U.S. FOOD & DRUG
ADMINISTRATION

Plan for

Issuance of Patient-Focused Drug Development Guidance

Under

21st Century Cures Act

Title III Section 3002

May 2017

This document outlines FDA's plan for development of the guidance required under Section 3002 of the 21st Century Cures Act. The statute specifies that FDA develop one or more guidances over a period of five years regarding the collection of patient experience data[1], and the use of such data and related information in drug development. The FDA plan targets the development of several guidances within the next five years. Table 1 provides a summary of key steps FDA will take over the next five years.

Background

Patients who live with a disease have a direct stake in drug development and in the outcome of the FDA review process for new drugs. Patients are also in a unique position to contribute to an understanding of benefit and risk considerations throughout the medical product development process. Under the 2012 FDASIA reauthorization of the Prescription Drug User Fee Act (PDUFA), FDA pioneered the use of patient focused drug development (PFDD) meetings[2] to help address the need for systematic collection of direct patient input. The twenty-two PFDD meetings we have held so far have each focused on a different disease area and have identified key findings including that patients living with a disease are experts on what it is like to live with the condition. In addition, the meeting highlighted that what patients care most about may not always be factored into clinical trials or approved labeling.

However, PFDD meetings alone will not address gaps in information on the patient perspective. Our next step is to bridge from PFDD-type meetings to methodologically sound fit-for-purpose tools to systematically collect key information about patients' experience (e.g., in clinical trials) including the burden of disease, benefit and burden of a therapy. Ideally, these patient-identified disease impacts, and potential measures of benefit and burden, would be explicitly considered from the early stages of drug development. In addition, these patient-identified key impacts and elements of disease experience could be translated into a measurement set that is validated for clarity to patients, reliability in capturing their reported experience, and responsiveness of the reporting scale to reflect changes in experience. For a given disease the set of elements used in different clinical studies would ideally reflect those that patients have identified as mattering most to them.

21st Century Cures Act -- Directing and Enabling Patient Focused Drug Development

[1] The statute defines patient experience data to mean data collected by any person (including patients, family members, and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers) that are intended to provide information about patients' experiences with a disease or condition. The term specifically includes data regarding (a) the impact of the disease or condition, or a related therapy, on patients' lives; and (b) patient preferences with respect to treatment of the disease or condition. (Section 3002(b))

[2] https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm368342.htm

On December 13, 2016, the 21st Century Cures Act (the Act) was signed into law and created for FDA both new directives and new opportunities to advance the science and efficiency of medical innovation in order to further address the critical unmet needs of US patients. Title III Section 3002 requires FDA to issue new guidance regarding methods and approaches to be used in capturing and measuring patients' experiences and perspectives. The Section further requires that FDA develop a plan for the issuance of draft and final versions of "one or more guidance documents over a period of 5 years," to address a series of topics outlined in the statute that will be of interest to stakeholders wishing to participate in or engage in patient focused drug development. This document provides the agency's plan.

In directing FDA to develop new guidance, Section 3002(c) specifies the content that should be addressed as follows:

(1) methodological approaches that a person seeking to collect patient experience data for submission to, and proposed use by, the Secretary in regulatory decision making may use, that are relevant and objective and ensure that such data are accurate and representative of the intended population, including methods to collect meaningful patient input throughout the drug development process and methodological considerations for data collection, reporting, management, and analysis;

(2) methodological approaches that may be used to develop and identify what is most important to patients with respect to burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease;

(3) approaches to identifying and developing methods to measure impacts to patients that will help facilitate collection of patient experience data in clinical trials;

(4) methodologies, standards, and technologies to collect and analyze clinical outcome assessments for purposes of regulatory decision making;

(5) how a person seeking to develop and submit proposed draft guidance relating to patient experience data for consideration by the Secretary may submit such proposed draft guidance to the Secretary;

(6) the format and content required for submissions under this section to the Secretary, including with respect to the information described in paragraph (1);

(7) how the Secretary intends to respond to submissions of information described in paragraph (1), if applicable, including any timeframe for response when such submission is not part of a regulatory application or other submission that has an associated timeframe for response; and

(8) how the Secretary, if appropriate, anticipates using relevant patient experience data and related information, including with respect to the structured risk-benefit assessment framework

described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decision making.

These provisions of Section 3002 provide several critical components that will serve to advance patient-focused drug development. The sections that follow provide more detail on the approach and planned time frames for implementation. Table 1 shows the targeted time frame for implementation of the provisions of Section 3002 over the next five years. The chart shows milestones, including planned public workshops, issuance of draft guidance, and issuance of final guidance.

Plan for Implementation of Section 3002(c)(1) Through (4)

Provisions (c)(1) through (4) of Section 3002 address methods and approaches that can be used by drug sponsors, patient advocacy groups and others to more systematically collect and rigorously measure disease and treatment impacts that matter most to patients. To implement these provisions, FDA intends to issue a series of four guidance documents to focus on approaches and methods to bridge from initial patient-focused drug development meetings to fit-for-purpose tools to collect meaningful patient and caregiver input for ultimate use in regulatory decision making.

