Stakeholder Interactions in the Drug Development Community

Introduction to Drug and Device Law and Regulation for Patient Organizations

Food & Drug Law Institute

December 3, 2020

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Stakeholder Interactions in Drug Development: Session Outline

1. Sponsor-Patient Group Engagement
2. The Role of Patient Experience Data and How Can Patient Advocacy Groups Influence it's Use in FDA Decision-making
3. Ways Patient Groups Can Engage Effectively with FDA
4. Payor Communications

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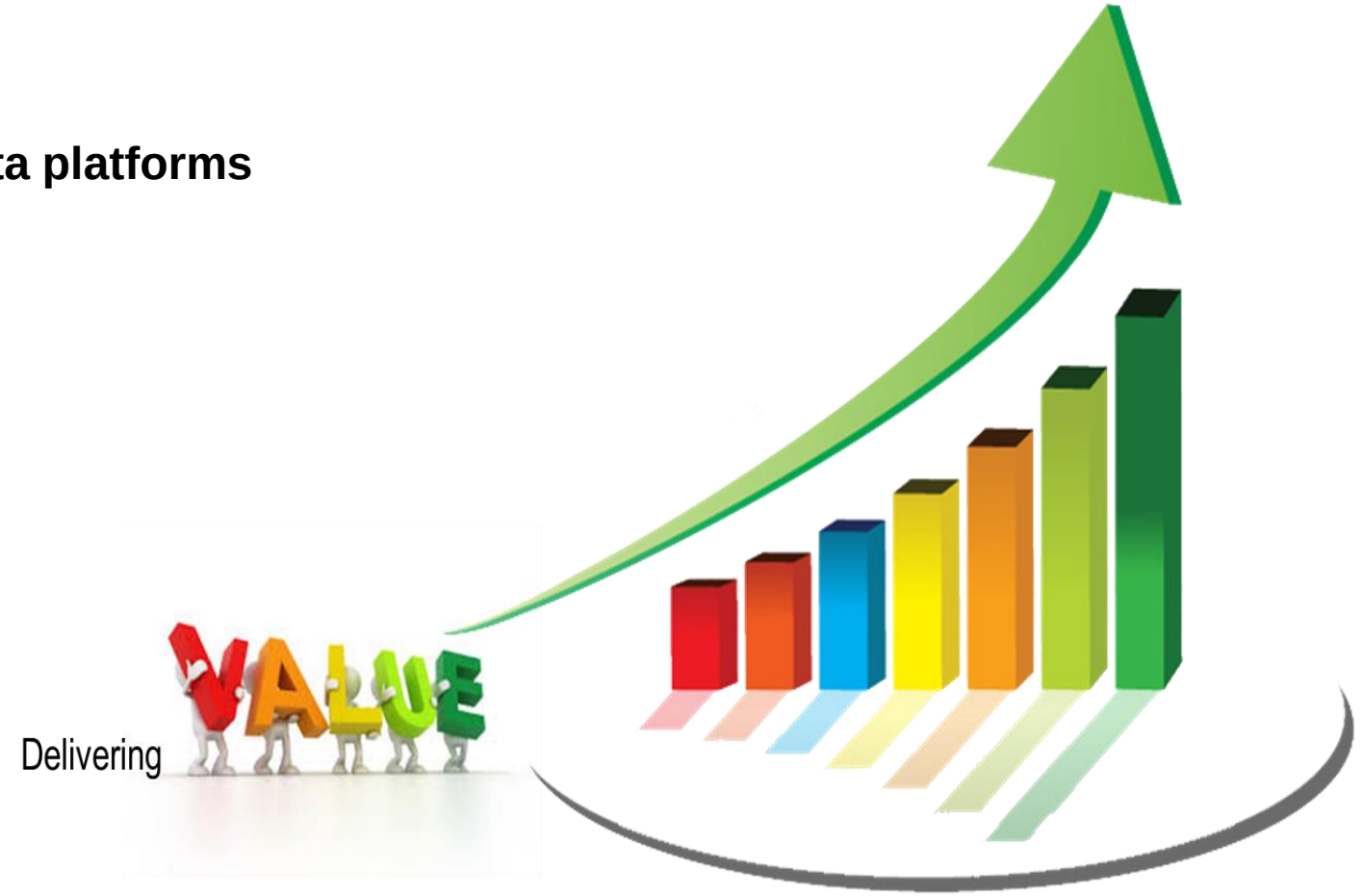
1. Sponsor-Patient Group Engagement

