Global Regulatory Policy

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
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MERCK
Research Laboratories

RE: Docket No. 03N-0158
Proposed Specifications: Annotated Electrocardiographic Waveform Data in Electronic Format

Merck & Co., Inc. is a leading worldwide human health product company. Merck's corporate strategy — to discover new medicines through breakthrough research — encourages us to spend nearly $3 billion annually on worldwide Research and Development (R&D). Through a combination of the best science and state-of-the-art medicine, Merck's R&D pipeline has produced many of the important pharmaceutical and biological products on the market today.

Merck is experienced in submitting both clinical and nonclinical datasets to FDA in accordance with the Guidance, *Providing Regulatory Submissions in Electronic Format – NDAs*. In addition, Merck is an active member of the CDISC Submission Data Standards group. Merck has been involved with CDISC since its inception as both a board member and with membership on several of the working groups. We feel that this experience with both electronic submissions and the CDISC standards qualifies Merck to comment on the proposed specifications, *Annotated Electrocardiographic Waveform Data in Electronic Format*.

Merck supports the Agency's goal of improving the evaluation of specific drug-induced cardiac toxicity by reviewing ECG waveform data with detailed, sponsor-generated annotations from the full spectrum of ECG devices. In general, we found the proposed specifications satisfactory. However, we found the HL7 website very difficult to navigate. While we acknowledge the helpful role that HL7 played in developing the ECG waveform specifications and the ease by which the FDA could link to the HL7 website, we found it difficult to thoroughly review the proposed specifications due to the form in which they appeared. It would be helpful if future versions of the specifications were accompanied by a nontechnical summary that is more relevant to a clinical audience.

Although we found the specifications satisfactory from a technical perspective, the narrative content of the HL7 website describes the process whereby sponsors submit digital ECG data to the Agency, even though a draft Guidance for Industry that describes the submission process has not yet been issued by the Agency. Therefore, we offer the

following comments to assist the Agency when developing the procedure through which digital ECG data is to be submitted by sponsors. In the meantime, we suggest that the HL7 website describe the submission process in very general terms and refer to the upcoming FDA Guidance for details.

The first paragraph of Section 4.1.1.1 states, *Sponsor decides to study effects of drug on cardiac electrophysiology*, without mention of baseline screening ECGs. While it is logical that ECGs from both baseline and on-study weeks should be transmitted digitally, it would be helpful if the FDA Guidance included a description of how sponsors should handle baseline screening ECGs.

The second paragraph of Section 4.1.1.1 mentions that the ECGs are collected from the subject for a visit and transferred to *a central ECG lab* for analysis. Although in many studies, a central laboratory may be used to analyze ECGs, this may not always be the case, especially for small Phase I studies. We recommend that the FDA not mandate that sponsors employ central laboratories to collect ECGs, but rather that the Agency permit sponsors to select the best means of collecting and analyzing ECG data, as study needs dictate.

We appreciate the opportunity to comment.

Sincerely,

Lauren M. Hetrick

for David Blois, Ph.D.
Senior Vice President
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