S. Albert Edwards, PharmD, RAC, FRAPS
16 Yorkshire Drive
Lincolnshire, IL 60069

July 21, 2021

Re: Docket No. FDA-2013-P-1509

Dear Dr. Edwards:

This letter responds to your citizen petition received on November 4, 2013, by the Food and Drug Administration (FDA or Agency) and your supplemental petition received on August 3, 2020 (collectively referred to as the Petition), requesting that FDA's Office of Business Informatics (OBI) meet with its Canadian counterparts at the Health Products and Food Branch (HPFB) in the Department of Health Canada (Health Canada) to create a common module 1 for the electronic common technical document (eCTD)/regulated product submissions (RPS).[1]

We have carefully considered the information submitted in the Petition. For the reasons set forth below, your Petition is denied.

I. BACKGROUND

The eCTD is the standard interface and format for submitting applications, reports, amendments, and supplements to FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER).[2] The structure and format of an eCTD submission is largely comprised of a set of standardized specifications, created by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and adopted and implemented by FDA, called the eCTD specification.[3] The eCTD specification helps a regulatory agency receive, process, review, and archive drug development data more efficiently and effectively because the specification is uniformly recognized and adopted by the pharmaceutical industry and regulatory agencies worldwide. While most of the eCTD specification is standardized across regulatory jurisdictions, additional specifications are also

[1] Petition at 1.

[2] The eCTD was developed by the ICH and adopted by FDA. ICH defines *the eCTD* as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, life cycle management, and archiving of the electronic submission. See the ICH M2 EWG electronic common technical document specification, *ICH eCTD Specification V 3.2.2* (ICH M2 eCTD Specifications) available at https://admin.ich.org/sites/default/files/inline-files/eCTD_Specification_v3_2_2_0.pdf. See also FDA's guidance for industry *Providing Regulatory Submissions in Electronic Format–Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (Revision 7) (February 2020) (eCTD Guidance); see also FDA's website on the Electronic Common Technical Document (eCTD), available at https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://fda.gov/regulatory-information/search-fda-guidance-documents.

[3] See FDA's eCTD Guidance.

often applied based on regional need. In the case of a submission made to FDA, the Agency layers additional and sometimes unique specifications onto its eCTD requirements, including PDF, transmission, file format, validation criteria, and supportive file types.[4] Other regional authorities often do the same based on specific requirements found in their drug regulatory schemes.

The eCTD is based on the Common Technical Document (CTD) format and contains five modules: (1) region-specific administrative information and prescribing information; (2) summary documents; (3) quality-related information (chemistry and manufacturing controls (CMC)); (4) nonclinical study reports; and (5) clinical study reports.[5] There are two categories of modules: regional (specific to each region) and common (common to all regions). The CTD, issued by the ICH and adopted across regulatory jurisdictions, describes the content of the common modules (modules 2, 3, 4, and 5), while the content of module 1 is described in documents issued by individual regions. The ICH acknowledges that due to the significant differences in documentation requirements across regions it is not expected that a single, global eCTD submission could be constructed and transmitted to multiple regions with each regional authority ignoring or deleting other regions' submission material.[6]

The eCTD module 1 was designed to capture regional requirements, specifically the administrative and prescribing information, such as the product information and labeling required by regional regulators.[7] For example, FDA asks for a cover letter and reviewer's guide, patient experience data, cross reference documents, labeling history, labeling samples, advertising and promotional material, marketing annual reports, information amendments, letters of authorization, field copy certifications, and Risk Evaluation and Mitigation Strategies (REMS) to be included in module 1 of a submission.[8] Specific file formats and backbone structure are required for this information to be processed by the Agency.[9] The contents and specifications outlined for FDA's module 1 are largely unique to the U.S. regulatory scheme.[10] Canada asks for its own set of content, format, nomenclature, and backbone specifications for its module 1 that differ from the U.S. module 1.[11] These differences are based on each region's unique regulatory scheme and drug approval pathways and are normally found in each region's intake and processing/validation criteria.

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[4] For the most recent versions of FDA's technical specifications, see the Agency's Electronic Common Technical Document (eCTD) website, available at https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd.

[5] See ICH M2 eCTD Specifications for further descriptions of the various modules.

[6] Id.

[7] Id.

[8] See FDA's *eCTD Technical Conformance Guide* (July 2020), available at https://www.fda.gov/media/93818/download.

[9] See FDA's eCTD Guidance; FDA's *Specifications for File Format Types Using eCTD Specifications* (August 2019), available at https://www.fda.gov/media/85816/download.

[10] See FDA's *The eCTD Backbone Files Specification for Module 1* (November 2020), available at https://www.fda.gov/media/76776/download. See also ICH M2 eCTD Specifications: "This module [1] contains administrative information that is unique for each region. Regional guidance will provide the specific instructions on how to provide the administrative forms and detailed prescribing information."

[11] See Health Canada's eCTD guidance documents, available at https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/ectd.html.

