POINT BIOMEDICAL

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

Re: Docket No. 98D-0785: Revised Draft Guidance for Industry on Developing Medical Imaging Drugs and Biologics (June 2000)

Dear Sir or Madam:

These comments on Food and Drug Administration's (FDA's) May 2003 draft "Guidance for Industry: Developing Medical Imaging Drugs and Biologics" (hereinafter the "Draft Guidance") are submitted by POINT Biomedical Corporation, a company involved in the research, development and manufacturing of medical imaging drug products.

POINT Biomedical has 2 major comments on the Draft Guidance Part 3:

1. Comparison to an approved agent (page 23, lines 855-869)

POINT Biomedical agrees with the paragraph in the Draft Guidance in its entirety and would not recommend that this section be changed. POINT feels very strongly that it is essential to use the clinically accepted truth standard in clinical trial design. It does not matter whether such a standard is invasive or non-invasive, what is important is that the standard selected has the highest known sensitivity and specificity currently available for the diagnosis of the disease under study. The use of a (non-invasive) less accurate comparator as a de facto truth standard could have serious consequences when considering interpretation of clinical trials. Thus use of such comparators as truth standards will not give the true state of a patient or true value of measurements. For example, the truth standard for the diagnosis of obstructive coronary artery disease is coronary angiography. The standard non-invasive comparator is radionuclide SPECT, but SPECT has only 80% sensitivity and 65% specificity for detection of obstructive coronary artery disease defined by coronary angiography (Fleishman et al. Exercise echocardiography or exercise SPECT imaging? a meta-analysis of diagnostic test performance. *JAMA* 1998; 280: 913-20). Accordingly the use of SPECT alone as both the comparator and the truth standard for presence of obstructive coronary artery disease

would lead to very misleading results if a new imaging modality (Such as ultrasound plus contrast) has superior performance to SPECT in detection of coronary artery disease. Paradoxically, cases in which it was superior would be treated as errors. In other words, use of a comparator known to have less accuracy than the truth standard in detection of certain disease endpoints will not permit an independent way of evaluating the same variable being assessed by the investigational medical imaging agent.

2. Protocol and Nonprotocol images (page 17, lines 625-640)

POINT Biomedical believes that all images specified by the protocol as pertaining to the efficacy end point must be sent to the blinded reader for review and interpretation. Any preselection of images by the investigators or sponsors introduces bias and should not be allowed. For example, in a perfusion imaging study, a video loop might include non protocol wall motion with a single protocol specified still frame indicating perfusion. The data acquisition can be performed such that the machine only acquires the still frame and not the intervening wall motion. The reader then is not biased by wall motion in the overall assessment of the patient. Conversely if the reader is shown a continuous loop but told to make an interpretation by freezing the video loop at a certain point in the cardiac cycle, the read of the protocol image will be contaminated by the non protocol wall motion. POINT believes that the language in the draft guidance (line 628 "primarily" and "ideally" and line 638 "in cases where preselection is thought to be needed") leaves open the potential for bias and should be revised such that image preselection is not used in efficacy determination. Accordingly, we recommend that FDA delete the words "primarily" and "ideally" in line 628, and also delete the sentence regarding preselection in lines 638-640.

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POINT Biomedical Corporation appreciates this opportunity to comment on the new Draft Guidance.

Respectfully,

Lee Rauch

Lee Rauch
Chief Business Officer
POINT Biomedical Corporation