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MEDICAL PRODUCTS DIVISION

February 16, 2000

Dockets Management Branch
Mail Code HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 10-61
Rockville, MD 20852

RE: Docket No. 99D-4396: Draft Guidance for Industry on Financial Disclosure by Clinical Investigators

Dear Sir or Madam:

W. L. Gore & Associates, Inc. would like to thank the agency for preparing the draft "Guidance for Industry—Financial Disclosure by Clinical Investigators." The company appreciates the agency's efforts to provide clarification of this complex issue.

W. L. Gore & Associates, Inc. is a member of the Health Industry Manufacturers Association (HIMA). HIMA has prepared comments on the draft Guidance for Industry on Financial Disclosure by Clinical Investigators. Those comments are attached to this letter.

W. L. Gore & Associates, Inc. would encourage the agency to consider HIMA's comments in its review of the draft guidance.

Sincerely,

Michael C. Morton
Regulatory Associate

99D-4396

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December 23, 1999

Dockets Management Branch
Mail Code HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 10-61
Rockville, MD 20852

Docket No. 99D-4396: Draft Guidance for Industry on Financial Disclosure by Clinical Investigators - Availability

Dear Madam or Sir:

These comments are submitted by the Health Industry Manufacturers Association (HIMA) in response to the FDA's notice announcing the availability of the FDA's Draft "Guidance For Industry - Financial Disclosure By Clinical Investigators." [64 Fed. Reg. 57640 (Oct. 26, 1999).] HIMA is a Washington, D.C.-based trade association and the largest medical technology association in the world. HIMA represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. HIMA's members manufacture nearly 90 percent of the \$62 billion of health care technology products purchased annually in the United States, and more than 50 percent of the \$147 billion purchased annually around the world.

HIMA appreciates the agency's effort to provide additional guidance for the final rule on financial disclosure by clinical investigators. The rule is complex, leading to many questions about its proper implementation. A guidance document will assist manufacturers in compliance. HIMA's comments, including suggestions for additional issues to be addressed in the guidance, appear below.

Section II, p.2 - Financial Disclosure Requirements/Disclosable Financial Information

Under items A. (compensation in which value could be affected by study outcome), B. (proprietary interest), and C. (equity interest whose value cannot be readily determined), it would be helpful to clarify that financial disclosure in these circumstances is required only in the case of studies used to support applications that are submitted to FDA on or after February 2, 1999. This limitation is contained in the December 31, 1998 amplification of the final rule [63 Fed. Reg. at 72173, col. 2.]

Question No. 5 - Definition of "Sponsor"

The guidance document should provide additional assistance to industry by clarifying the entity that is considered to be the "sponsor" of a clinical study for purposes of financial disclosure requirements in the event that more than one company pays for the expenses of the clinical trial. Although the answers to questions 5 and 7 define sponsor to be any party that provides "material support" to the study, this is not a definite enough criterion to be useful to industry. More specific guidance is needed, particularly since joint development agreements have become much more common for industry-supported clinical trials in today's business environment.

HIMA suggests that the guidance document specifically recognize that companies can contractually define in the joint development agreement which company will be the sponsor for purposes of financial disclosure. Another way in which FDA can provide more specific guidance in the case of multiple companies funding a study is to define a funding threshold to determine whether a company is the sponsor. For example, the guidance document can specify that the

company providing the greater percentage of the funding is considered the sponsor for financial disclosure purposes.

In addition, FDA should clarify in the guidance document that in clinical trial programs operated by the government (e.g. NIH) the manufacturer who merely supplies product(s) for testing is not considered the "sponsor" for purposes of financial disclosure requirements.

Question Nos. 8, 13 and 28 - Extent of Recordkeeping Requirements

The guidance document should state in the answer to one, if not all, of these questions that a manufacturer is entitled to rely on financial information provided by the investigator to the company (e.g. in response to a company questionnaire or recorded in the company files after contact with the investigator) as sufficient recordkeeping to comply with the financial disclosure requirements, as long as the information from the investigator contains adequate detail and is properly updated. Such guidance would be consistent with the advice given to industry by Mary C. Gross, Senior Policy Analyst, Office of International and Constituency Relations, Office of the Commissioner, FDA, at the November 1, 1999 Drug Information Association conference in Washington, D.C. on Financial Disclosure by Clinical Investigators.

As FDA is aware, large companies, particularly those with global operations, have multiple divisions and departments from which various types of payments (e.g. cash equivalents or significant payments of other sorts) to investigators can be made (e.g. clinical, professional services, marketing.) It is important for the ease of administration of the financial disclosure requirement that manufacturers not be forced to establish entirely new computer systems or programs to track these corporate payments to clinical investigators. Without an explicit statement by FDA in the guidance that provides manufacturers an assurance that they can rely on responses from clinical investigators, many manufacturers will invest extensive resources into new computer systems or programs to track payments.

As FDA notes in the draft answer to question no. 8, "companies have the flexibility to collect the information in as efficient and least burdensome manner as possible." To ensure this actually is an achievable result for industry, the agency's guidance needs to specify that manufacturers can rely on the disclosures made to them by clinical investigators rather than setting up a separate corporate system to capture this information.

