Heart House
9111 Old Georgetown Rd.
Bethesda, MD 20814-1699
USA

301-897-5400
800-253-4636
Fax: 301-897-9745
www.acc.org

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

RE: Docket No. 98D-0785 – Revised Draft Guidance for Industry: Medical Imaging Drugs and Biological Products (May 2003)

To Whom It May Concern:

The American College of Cardiology (ACC) and the American Society of Nuclear Cardiology (ASNC) welcome the opportunity to comment on Food and Drug Administration's (FDA) revised draft guidance on medical imaging drug and biological products. The ACC is a 28,000-member nonprofit professional medical society and teaching institution whose purpose is to foster optimal cardiovascular care and disease prevention through professional education, promotion of research, and leadership in the development of standards and formulation of health care policy. ACC represents over 90 percent of the cardiologists practicing in the United States. ASNC is a professional medical society, international in scope, of some 4,300 members which provides a variety of continuing medical education programs related to Nuclear Cardiology, develops standards and guidelines for training and practice, promotes accreditation and certification in this sub-specialty field, and is the principal advocacy voice for Nuclear Cardiology.

The ACC and ASNC appreciate the FDA's willingness to develop this guidance with input from members of the medical imaging community and professional medical organizations. ACC and ASNC have concerns with certain provisions in the draft guidance. They are briefly summarized below by section in which they appear.

Part 1

- Repeat dose toxicity studies in products with long residence time. ACC and ASNC are concerned that FDA proposes to modify its guidance which states that long-term, repeat dose toxicity studies in animals usually can be eliminated, to create exceptions for long residence time. ACC and ASNC question whether the change is necessary as a longer residence time does not necessarily require long-term, repeat dose studies. Further, physicians are not likely to administer frequent, multiple doses of contrast agents or radiopharmaceuticals.

98D-0785 C 30

- Waivers for long-term rodent carcinogenicity studies. ACC and ASNC do not necessarily object to filing a waiver request but question what is accomplished by requiring that a waiver request be submitted for long-term rodent carcinogenicity studies using contrast agents.

- Necessity for expanded single-dose toxicity studies if short-term repeat dose studies have been completed. FDA's June 2000 draft guidance stated that if short-term, repeat-dose studies have already been completed, then non-expanded single-dose studies may be sufficient. ACC and ASNC support retaining this provision in the May 2003 guidance.

- Adverse events causing switch to Group 2 medical imaging drugs. The draft guidance states that in the event of adverse events associated with a Group 1 drug, the drug should be reconsidered as a Group 2 medical imaging drug. ACC and ASNC recommend that a group designation switch should not be made unless the emergent adverse events have potential clinical consequences.

Part 2

- Abnormal anatomy and disease detection claims. The draft guidance provides examples of agents that distinguish between normal and abnormal anatomic structures, and states that 'the agent's ability to outline abnormal anatomy approaches a disease detection indication.' ACC and ASNC suggest that the indication is determined by the labeled claim sought by the manufacturer and that a claim that an agent is effective in distinguishing abnormal structures does not mean that it can detect a specific disease.

- Functional, physiological or biological (FPB) patient assessment. The draft states that a FPB assessment is appropriate for previously-diagnosed patients when new information may be obtained that would have a clinically useful effect on management. ACC and ASNC ask FDA to clarify whether this is true only for patients with a previous diagnosis. Should it not also apply to other patients?

- Functional indication studies. Requiring functional indication to be studied in a wide spectrum of diseases and severity does not appear warranted and dates back to pre-Food and Drug Administration Modernization Act (FDAMA) standards when FDA required separate studies in numerous diseases to support a functional claim.

- Clinical usefulness – structure delineation and disease detection claims. ACC and ASNC request that FDA clarify that Section B (pages 10-11) must be read in conjunction with the introductory comments, since Section B appears to apply to all indications.

- Page 11, line 416 – "both aspects of effectiveness." ACC and ASNC request that FDA clarify what "both aspects of effectiveness" refers to.

Part 3

- Statistical analysis plan and study protocol. ACC and ASNC request that FDA modify the provision that would require a statistical analysis plan to be submitted to the protocol before images have been collected. This is inconsistent with International Conference on Harmonisation Guidelines and should be changed to require submission of the plan before the blinded image evaluations.

- Test drug and comparator compared to truth standard. ACC and ASNC suggest that the truth standard is not appropriate in all cases, such as when the truth standard is no longer the standard of care. We recommend that the comparator be used as the truth standard in appropriate cases.

Again, the ACC and ASNC appreciate the opportunity to provide comments on this draft guidance. Should you have any questions, please do not hesitate to contact Carrie Kovar of ACC at 301-493-2352, or ckovar@acc.org, or James A. Boxall, Jr., ASNC Director, Health Policy, at 301-493-2366 or boxall@asnc.org

Sincerely,

Carl J. Pepine, MD, MACC
President
American College of Cardiology

Ernest V. Garcia, PhD
President
American Society of Nuclear Cardiology

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