II. DISCUSSION

The Petition requests that FDA and Health Canada create a common module 1 for use by both countries.[12] It claims that based on the geographic proximity of the United States and Canada, a common module 1 would ease the filing burden for many regulated firms conducting business in both countries because it would simplify the filing process.[13] The Petition also claims a common module 1 would make it easier for FDA's OBI staff to process submissions.[14]

The eCTD (and the CTD on which eCTD is based) was intended to include modules that would contain common and standardized information needed for drug development across regions, and a module that would allow each region to incorporate information unique to the individual region.[15] Modules 2, 3, 4, and 5 of the eCTD contain scientific and technical information that is specific to the drug, such as current good manufacturing practices, CMC and clinical and non-clinical study reports.[16] The regulatory requirements for this type of information have been largely standardized worldwide and are appropriate for use in common modules. Module 1 of the eCTD, however, contains administrative information that is specifically required by an individual region's regulatory scheme. Module 1 does not prevent different regions from harmonizing, but harmonizing Module 1 would first require harmonization of regulatory requirements across regions. Doing so typically would entail a significant commitment from the regions involved.

FDA's eCTD module 1 is based on the Agency's unique regulatory and submission processing requirements.[17,18] While it may contain some similarities, Health Canada's eCTD module 1 is tailored to its own regulatory requirements, which differ from FDA's requirements.[19] For a harmonized module 1 to be useful to both countries, the United States and Canada would first have to harmonize their regulatory requirements and approval standards for drug and biological products.

The Petition claims that the burden on regulated industry doing business in both countries would be reduced by harmonizing module 1.[20] While FDA cannot definitively speak to whether

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[12] Petition at 1.
[13] Id.
[14] Id.
[15] See ICH M2 eCTD Specifications: "This document describes the parts of the registration application that are common to all regions and some of the life cycle requirements for products. The parts of the registration application that are specific to a region will be covered by regional guidance. However, this backbone has been developed to handle both the regional and common parts of submissions."
[16] See FDA's guidance for industry *M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use* (October 2017).
[17] See, e.g., 21 CFR 314.50.
[18] See e.g., FDA's *The eCTD Backbone File Specifications for Module 1* (November 2020), available at https://www.fda.gov/media/76776/download; FDA's *eCTD Technical Conformance Guide* (July 2020), available at https://www.fda.gov/media/93818/download.
[19] See Canadian Food and Drugs Act (R.S.C., 1985, c. F-27) as amended, available at https://laws-lois.justice.gc.ca/eng/acts/F-27/index.html; Canadian Food and Drug Regulations (C.R.C., c. 870) as amended, available at https://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._870/index.html.
[20] Petition at 1.

harmonization of module 1 would lead to a burden reduction for regulated industry, we are not persuaded that harmonization of module 1 alone would save a significant amount of time or effort for submitters. FDA and Health Canada have separate legal authority, regulations, and processing systems. Therefore, regardless of a harmonized eCTD module 1, submissions would still have to comply with the different regulatory and submission requirements of each country. While harmonization of eCTD module 1 would mean that a submitter could prepare a single eCTD module 1 for both the United States and Canada, separate approval packages would still have to be created and separate country-based filing validation requirements would have to be met. For example, FDA requires most regulatory submissions to be submitted electronically using specific formats that must pass an FDA-specific validation system to be accepted for review.[21] Thus, unless Health Canada's submission and filing system were identical to the one used by FDA, and it is not, we are not persuaded that a common module 1 would substantially reduce a submitter's filing burden.

The Petition also claims that harmonization of module 1 would make it easier for FDA to process electronic submissions. We disagree. As an initial matter, it is difficult to assess whether and to what extent FDA would achieve process efficiencies if it were to harmonize module 1 with Health Canada. But even if could result in process efficiencies, such efficiencies would need to be weighed against the time and resources required to harmonize eCTD module 1 across the two jurisdictions. To utilize a harmonized eCTD module 1 that changes our current review processes or information requirements, FDA likely would need to revise a number of our regulations and guidance documents; revisions that would take time and resources to accomplish. Moreover, FDA's use of a harmonized eCTD module 1 with its new format and information content likely would take additional time and effort to implement within the Agency's review divisions and could at least initially slow down the drug approval process as the Agency transitions to the new module. Consequently, FDA has not determined that harmonizing eCTD module 1 would generate efficiencies that would justify its implementation, nor would it lessen the burden on submitters and the Agency as the Petition claims. While FDA and other drug regulatory agencies worldwide embrace and encourage efforts designed to implement data standardization, we are currently focused on efforts other than creation of a common eCTD module 1. Moreover, under the current global healthcare environment, i.e., the coronavirus disease 2019 (COVID-19) pandemic, FDA and Health Canada are unlikely to make this harmonization initiative a high priority at this time.

III. CONCLUSION

As explained above, the Agency has not determined that harmonizing eCTD common module 1 with Health Canada would significantly reduce the filing burden on either submitters or FDA. While the Agency continues to look for ways to improve its drug submission process, the Petition has not convinced FDA that harmonizing eCTD module 1 with Health Canada would advance that goal at this time. Accordingly, your Petition is denied.

[21] See FDA's eCTD Guidance.

Sincerely,

Douglas C. Throckmorton -S

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Patrizia Cavazzoni, M.D.
Acting Director
Center for Drug Evaluation and Research