Question No. 10 - Definition of "Clinical Investigator"

Although in general it is helpful to refer to investigator agreements to determine who is a clinical investigator and who is a subinvestigator for the purposes of financial disclosure, the guidance should make clear that the key factor in the determination is the role of the person in the clinical study. The person who makes a "direct and significant contribution to the data" is within the scope of the rule, and not someone who, although part of the investigator agreement, plays a support role in the clinical study. Examples of such supporting personnel include study coordinators, medical device technical support personnel, physician house staff and/or nurses. The guidance document should specifically state that these types of support personnel are not considered to be "clinical investigators or subinvestigators" for the purposes of financial disclosure even if they are listed in the investigator agreement.

In addition, some clarification would be useful about the financial disclosure situation in which an investigator or subinvestigator in a covered clinical study leaves the study or institution prior to its completion. In some cases, a clinical investigator or subinvestigator may have left years before the study is completed. Financial disclosure in this situation would not seem relevant or useful to the agency.

Question No. 11 - Large Multicenter Efficacy Studies

FDA indicates that it considers the financial disclosure reporting requirements to apply to large, multicenter efficacy studies because data from one investigator with a small number of patients may still affect the study results. HIMA believes that FDA should reconsider this interpretation. Ultimately, the purpose of the financial disclosure rule is to minimize bias. Large, multicenter studies have a study design that inherently minimizes bias since the data is aggregated from all participating sites. FDA should therefore exempt these studies from the financial disclosure requirements.

Question No. 12 - Definition of "Completion of the Study"

Completion of the study should be defined as the point at which the last subject has his or her last visit for evaluation of the primary endpoint at the last trial site. This is a more defined point in time for sponsors during a study program and easier to record than the subjective and vague criterion mentioned currently in the agency's draft answer to question no. 12 (when "all study subjects have been enrolled and follow up of primary endpoint data on all subjects has been completed in accordance with the clinical protocol.")

Question No. 17 - Clinical Investigators Outside the United States

Many countries have strict privacy laws to protect financial information. For example, our understanding is that in Germany it is illegal for a company to release any financial information regarding payments to vendors, including clinical investigators. Thus, company records in Germany may not be used as a source for this information but the company can contact the clinical investigator to request that he or she voluntarily provide the information to the company. In addition to the legal issues involved in obtaining financial data in countries outside the United States, there are different cultural perspectives concerning personal privacy.

It would be useful for industry if FDA confirmed, either in the answer to question no. 17 or in a separate question and answer, that sponsors can still include in a covered clinical study an investigator located in a country outside the United States, if the sponsor can demonstrate due diligence in requesting the information from the foreign investigator and if the sponsor can demonstrate the steps it took to minimize the potential for bias in that clinical study.

In addition, it is not uncommon for a company subsidiary in one country to perform a clinical trial with the intent of regulatory approval in the country in which the subsidiary is located and the U.S. subsidiary may later decide to use this study in an application to FDA. The study would not contain any financial disclosure information since it is a clinical study conducted outside the U.S., by investigators located outside the U.S., not under an IDE, and therefore not subject to the financial disclosure rule. It would be useful to industry for FDA to confirm that this type of study is acceptable in an application to the agency under the terms of 21 C.F.R. §814.15 despite the lack of financial disclosure information.

Question No. 22 - Applicability to In Vitro Diagnostic Products

The guidance document should specify that while the testing of in vitro products at a clinical site is considered a 'covered clinical study,' testing of in vitro products performed by a manufacturer's employee(s) within the company's facilities is not a 'covered clinical study.' Although this distinction is made in 21 C.F.R. §54.4, which provides that full-time and part-time employees of the sponsor do not have to submit financial disclosure information, it would be helpful for industry to have this concept reinforced in the guidance document.

The guidance document should also specify that in vitro research studies of medical products involving collection of blood and blood components from routine donors (not for transfusion or re-infusion) are not 'covered clinical studies' for the purpose of financial disclosure. Blood products are commonly obtained from 'subjects' (typically routine, volunteer blood donors) for in vitro evaluation and analysis of medical products to confirm a product's performance prior to conducting a clinical study in which evaluations may be made in vivo. The in vitro evaluation and analysis may be made at a blood bank facility (or within the manufacturer's facility as discussed in the paragraph above.) These types of in vitro analyses should not be considered 'covered clinical studies' because they are not in essence a 'clinical' study - they are not studies performed in humans, but rather are conducted in vitro. In addition, these studies involve non-therapeutic research because they do not produce a diagnostic, preventative or therapeutic benefit to the subject from whom the blood products were obtained. For these reasons, this type of in vitro study should not be subject to the financial disclosure requirement.

* * * *

HIMA appreciates the opportunity to comment on these issues.

Respectfully submitted,

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and Associate General Counsel

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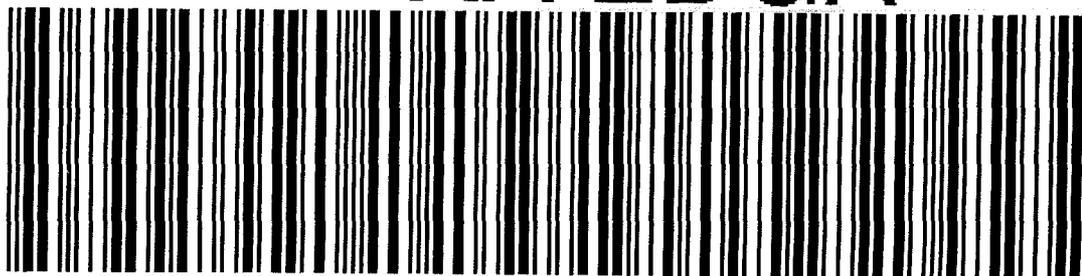
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