



**AMERICAN
SOCIETY FOR
MICROBIOLOGY**

December 7, 1999

4644 '00 JAN 12 P1:44
Public and Scientific Affairs Board

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

RE: Medical Devices: Draft Guidance on Premarket Approval applications for Assays Pertaining to hepatitis C Viruses (HCV) That Are Indicated for Diagnosis or Monitoring of HCV Infection or Associated Disease; Availability.

In response to the notice published October 8, 1999, in the *Federal Register*, the ASM would like to comment on the draft Guidance on Premarket Approval Application for Assays Pertaining to hepatitis C Viruses (HCV).

The American Society for Microbiology (ASM) is the premier education, professional, and scientific society dedicated to the promotion of the microbiological sciences and their application for the common good. The Society represents more than 42,000 microbiologists, including scientists and science administrators in academic, industry and government institutions working in a variety of areas, including applied and environmental microbiology, food science, and medical microbiology.

The ASM applauds the FDA's initiative to offer guidance on premarket approval applications for assays pertaining to hepatitis C viruses. This guidance document is extremely detailed and complete and should be of significant assistance to manufacturers in the design of studies for review of data and preparation of PMAs, as well as for the FDA staff in assisting manufacturers in their review of PMAs. In support of this guidance, the ASM offers the following comments:

Information on the utility of antigen or RNA detection assays should be emphasized, in confirming the presence of an active disease. It is well recognized that RNA is detectable in serum or plasma within a few days of exposure, long before the onset of symptoms, while antibodies are not seen until after the appearance of symptoms and sometimes weeks after that. In that regard, antigenemia and molecular-based tests will be far more useful in confirming the presence of a disease, as opposed to just indicating prior exposure to the virus, which is the role of antibody assays.

The intended use for new tests should be fully and explicitly described, especially discussing the distinct utilities of qualitative vs. quantitative RNA assays. The former could be used for confirmation as well as for following therapy, while the latter has more practicality in following therapy and prognosis. When such intended uses are stipulated, there must be substantial evidence that quantitative testing can monitor the clinical state of the disease.

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When evaluating the specificity of RNA assay agents associated with "other HCV-associated syndromes" are to be tested. The document should stipulate HIV and CMV because of the frequency of co-infection with these specific viruses.

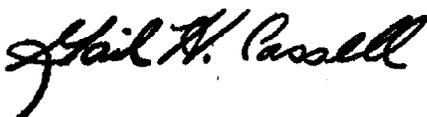
When reporting the results of quantitative assays, consideration should be given to presenting the values in logs, i.e., 6×10^5 , unless the reproducibility and analytical accuracy is determined, or that more precise values are of clinical utility.

When evaluating quantitative assays it is also recommended to select specimens that contain "high concentrations" of the analyte. For instance, some workers feel that RNA assays should be linear enough to detect 1 or 2 million copies of RNA/ml. Current assays (not FDA-approved) will not detect RNA levels greater than 500,000 accurately and the high level controls that are provided are less than 100,000. Furthermore, consideration must be given to the clinical significance of the various detectable levels of HCV RNA.

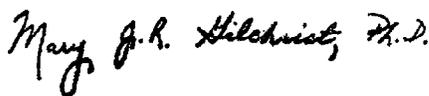
No mention is made of HCV genotyping. The ASM believes this test has a role in the therapy of HCV disease. The type, length, and consequently, the cost of therapy will be affected by the specific genotype. Although these latter issues are not in the FDA's purview, manufacturers will mention them in package inserts and should be considered.

The ASM is pleased to have the opportunity to provide comments on the draft guidance on premarket approval applications for assays pertaining to Hepatitis C viruses. The ASM believes that it will assist manufacturers and the FDA and thus provide an improved diagnostic test for health care providers.

Sincerely,



Gail Cassell, Ph.D.
Chair, Public and Scientific
Affairs Board



Mary Gilchrist, Ph.D.
Chair, Laboratory Practices
Committee



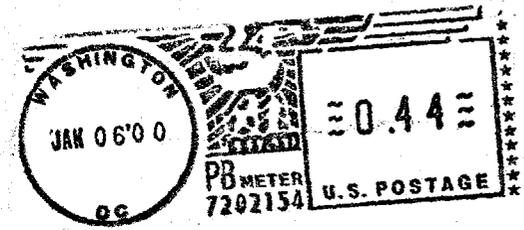
Ronald Zabransky, Ph.D.
Chair, Subcommittee on Microbiology
Devices

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