FDA plans to conduct a public workshop prior to the issuance of each of the draft guidances, to gather input from the wider community of patients, parents, caregivers, patient advocacy organizations, academic and medical researchers, expert practitioners, industry, and other stakeholders and inform the draft guidance.

To address Section 3002(c)(1), by the end of the second quarter of calendar year (CY) 2018, FDA will publish a draft guidance describing approaches to collecting comprehensive and representative patient and caregiver input on burden of disease and current therapy. This draft guidance will address topics including: standardized nomenclature and terminologies, methods to collect meaningful patient input throughout the drug development process, and methodological considerations for data collection, reporting, management, and analysis.

To address Section 3002(c)(2), by the end of the second quarter of CY 2019, FDA will publish a draft guidance describing processes and methodological approaches to development of holistic sets of impacts that are most important to patients. The draft guidance will address topics including: methods for sponsors, patient organizations, academic researchers, and expert practitioners to develop and identify what are most important to patients in terms of burden of disease, burden of treatment, and other critical aspects. The draft guidance will address how patient input can inform drug development and review processes, and, as appropriate, regulatory decision making.

To address Section 3002(c)(3), by the end of the second quarter of CY 2020, FDA will publish a draft guidance describing approaches to identifying and developing measures for an identified set

of impacts (e.g., burden of disease and treatment), which may facilitate collection of meaningful patient input in clinical trials. The draft guidance will address methods to measure impacts in a meaningful way, and identify an appropriate set of measure(s) that matter most to patients.

To address Section 3002(c)(4), by the end of the second quarter of CY 2020, FDA will publish a draft guidance on clinical outcome assessments, which, when final, will, as appropriate, revise or supplement the 2009 Guidance to Industry on Patient-Reported Outcome Measures. The draft guidance will also address technologies that may be used for the collection, capture, storage, and analysis of patient perspective information. The draft guidance will also address methods to better incorporate clinical outcome assessments into endpoints that are considered significantly robust for regulatory decision-making.

It is anticipated that these draft guidance documents, when finalized, will provide industry sponsors with the information needed to support the integration of patient experience in their drug development programs, and will also help guide next steps that external stakeholders (e.g., patient advocacy groups, researchers, industry and others working via public-private partnerships) may want to undertake to develop tools in a given disease area, e.g., in a precompetitive environment via Drug Development Tool qualification.

For each of the guidance documents identified above FDA will issue the final guidance eighteen months after the close of public comments on the draft guidance.

Plan for Implementation of Section 3002(c)(5)

Section 3002(c)(5) requires FDA to issue guidance on how a person seeking to develop and submit proposed draft guidance relating to patient experience data for consideration by FDA may submit such proposed draft guidance to the agency. This information may be particularly useful to persons with particular knowledge of, or access to, the patient community, including both patients and caregivers dealing with a particular disease, as well as others. The guidance required by Section 3002(c)(5) should cover both the work products generated by public stakeholders that could be helpful to submit as proposed draft guidances, and other documents and work products that stakeholders may develop related to patient experience that may provide helpful information to support patient-focused drug development.

Proposed draft guidance that may specially benefit from the experiences and insights of persons with particular knowledge of or access to the patient community may include documents that address the planning and conduct of clinical trials to be more patient focused, enhancing patients' ability to enroll and continue to sustain participation in clinical studies, and the quality of their experiences as participants in such studies. It might also include proposed draft guidance that adds to an existing guidance document to further address special considerations for enrolling patients or conducting trials with a particular disease focus, or the special needs of a patient subpopulation (e.g., a pediatric, elderly, or a subpopulation with particular co-morbidities).

Another potential area of opportunity may concern development of proposed draft guidance that adds to existing guidance on disease-specific endpoints that may be considered for inclusion in clinical development programs in that disease area.

To address Section 3002(c)(5), FDA will issue draft guidance by the end of the first quarter of CY 2018 and will issue final guidance eighteen months after the close of public comments on the draft guidance.

Plan for Implementation of Section 3002(c)(6)

Section 3002(c)(6) requires FDA to issue guidance on *the format and content* required for submissions to FDA under Section 3002, including with respect to the information described in paragraph (1). To meet this requirement, FDA plans to address the format and content requirements within the body of each of the guidance documents that will cover particular approaches and methods for identifying, measuring and collecting patient experience data, where appropriate in the guidance developed under Section 3002(c)(1) through (4).

Plan for Implementation of Section 3002(c)(7)

Section 3002(c)(7) requires FDA to issue guidance on how the agency intends to respond to submissions of information described in paragraph (1), if applicable, including any timeframe for response when such submission is not part of a regulatory application or other submission that has an associated timeframe for response. FDA recognizes that the guidance developed under Section 3002(c)(1) through (4) will inform both the work of drug sponsors working to collect patient experience data to advance proprietary drug development programs and the work of patient advocates, sponsors, and other organizations that may work individually or collaboratively to develop collection tools for qualification and public availability as drug development tools (DDTs). These guidances will address, when appropriate, how the FDA will respond to submissions of information in each guidance developed under section 3002(c)(1) through (4).

