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October 22, 2018

Via Electronic Submission

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-N-0377 (83 Fed. Reg. 42,664, August 23, 2018)—Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Tobacco Health Document Submission"

Altria Client Services ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA"), John Middleton Company ("JMC"), Sherman Group Holdings LLC and its subsidiaries ("Nat Sherman"), U.S. Smokeless Tobacco Company LLC ("USSTC"), and Nu Mark LLC ("Nu Mark"),[1] submits these comments to the Food and Drug Administration's ("FDA" or the "Agency") docket entitled "Agency Information Collection Activities; Proposed Collection; Comment Request; Tobacco Health Document Submission" ("Notice").

In April 2010, FDA published draft guidance to clarify the requirements of Section 904(a)(4) of The Family Smoking Prevention and Tobacco Control Act ("TCA")[2] requiring the submission of certain categories of documents.[3] FDA revised the guidance in November 2016 to reflect

[1] PM USA, JMC, Nat Sherman, USSTC and Nu Mark are wholly-owned subsidiaries of Altria Group, Inc. ("Altria"). PM USA manufactures cigarettes, JMC manufactures cigars and pipe tobacco and Nat Sherman manufactures cigarettes, cigars, and pipe tobacco. USSTC manufactures smokeless tobacco products and oral tobacco-derived nicotine products and Nu Mark manufactures e-vapor products. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout to refer to PM USA, JMC, Nat Sherman, USSTC, and Nu Mark.

[2] Public Law 111-31, 123 Stat. 1776, June 22, 2009. Codified at 21 U.S.C. § 301.

[3] We incorporate by reference and attach below our prior submission to this docket entitled "Comments on Agency Information Collection Activities; Proposed Collection; Comment Request; Tobacco Health Document Submission" dated June 10, 2013. See Attachment. That submission is also available at https://www.regulations.gov/document?D=FDA-2013-N-0377-0003.

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changes in the Agency's authority over "deemed" tobacco products and revised the guidance again in October 2017 to reflect various changes to compliance dates. In response to the Notice, we share several suggestions below that would more efficiently implement the TCA. Specifically, FDA should exercise enforcement discretion on redundant health document submissions and FDA should define key terms governing health document submissions.

I. FDA Should Exercise Enforcement Discretion on Redundant Health Document Submissions

The TCA requires manufacturers to submit health documents. FDA has indicated it will exercise enforcement discretion in this area.[4] The related guidance, however, outlines an ongoing, overly broad retention policy that requires manufacturers to "[p]reserve all health documents, including those that relate to products for further manufacturing and those developed after December 31, 2009, for future submission to FDA."[5]

This retention policy "for future submission to FDA" is unnecessary because the TCA provides FDA with multiple means to collect the information necessary to effectively regulate and reduce the harm associated with tobacco products.[6] Rather than rely on this overly broad health documents retention and collection policy, FDA should instead use the best tools at its disposal and only collect the information needed to properly inform a specific issue or question. FDA can best accomplish this by using its authorities under 904(b)(1), ingredient disclosures and the Premarket Tobacco Product Application and Substantial Equivalence processes.

These avenues provide greater focus for targeting relevant information requests. Therefore, FDA should indefinitely suspend the 904(a)(4) health documents submission requirement, which by its very nature, is not focused on a particular product or issue before FDA. If not, thousands of hours will continue to be spent by manufacturers preparing for future submissions and by the Agency in reviewing and processing overly broad, non-specific document productions.

II. FDA Should Define Key Terms Governing Health Document Submissions

If FDA does not suspend the broad health documents submission requirement, it should narrow its scope. The TCA provides FDA with the ability to collect health documents from manufacturers related to "health," "toxicological," "behavioral," or "physiologic" information.[7]

Current FDA guidance does not appropriately define the scope of those terms. For example, the guidance on health documents states, "FDA interprets 'health, toxicological, behavioral, or

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[4] "Although section 904(a)(4) requires ongoing submission of health documents, at this time, FDA does not intend to enforce section 904(a)(4) with respect to documents developed after December 31, 2009." Guidance for Industry, *Health Document Submission Requirements for Tobacco Products (Edition 3)* (Oct. 2017), p. 14, *available at* https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM208916.pdf.

[5] *Id.*

[6] *See, e.g.,* TCA §§ 904(b), 904(c), 905(j), 910.

