Alan Goldhammer, PhD
Associate Vice President,
US Regulatory Affairs

PhRMA

2223 '03 APR 28 P3:48

April 28, 2003

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

Re: Docket Nos. 03D-0060, 99D-1458, 00D-1538, 00D-1543, 00D-1542, and 00D-1539; Draft Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures- Scope and Application;" Availability of Draft Guidance and Withdrawal of Draft Part 11 Guidance Documents and a Compliance Policy Guide

Dear Sir/Madam:

The following comments on the above noted draft guidance are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. Our member companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. In 2002, our members invested over $32 billion in the discovery and development of new medicines.

PhRMA welcomes this draft guidance on the scope and application of Part 11 and strongly supports the Agency's adoption of a risk-based approach to compliance. This risk-based approach is, in PhRMA's view, a more realistic and effective way to protect the public health. PhRMA cautions, however, that because Part 11 applies so broadly, affecting companies and products regulated by all the Food and Drug Administration's (FDA's) centers and the Office of Regulatory Affairs, the finalization of this guidance represents a massive undertaking, and much remains to be done. Integrating risk based processes into Part 11 computer system validation, audit trails, and electronic data retention will take time, and this reality should be clearly recognized in FDA's plans for future guidance, enforcement and internal training.

PhRMA is a founding member of the Industry Coalition on 21 CFR Part 11, a group of 14 trade associations that have engaged FDA in a dialogue on regulatory and compliance issues associated with this regulation over the past three years. PhRMA supports the Coalition's comments on this draft guidance. The remainder of this letter details PhRMA's specific points with respect to the draft guidance.

The scope of Part 11 should be further clarified. The guidance currently indicates that Part 11 applies to "records required by predicate rule." Some record keeping requirements are explicitly stated in FDA regulations, while others are implicit. For example, records are kept "to demonstrate compliance" for the engineering design of a sterile facility, for the design of various types of water systems, and for cGMP training, even though in each case there is no record-keeping requirement explicitly stated in the predicate rule. While there is no question that this documentation must be kept, the sponsor will have a process and SOP in place for maintaining

99D-1458 C 9

all relevant records following a risk based approach and insuring product quality. This fits appropriately within the framework that FDA proposes.

Another area in which the scope of Part 11 could be clarified is the definition of legacy systems. It is routine practice to upgrade or otherwise modify systems over time, and the implementation of Part 11 in August 1997 along with the Y2K event accelerated some of these activities. The section on legacy systems does not explicitly address legacy systems that have undergone minor or major modifications since the effective date of Part 11. There is a clear need for a broader definition of legacy system that takes into account the normal maintenance and changes to systems that are necessary to keep them running properly and satisfying the needs of the enterprise. This matter is worthy of ongoing discussion with FDA both in regard to which system modifications present significant compliance concerns under this new definition and how the "exercise of enforcement discretion" will be employed

FDA regulations require clinical investigators to retain records, electronic or paper, for two years following the approval of a marketing application. 21 CFR §312.62(c). There is need for a practical solution for retaining these data "electronically. Although these records theoretically can be kept locally, this usually is not practical or even possible for many sites to manage. One possibility is that data could be maintained by a trusted third party, but this will require revision of GCP guidelines 21 CFR Part 312.62 (b) and (c).

Additional clarification is needed regarding the statement "You should allow inspection, review, and copying of records in human readable form, on your site, using your hardware and software, following your established procedures and techniques for accessing those records." We have no objection to providing an electronic copy of requested records, but electronic inspection and review appear to be new expectations that are potentially in conflict with Section 527.4 in the FDA's Investigations Operations Manual. That reference states that investigators "should not use the audited firm's equipment or personnel to perform extensive queries or manipulation of the audited firm's own computerized data." The Part 11 guidance should be clarified to state "You should make provision for **copying** of records in human readable form, on your site, using your hardware and software, following your established procedures and techniques for accessing those records."

PhRMA trusts that these comments are useful to FDA as this critical guidance document is finalized and looks forward to working with other Industry Coalition members and the FDA on Part 11 issues.

Sincerely,

Alan Goldhamer