications.

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We are concerned, however, that the Draft Guidance does not provide sufficient clarity to allow industry and other stakeholders to assess, interpret, and utilize this information in a meaningful way. Unless resolved, this ambiguity undermines the usefulness of the Draft Guidance to industry, stakeholders, and FDA.

These comments outline where we believe there is room for clarification in the Draft Guidance and where we would appreciate receiving additional guidance from the FDA.

New Contrast Indication Definition

We believe there is ambiguity in the Draft Guidance's definition of a "new contrast indication" for drugs and devices and in how the Agency will apply this definition in practice. Section III of the Draft Guidance defines a contrast indication as "a *statement* in the indication or intended use section of the labeling of either an imaging drug or imaging device using an imaging drug or biological product, including radiopharmaceuticals" (emphasis added). This definition does not give clear guidance as to when a new device feature will constitute a new contrast indication and when it will not. Our members have engaged in extensive evaluation of this definition and the limited hypothetical examples offered in that document and have indicated that the ambiguity in definition and proposed application makes it difficult to provide an effective comment.

In order to fully understand how the Draft Guidance will affect current and future molecular imaging products, as well as product development, we respectfully request FDA to provide more specific information and examples of the device characteristics the Agency will consider in its determination of what is or is not considered a "new contrast indication."

Premarket Approval (PMA) and 510(k) Pathways

Second, we find the Draft Guidance is unclear and inconsistent in defining and describing when FDA will require a company to follow the PMA versus 510(k) pathway. Nor do we agree with the rationale underlying the Agency's presumption that in most cases, a PMA is the appropriate pathway.

Section VI.1. outlines the circumstances under which only a device application is required:

> When an imaging device or device modification enables the device to be used with an *approved imaging drug* (i.e., at its approved formulation, dose, rate, and route of administration) *for a contrast indication that is consistent with the drug's approved indication.* (emphasis added).

The Draft Guidance then in Sections VII.C.1 and VII.C.2 states that "*most* proposed new contrast indications" meeting this criteria *should be sought in a PMA*" (emphasis added)

because "new indications for devices using imaging drugs *are likely* to raise new types of safety and effectiveness questions that require review of a PMA." (emphasis added).

We respectfully disagree with this presumption. Granted, there may be isolated circumstances where a new contrast indication for a device might raise new safety or effectiveness concerns that necessitate submission of a PMA. IMT members, however, believe these circumstances to be the exception rather than the rule. As such, for the majority of cases for which FDA indicates a device application alone is sufficient (*i.e.* use of an approved imaging drug for a contrast indication consistent with the drug's approved indication), we believe the 510(k) process remains the appropriate presumptive pathway.

We perceive that the Draft Guidance is inconsistent on this point. Section VII.C.2 suggests only that submission of a 510(k) "for the new indication *might* be appropriate . . . if the approved imaging drug and cleared imaging device *are already indicated for the same or consistent contrast indication*." Yet, as noted above, Section VII.C.1 indicates that this very situation -- a stand-alone device application for a new contrast indication that is consistent with the drug's approved indications -- will, in most cases, require a PMA.

Given the uncertainty raised by the Draft Guidance, we ask FDA to provide further clarification on this issue. Specifically, we request additional information concerning what criteria the Agency will consider in determining whether a new contrast indication is consistent with the drug's approved indication and also when it raises new safety and effectiveness questions.

Class Labeling

Third, the Draft Guidance uses the terms "classes of drugs" and "classes of devices" in Sections VII.A.1 and VII.A.2. The Draft Guidance specifically discusses the imaging drug class considerations and device class considerations that a manufacturer should follow when developing clinical trials for potential new contrast indications. We appreciate FDA's interest in reducing redundancy in seeking approval for similarly situated products and the potential for expanding the range of imaging products that may be used together.

Nonetheless, the Draft Guidance does not describe how FDA defines a class of drugs or devices for these purposes. We request additional clarification and information on how the Agency intends to define a "class" for purposes of implementing the Draft Guidance.

Stakeholder-FDA Forum

Finally, we would like to supplement our comments through a public forum that would bring together and seek input from both the Agency and industry stakeholders in addressing these important issues. Given the uncertainty of the issues presented, we

believe it would be useful to meet in an open forum to discuss them further. Our members have significant experience and expertise dealing with these issues, and it would be helpful to facilitate a dialogue with Agency staff. We believe such a forum would provide an appropriate venue for industry stakeholders and the Agency to exchange information and provide constructive detail on the Draft Guidance's potential application to existing and future product development. We would respectfully invite Agency staff to participate in a discussion with IMT members in January, and we would be glad to work with you to facilitate such a meeting.

Again, we appreciate the opportunity to comment on this important Draft Guidance. We look forward to your response, and we welcome the opportunity to meet with the Agency to further discuss these critical issues related to molecular imaging.

Respectfully,

Tim McCarthy
President , AMI

Richard Frank, MD, PhD, FFPM
Chairman, IMT

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