[7] TCA §§ 904(a)(4), 904(b).

physiologic' broadly to include, for example, cell-based, tissue-based, animal, or human studies, computational toxicology models, information on addiction, intentions to use, cognition, emotion, motivation, and other behavioral effects at both the population-level (epidemiology) as well as the individual level (such as abuse liability)."[8] This type of broad definition is far beyond what was contemplated by the TCA and results in the FDA receiving documents that provide no relevant information to further the TCA's mission. On several occasions we have provided FDA with proposed definitions for these terms that we believe will allow the Agency to receive relevant documents while limiting irrelevant materials. Those definitions are as follows:

- Health Effects – diseases and adverse reproductive effects in humans from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.

- Toxicological Effects – adverse effects in humans, animal, or cells from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.

- Behavioral Effects – dependence, cognitive effects, and behavioral disorders in humans or animals from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.

- Physiologic Effects – changes to processes or functions of humans, animal or cells from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.

Conclusion

We urge FDA to adopt our recommendations as they will help drive simplicity and efficiency into the Agency's regulatory approach. The changes will decrease costs for FDA and regulated entities and help the Agency better focus on its public health mission.

We appreciate the opportunity to provide our input on this Notice and would be happy to discuss our suggestions in more detail. If you have any questions, please contact me at (804) 335-2879.

Sincerely,

[8] Guidance for Industry, Health Document Submission Requirements for Tobacco Products, (Oct. 2017) p. 7. *Available at* https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM208916.pdf

Attachment

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James E. Dillard III
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June 10, 2013

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

Re: Docket No. FDA-2013-N-0377 – Comments on Agency Information Collection Activities; Proposed Collection; Comment Request; Tobacco Health Document Submissions

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments in response to the above-referenced docket and April 10, 2013, Federal Register notice (the "Notice").[2] The Notice seeks input on FDA's collection of health documents created from June 23, 2009 through December 31, 2009.

We attach ALCS' June 2010 comments on FDA's 2010 *Draft Guidance on Tobacco Health Document Submissions*[3]. In our June 2010 comments, we urged FDA to reconsider its recommendation that manufacturers submit health document drafts.[4]

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[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ("Altria"). ALCS provides certain services, including regulatory affairs, to the Altria group of companies. "We" and "our" are used throughout to refer to PM USA and USSTC.
[2] 78 Fed. Reg. 69 (April 10, 2013).
[3] See Docket No. FDA-2009-D-0600
[4] FDA's *Draft Guidance for Industry: Tobacco Health Document Submission* had indicated that manufacturers should produce all drafts of a research study, with the exception of identical copies, and "documents that do not affect the meaning or substance of the [prior] document...."

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We note that FDA's most recent document submission requests have appropriately excluded draft documents.[5] For example, FDA's *Request for Submissions Related to Dissolvable Tobacco Products June 10, 2011* requested "only the final version, or in the absence of a final version, the most recent draft of each document."[6]

We believe this approach reflects an appropriate balance that will provide FDA with information it may find of use while not unduly burdening either manufacturers or the Agency. We encourage FDA to maintain this approach as it considers future document collections.

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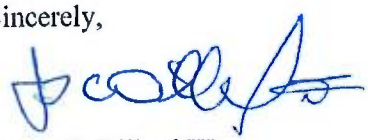
We thank the FDA for this opportunity to provide our views.

Sincerely,



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[5] *See* FDA "Letter: Request for Submissions Related to Menthol" (May 26, 2010) and "Letter: Request for Submissions Related to Dissolvable Tobacco Products June 10, 2011 (Other Tobacco Products Companies)" (June 10, 2011).

[6] *See* "Letter: Request for Submissions Related to Dissolvable Tobacco Products June 10, 2011 (Other Tobacco Products Companies)" page 3.

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January 22, 2010

Division of Documents Management (HFA-305)
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Re: **Docket No. FDA-2009-D-0600**
Comment: Draft Guidance on Tobacco Health Document Submission

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") welcome this opportunity to comment on FDA's Draft Guidance for Industry: Tobacco Health Document Submission, dated December 2009 ("Draft Guidance"), as published at http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm195093.htm.[1]

The Draft Guidance contains a number of recommendations that clarify section 904(a)(4) of the Federal Food, Drug and Cosmetic Act, requiring the submission of certain categories of documents. The Draft Guidance generally encourages tobacco product manufacturers to submit documents to FDA that are relevant;[2] consistent in form and format; timely delivered to the Agency; and accessible for FDA's purposes.

We have been working diligently to comply with section 904(a)(4) and appreciate many of the recommendations the Draft Guidance contains. However, we have several concerns with the breadth of the Agency's interpretations and suggested procedures. In particular, we are concerned that certain procedures are likely to unduly burden tobacco product manufacturers without corresponding benefit to FDA. We also believe it would be impossible for us to implement all of the recommendations within the Draft Guidance's timeframes. Given our substantial experience in managing and producing documents for other purposes, we suggest an alternative and, we believe, more efficient and effective approach.

