

Implementing the 21st Century Cures Act: Supporting Orphan Drug Development



**Rare Disease Congressional Caucus Briefing
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Energy & Commerce Subcommittee on Health



- Frank Sasinowski’s testimony at this 1st hearing focused on expanding use of Subpart H/Accelerated Approval pathway and importance of including patient voice in FDA regulatory processes

Topic 1 – Patient Experience Data

1. Patient Experience Data



- Pure Food & Drug Act (1902): Nation's 1st Law on Medicines
- FDASIA Law (2012) directs FDA
 - “to develop and implement strategies to solicit the views of **patients** during the medical product development process and consider the perspectives of patients during regulatory discussions”
- 21st Century Cures significantly expands this, recognizing the role for those to be benefitted by medicines: **patients!**

1. Patient Experience Data



- Section 3001 requires FDA to state the “patient experience data” submitted/reviewed as part of an NDA/BLA. This section is effective 180 days after the date of enactment.
- Section 3002 requires FDA issue guidance documents, over 5 years, on the collection and use of patient experience data.
- Section 3004 requires FDA to issue reports in June 2021, 2026, and 2031 on the use of patient experience data.

1. Patient Experience Data

Opportunities for Patient Experience Data

- April 25, 2015: PCNS Advisory Committee meeting for eteplirsen
 - JF provided a written report of findings to the committee (<http://bit.ly/JFreport>)
 - Christine McSherry of JF is *the first ever* patient advocate to present during “core” sponsor presentation (<https://youtu.be/-rtiH2oGwOo>)



1. Patient Experience Data

Opportunities for Patient Experience Data

➤ A Patient Representative as part of FDA Review Team

- Ms. House is Chair of the International Pompe Association
- As a Patient Representative, she was consultant to FDA Division of Neurology Products & ad hoc member of the Advisory Committee for Myozyme
- After the Myozyme review, FDA medical reviewers have stated that they learned from Ms. House that being stable for a person with a uniformly progressive disease is a HUGE benefit
- Patient perspective is a key factor for evaluating both safety and efficacy



Ms. House speaking at FDA's Inaugural Rare Disease Patient Advocacy Day on March 1, 2012

1. Patient Experience Data



Opportunities for Patient Experience Data

➤ Patient Surveys

- Huntington's Disease Society of America, presented the findings of a survey at an FDA PFDD meeting on September 22, 2015
- Highlighted that opinions of the most impactful symptoms vary between patient and neurologist:
 - Patients rated declines in cognitive and executive functions and inability to work as among the most impactful symptoms
 - Neurologists rated chorea and ability to speak clearly as most impactful symptoms and did not even recognize ability to work as an issue at all for patients



1. Patient Experience Data



Opportunities for Patient Experience Data

➤ Externally-Led PFDD Meetings

- Under PDUFA V, CDER/CBER led 20+ disease-specific PFDD meetings
- In December 2015, CDER announced opportunity for patient groups to host externally-led PFDD meetings
- *First ever* externally-led PFDD meeting was hosted by the Myotonic Dystrophy Foundation on September 15, 2016
 - Attended by several FDA officials, including Drs. Woodcock, Goldsmith, and Dunn
 - Several more scheduled for 2017
- Externally-submitted “Voice of the Patient” reports will be posted on FDA website



MYOTONIC
DYSTROPHY
FOUNDATION

1. Patient Experience Data



- Opportunities for Patient Experience Data
 - Commitments and resources for patient engagement in PDUFA 6 (you'll hear more in the next presentation)
 - Monitor issuance of FDA guidance documents and reports to ensure FDA endorses a broad range of opportunities for patient input
 - Keep an ear to the ground with rare disease patient organizations like the EveryLife Foundation

Topic 2 – Qualification of Drug Development Tools

2. Qualification of Drug Development Tools



- Directs FDA to establish process for qualification of drug development tools (i.e., biomarker, clinical outcome measure)
- Timeframes: 2 years for public meeting, 3 years to issue guidance, 5 years to issue report

2. Qualification of Drug Development Tools



- Need oversight to ensure it is used to reform the existing, overly-cumbersome qualification program

	All Drug Development Tool (DDT) Qualification Programs	DDT - Animal Model Qualification Program	DDT - Biomarker Qualification Program	DDT - Clinical Outcome Assessments
Total Number of Active Projects	79	8	23	48
Number in <i>Initiation Stage</i>	22	3	4	15
Number in <i>Consultation and Advice Stage</i>	49	5	15	29
Number in <i>Review Stage</i>	8	0	4	4
Number Qualified	8	0	6	2

Source: FDA.gov (ucm409960), last accessed 1/6/17

Topic 3 – Priority Review Vouchers

3. Priority Review Vouchers



- Reauthorized FDA's rare pediatric disease PRV program by extending sunset date from December 31, 2016 to September 30, 2020.
 - If a drug is designated as a drug for a “rare pediatric disease” prior to September 30, 2020, it is eligible for a pediatric PRV if it is approved by September 20, 2022.
- Requires GAO to conduct a study and issue a report that evaluates the PRV programs (due Jan. 31, 2020).

Topic 4 –
Regenerative Advanced Therapies (RAT)

4. Regenerative Advanced Therapies



- Section 3033 creates process and requirements for designating a drug as a RAT
 - Noteworthy effect of designation: ***eligible for accelerated approval*** under current FDA preapproval standards but with new postapproval requirements
 - Therefore, RAT is an opportunity to increase the visibility and use of accelerated approval as it is one visible sign of movement to expand use of accelerated approval beyond cancer and AIDS
- Section 3034 - requires FDA to issue guidance within 1 year
- Section 3035 - requires HHS to report annually to Congress the ***number of applications granted accelerated approval***

4. Regenerative Advanced Therapies



- When providing oversight:
 - Ask whether FDA and sponsors routinely consider whether therapies could be candidates for accelerated approval at key FDA-sponsor meetings and Advisory Committee meetings (major recommendation of Sasinowski in May 2014 testimony)
 - Ask whether FDA has utilized new options for postapproval requirements for accelerated approvals (e.g., clinical studies; patient registries; other sources of real world evidence, such as electronic health records; or postapproval monitoring of all patients treated with such therapy prior to approval of the therapy)
- Opportunities:
 - Technical amendment to explicitly include gene therapies in definition of RAT
 - In PDUFA 6, expand this designation and its benefits (e.g., relaxing postapproval requirements under accelerated approval) to other innovative categories of therapies (such as anti-sense oligonucleotides or ASO therapies, e.g., Spinraza approved Dec. 23, 2016 for spinal muscular atrophy, including “floppy babies”).

Topic 5 – Targeted Drugs for Rare Diseases

5. Targeted Drugs for Rare Diseases



- For genetically targeted drugs to treat serious and life-threatening rare diseases that meet unmet medical needs:
 - Allows FDA, consistent with its existing approval standards, for a genetically targeted drug (i.e., a drug that modulates function of a gene) or a variant protein targeted drug to rely on data and information that was previously developed by the same sponsor and that was submitted by that sponsor in support of one or more previously approved NDAs or BLAs if the new drug relies on the same or similar technology as the approved drug
- Opportunity:
 - In PDUFA 6, expand this concept of relying on data/information from previous approvals to other types of targeted “platforms” that address rare diseases with a common pathophysiology (e.g., across mitochondrial diseases)