Guidance on how the agency intends to respond and timeframes for response to submissions made for the DDT qualification program for Clinical Outcome Assessments and Patient Reported Outcomes will also be included and addressed in the guidance issued to implement the Section 3011 process for qualification of DDTs. FDA plans to issue this draft guidance by the end of the fourth quarter of CY 2019 and to issue final guidance six months after the close of the public comment period for the draft guidance.

Plan for Implementation of Section 3002(c)(8)

Section 3002(c)(8) requires FDA to issue guidance on how the agency, if appropriate, anticipates using relevant patient experience data and related information, including with respect to the

structured risk-benefit assessment framework described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decision making. As appropriate, FDA will integrate into its clinical review templates the regulatory review and decision making considerations developed and included in the guidance under provisions (1) through (4) of Section 3002.

The agency will also integrate this information into the further development of the benefit risk assessment framework for new drugs and biologics. To further inform the development of this guidance, FDA will hold a public meeting by the end of the second quarter of CY 2019. FDA will publish a draft guidance on benefit-risk assessments for new drugs and biologics that will articulate FDA's decision-making context and framework for benefit-risk assessment, including the integration of patient experience data available for that assessment. The draft guidance will illustrate the application of the benefit-risk framework throughout the human drug lifecycle, using a case study approach, if appropriate, and discuss appropriate interactions between a sponsor and FDA during drug development to understand the therapeutic context (i.e., the severity of disease that represents the targeted indication and the extent of unmet medical need in the target population) regarding regulatory decisions for the product at the various stages of drug development and evaluation.

To address Section 3002(c)(8), FDA will issue draft guidance by the end of the second quarter of CY 2020 and will issue final guidance eighteen months after the close of public comments on the draft guidance.

Summary

Title III of the 21st Century Cures Act gives FDA both new directives and new opportunities to advance the science and efficiency of medical innovation to address the critical unmet needs of US patients. In FDA's work to meet key PDUFA commitments under FDASIA, the agency learned that a more systematic and rigorous approach to collecting the patient's perspective and patient experience data was needed to better advance patient-focused drug development. Key provisions of Section 3002 address this important need to more comprehensively and systematically include the patients' perspectives and experience with a disease or condition, and experience and preferences related to therapy, into drug development. FDA plans an approach that will feature public workshops to inform and precede the issuance of draft guidance documents to address the contents specified under Section 3002(c)(1) through (8), and will plan to issue final guidance 180 days after the close of public comments on draft guidance. These guidances will provide information that FDA, patient stakeholders, researchers, and regulated industry have identified as important to continued progress in developing new medicines to respond to patients' needs.

Table 1 – Planned Timeframe for Guidance Development

21st Century Cures Act	CY 2017	CY 2018	CY 2018	CY 2019	CY 2019	CY 2020	CY 2020	CY 2021	CY 2021
Provisions of Section 3002	**Q4**	**Q2**	**Q4**	**Q2**	**Q4**	**Q2**	**Q4**	**Q2**	**Q4**
(1) methodological approaches that a person seeking to collect patient experience data for submission to, and proposed use by, the Secretary in regulatory decision making may use, that are relevant and objective and ensure that such data are accurate and representative of the intended population, including methods to collect meaningful patient input throughout the drug development process and methodological considerations for data collection, reporting, management, and analysis; (6) the format and content required for submissions	Q4 2017: Public Workshop	Q2 2018: Draft Guidance				Q1 2020: Final guidance			
(2) methodological approaches that may be used to develop and identify what is most important to patients with respect to burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease; (6) the format and content required for submissions			Q4 2018: Public Workshop	Q2 2019: Draft Guidance				Q1 2021: Final guidance	
(3) approaches to identifying and developing methods to measure impacts to patients that will help facilitate collection of patient experience data in clinical trials; (6) the format and content required for submissions					Q4 2019: Public Workshop	Q2 2020: Draft Guidance			Q4 2021: Final guidance
(4) methodologies, standards, and technologies to collect and analyze clinical outcome assessments for purposes of regulatory decision making; (6) the format and content required for submissions				Q2 2019: Public Workshop		Q2 2020: Draft Guidance			Q4 2021: Final guidance
(5) how a person seeking to develop and submit proposed draft guidance relating to patient experience data for consideration by the Secretary may submit such proposed draft guidance to the Secretary;		Q1 2018: Draft Guidance			Q4 2019: Final guidance				
(6) the format and content required for submissions under this section to the Secretary, including with respect to the information described in paragraph (1); SEE guidance for (1) through (4) above									
(7) how the Secretary intends to respond to submissions of information described in paragraph (1), if applicable, including any timeframe for response when such submission is not part of a regulatory application or other submission that has an associated timeframe for response; and					Q4 2019 : Draft Guidance		Q3 2020: Final Guidance		
(8) how the Secretary, if appropriate, anticipates using relevant patient experience data and related information, including with respect to the structured risk-benefit assessment framework described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decision making				Q2 2019: Public Workshop		Q2 2020: Draft Guidance			Q4 2021: Final guidance