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[1] PM USA and USSTC are wholly owned subsidiaries of Altria Group, Inc. ("Altria"). Altria Client Services is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs and research and development, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] Section 904(a)(4) requires the submission of documents that relate to "the health, toxicological, behavioral, or physiologic effects of current or future tobacco products....." Throughout this comment, we refer to these as "health documents."

I. The Draft Guidance Provides Recommendations that Facilitate Relevant, Consistent, Timely and Accessible Health Document Submissions.

The Draft Guidance contains certain recommendations that promote relevant, consistent, timely and accessible document submissions by tobacco product manufacturers. We believe that the recommendations, if retained in the final guidance, both serve the goals of the Agency and can be implemented by the companies within the Draft Guidance's timeframes. These recommendations are to:

- organize or label each document according to its relevance to the categories of health, toxicological, behavioral and/or physiologic effects;
- scan and OCR paper documents;
- submit all documents in digital format that is text searchable;
- provide seven objective fields of data for each document;
- Bates number each page;
- translate foreign documents into English; and
- submit a glossary of abbreviations, jargon or internal names found in health documents.

The key recommendation is that the manufacturers submit all documents in text searchable format. That capability will enable the Agency to search, retrieve, organize and evaluate appropriately formatted documents as necessary.

The Draft Guidance also incorporates concepts from the Federal Rules of Civil Procedure ("FRCP") including its definition of "document." While defining the term broadly, the Federal Rules limit the scope of documents subject to production to those that contain relevant information. *See* FRCP 26, 34. The same scope limitation should apply here to limit health document submissions to only those documents that substantively relate to the four topics identified in the statute. Transmittal documents, meeting notices and other types of "transactional" documents that might relate only tangentially to the four topics listed in section 904(a)(4) should be excluded from the submissions.

II. Certain of the Draft Guidance's Recommendations Would Impose Unreasonable Burdens on Manufacturers Without Producing Corresponding Benefits for FDA.

We are particularly concerned with four elements of the Draft Guidance. First, it fails to define section 904(a)(4)'s key terms. Second, it recommends complex classification and coding of health documents. Third, the Draft Guidance recommends that drafts be submitted. Finally, the Draft Guidance's timing and frequency recommendations are unachievable. These elements, if not addressed in the final guidance, will likely result in inconsistent and unnecessarily burdensome health document submissions, and will make the timeframes suggested in the Draft Guidance unachievable.

Each of our specific concerns is discussed more fully below.

- **The Draft Guidance Fails to Define Section 904(a)(4)'s Key Terms.**

The Draft Guidance does not define the key terms that establish the substantive scope of section 904(a)(4). We propose definitions for the terms "health effects," "toxicological effects," "behavioral effects" and "physiologic effects." We developed these definitions using scientific and public health resources[3] to aid us in identifying relevant documents for potential submission under section 904(a)(4).

- Health Effects – diseases and adverse reproductive effects in humans from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.
- Toxicological Effects – adverse effects in humans, animals, or cells from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.
- Behavioral Effects – dependence, cognitive effects, and behavioral disorders in humans or animals from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.
- Physiologic Effects – changes to processes or functions of humans, animals, or cells from exposure to tobacco products, their constituents (including smoke constituents), ingredients, components, and additives.

We request that FDA incorporate these definitions into the final guidance. All tobacco product manufacturers and importers who are subject to the requirements of section 904(a)(4) will be able to comply with its requirements based on a common understanding of its scope.

- **The Draft Guidance Recommends Complex Classification and Coding of Health Documents.**

The Draft Guidance recommends that manufacturers submitting health documents subjectively classify and code the documents by their relevance to the categories of health, toxicological, behavioral and/or physiologic effect and by:

- current or future tobacco products, using unique commercial or identifying names;
- ingredient, using the ingredients listing framework;
- additive, using the ingredients listing framework;
- constituent, using the ingredients listing framework;
- smoke constituent;
- component; and

[3] The resources we consulted include, but are not limited to: CDC Smoking and Tobacco Use website; Society of Toxicology website; Institute of Medicine's "Clearing the Smoke" (2001); and S. Trent Rosenbloom, et al., *Adequacy of Representation of the National Drug Reference Terminology Physiological Effects reference hierarchy for commonly prescribed medications*, American Medical Informatics Annual Symposium Proceedings, 2003.

- keyword, using relevant keywords from the National Library of Medicine's Medical Subject Headings ("MeSH").

We appreciate that FDA is seeking consistency and accessibility when it recommends this complex taxonomy for document classification and coding. Based on our extensive experience with document collection and review, however, we suggest that this taxonomy will not achieve the Agency's intended goal and will lead to less rather than more accessibility to important information in the documents. Additionally, the process is not practicable and will be unduly burdensome for manufacturers. We believe, however, that the recommendation that manufacturers submit documents with full-text search capability, combined with the section 904(a)(1) ingredients listing, other regulatory submissions, and the glossary recommended in the Draft Guidance, will afford FDA effective and efficient access to the health documents it needs.

The classification and coding proposed by FDA is inconsistent with best practices that have developed in the litigation context. Human coding of documents is unavoidably subjective and inconsistent.[4] Consequently, most document productions have moved away from subjective, keyword coding to more reliable objective coding and full-text search capability.

Two of the proposed recommendations illustrate both the burden and limited utility of the Draft Guidance's approach to health document classification and coding.

- Section III(C)(1)(a)(ii) of the Draft Guidance states:

> *FDA requests that you identify constituents and ingredients using the identification framework described in section III.C.3 of the FDA's Final Guidance for Industry: Listing of Ingredients in Tobacco Products...*

Section III(C)(3) of FDA's November 2009 Final Guidance For Industry: Listing Of Ingredients In Tobacco Products[5] establishes the requirements for ingredient identification under section 904(a)(1).[6] Coding each of the thousands of health documents that will be submitted over time under section 904(a)(4) – by ingredient, additive, constituent, smoke constituent and component, as well as by existing and/or

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[4] *See* The Sedona Conference Commentary on the Use of Search and Information Retrieval Methods in E-Discovery, 2007 ("Human review of documents in discovery is expensive, time consuming, and error-prone."); *see also* D.W. Oard, B. Hedin, S. Tomlinson, & J. R. Baron, Overview of the TREC 2008 Legal Track, at p. 18, Table 7 (indicating that there is approximately a 71% rate of agreement among manual assessors of the same documents for the same topics).

[5] *See* http://www.fda.gov/ TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm191982.htm

[6] For example, an ingredient that is a "Complex Purchased Ingredient" must be further classified by: 1) name of manufacturer; 2) uniquely identifying name or number used by the manufacturer; 3) information to uniquely identify each specified ingredient (i.e., all classifications required for an individual ingredient); 4) the quality (e.g., percent purity) of each specified ingredient; 5) the expected function(s) of each ingredient; 6) the internal identification number used by the manufacturer (e.g., SKU, product code); 7) any additional specifications for the complex ingredient (e.g., release specifications, acceptance criteria, a sample certificate of analysis); and, 8) alternative sources of supply for interchangeable ingredients. Thus, the Draft Guidance essentially recommends that a manufacturer submitting health documents containing ingredient information code as many as several dozen (for complex purchased ingredients) additional pieces of information. This simply is not practicable.

"future" products – would present the manufacturers with daunting challenges. Employees charged with document coding (the "coders") must know what ingredients, constituents, etc., have been listed and then look for those words in every health document submitted. For some health documents the task may not be difficult. But for many other documents – such as formal research papers, a scientist's notes, or a lengthy presentation on a relevant study – the task will be exceedingly complex.

- Section III(C)(1)(b) (bullet 3) recommends that tobacco manufacturers:

> *Label each document with relevant keywords – FDA recommends that keywords be chosen from the National Library of Medicine's Medical Subject Headings, available at www.nlm.nih.gov/mesh/*

The Draft Guidance explains that its "keyword" protocol will "ensure accessibility" of tobacco manufacturer documents and "facilitate more fluent and efficient communication" between tobacco manufacturers and the FDA. We respectfully disagree. A keyword classification system such as the MeSH index offers *tens of thousands* of scientific and medical terms from which to choose. Even with comprehensive, ongoing training, it will be impossible to achieve reasonable consistency in applying these keywords to thousands of documents.

An October 2009 solicitation posted by the National Institute of Health's National Library of Medicine ("NLM") illustrates the impracticability of implementing this coding system. The solicitation seeks vendors who can perform MeSH indexing in connection with the posting of life sciences journal articles to the NLM's MEDLINE online resource.[7] Accompanying the solicitation is a 45-page statement of work that lists the training coders are expected to undergo – including a two-month onsite training program at NLM, with weekly follow-on training during the next two years. Even with such training, however, it would be impossible to achieve the consistency necessary to make the results useful to the FDA.

- **The Draft Guidance Recommends that Drafts be Submitted.**

We urge the Agency to reconsider the recommendation that manufacturers submit health document drafts. We do not believe that drafts will be useful to the FDA and may, in fact, complicate FDA's efforts to obtain the information it needs. For example, a final report (including supporting data) on the toxicological effects of an ingredient proposed for inclusion in a tobacco product is likely within the scope of section 904(a)(4). Multiple prior drafts of that report will not reflect final work or final manufacturer views on a given topic, and so will provide no incremental benefit to the Agency.

We will, of course, submit the final (i.e., last created) version of relevant health documents, regardless of whether they are labeled as "Final," "Draft" or not labeled at all. This more targeted, final version approach will not prejudice, and may well simplify, FDA's ability to access tobacco product manufacturers' scientific research. Moreover, section 904(b) permits the Agency to specifically require the companies to provide

[7] *See* Indexing of Journal Articles for MEDLINE, Solicitation Number: NLM-10-001-UHP at https://www.fbo.gov/index?s=opportunity&mode=form&id=3422502f647d2e221c3aee78c5dfd336.

documents on a range of topics, including health documents, at any time. Because we preserve for litigation purposes all health documents – including drafts – such documents will remain available.

- **The Draft Guidance's Health Document Submission Timing and Frequency Recommendations are Unachievable.**

Both the proposed timing and frequency for submissions will present significant challenges. First, FDA should allow 90 days following the submission period cut-off date to complete the collection and preparation of documents. It is not possible to collect, review, scan, OCR and provide even objective coding within 30 days. In a 90-day period, we believe that we will be able to provide health document submissions as described in section I.

If the Agency's final guidance includes classification and coding recommendations, they should apply only to documents developed after January 1, 2011, to permit time for tobacco product manufacturers to adapt their practices. To implement the Draft Guidance's current recommendations, we would need to recruit and train document coders to code existing health documents, and build into our processes and systems ways to automate the capture of this information going forward. This is not work that can be completed in several months.

Second, we urge FDA to recommend annual, rather than quarterly, health document submissions, as stated in the Agency's September 1, 2009 Paperwork Reduction Act ("PRA") notice.[8] An annual schedule will reduce significantly submission of health documents that reflect work-in-progress – documents which are, by definition, incomplete.

Finally, the Draft Guidance's recommendations constitute a substantive and material change to FDA's information request under the PRA. FDA's Federal Register notice under the PRA estimated the reporting burden to be one hour per submission, and represented that the frequency of submissions would be once per year. The one hour per submission estimate is inconsistent with the volume of documents to be submitted, and does not take into account any of the classification and coding recommendations. As such, the Draft Guidance constitutes a "substantive or material modification" to a previously approved information collection request and it should be submitted to OMB for clearance.[9]

[8] 74 Fed. Reg. 45219-20, Table 1 (Sept. 1, 2009)
[9] *See* 5 C.F.R. § 1320.5(g) (2010).

The benefits to both FDA and manufacturers in taking a reasonable approach to section 904(a)(4) submissions are clear.[10] Manufacturers will be able to submit their relevant health documents in a consistent and accessible form. FDA will avoid implementing guidance of limited utility that will introduce unnecessary delays into the process. In addition, we urge FDA not to overlook the challenges it will encounter in storing and managing a collection of electronic documents that will grow with each submission.

III. A Proposal for Developing Final Guidance for Health Document Submissions.

The Agency has invested considerable time and thought in developing the Draft Guidance. However, FDA is not yet familiar with the types of health documents that we develop. If the Agency does not believe it is appropriate to modify the Draft Guidance as we have suggested, we are prepared to submit to the Agency health documents that were developed between June 22, 2009 and December 22, 2009, in compliance with the seven elements discussed in section I, our other proposals and the current April 30, 2010 deadline. With six months' worth of tobacco health documents in text searchable format, the Agency will be better able to evaluate whether it can access and manage the documents to fulfill its regulatory obligations. We believe that this experience with actual health documents will confirm the utility of our recommendations in section I. We further believe that such experience will provide FDA a sound basis to issue final guidance.

In addition to, or in lieu of, this alternative, we stand ready to meet with FDA to provide additional information or to answer any questions that may remain.

We thank the FDA for this opportunity to provide our views on the Draft Guidance.

Sincerely,

James E. Dillard III

[10] The Draft Guidance's approach is at odds with FDA's general approach to document submissions for other products. As the Agency noted in 2009, in its Draft Guidance for Industry, User Facilities and FDA Staff eMDR – Electronic Medical Device Reporting:

> "We believe we should consider the least burdensome approach in all areas of medical device regulation. This guidance reflects our careful review of the relevant scientific and legal requirements and what we believe is the least burdensome way for you to comply with those requirements."