Sponsor-Patient Group Engagement: A range of relationships and tools

1. **Pre-competitive patient perspectives**
2. **Jointly funded research**
3. **Clinical trials recruitment**
4. **Sponsorship and promotion**
5. **Patient registries and other data platforms**
6. **Natural history studies**
7. **Etc.**



Remember: Eyes Are On You!

The Washington Post
Democracy Dies in Darkness

Health & Science

Patient Advocacy Groups Take In Millions From Drugmakers. Is There A Payback?

By **Emily Kopp, Kaiser Health News and Sydney Lupkin, Kaiser Health News and Elizabeth Lucas, Kaiser Health News**
April 6

Pharmaceutical companies gave at least $116 million to patient advocacy groups in a single year, reveals a new database logging 12,000 donations from large publicly traded drugmakers to such organizations.

Even as these patient groups grow in number and political influence, their funding and their relationships to drugmakers are little understood. Unlike payments to doctors and lobbying expenses, companies do not have to report payments to the groups.

The database, called "Pre$cription for Power," shows that donations to patient advocacy groups tallied for 2015 — the most recent full year in which documents required by the Internal Revenue Service were available — dwarfed the total amount the companies spent on federal lobbying. The 14 companies that contributed $116 million to patient advocacy groups reported only about $63 million in lobbying activities that same year.

Though their primary missions are to focus attention on the needs of patients with a particular disease — such as arthritis, heart disease or various cancers — some groups effectively supplement the work lobbyists perform, providing patients to testify on Capitol Hill and organizing letter-writing and social media campaigns that are beneficial to pharmaceutical companies.

Pre$cription For Power

Investigating the relationships between patient advocacy groups and Big Pharma

By Emily Kopp, Elizabeth Lucas and Sydney Lupkin

Patient advocacy groups campaign to raise awareness of diseases, to fund research and to promote policies favorable to their causes on Capitol Hill and at the Food and Drug Administration. But do they represent patients or Big Pharma? Kaiser Health News has compiled and analyzed disclosures to shed light on the flow of money between the pharmaceutical industry and patient advocacy groups. The database currently covers 2015 and will be updated as additional data become available.

Use the search bar to find a drug company or patient group, or click the "View All" links.

SCOPE OF THE PRESCRIPTION FOR POWER DATABASE

14	$116,011,433	594
Number of Pharmaceutical Companies	Tracked Donations	Number of Patient Advocacy Groups
View All		View All

Search Pre$cription For Power database

NOTABLE PATIENT ADVOCACY GROUPS

Some drugmakers gave seven-figure donations to patient advocacy groups whose communities depend on blockbuster medicines made by those companies. This relationship could inhibit patient advocates from calling for lower drug prices, watchdogs say.

Crohn's & Colitis Foundation

The Crohn's & Colitis Foundation accepted $2.7 million from AbbVie in 2015. AbbVie's Humira treats inflammatory conditions like Crohn's disease and colitis for the list price of $63,000 annually. AbbVie has dozens of patents on the drug, according to a 2016 lawsuit.

TOP COMPANY DONORS:

AbbVie Inc.

The American Diabetes Association

Eli Lilly gave $2.9 million to the American Diabetes Association in 2015. The drugmaker has hiked the price of its insulin brand Humalog 30 times in 20 years, according to data provided by Truven Health Analytics, now IBM Watson Health.

TOP COMPANY DONORS:

Eli Lilly

Patient Access Network Foundation

The Patient Access Network Foundation helps patients cover their drug copays. PAN received $31 million from just two companies: AbbVie and Pfizer. A 2007 advisory opinion by the Inspector General for the U.S. Department of Health and Human Services precludes the foundation from disclosing donors, a spokeswoman said.

TOP COMPANY DONORS:

Pfizer Inc.

AbbVie Inc.

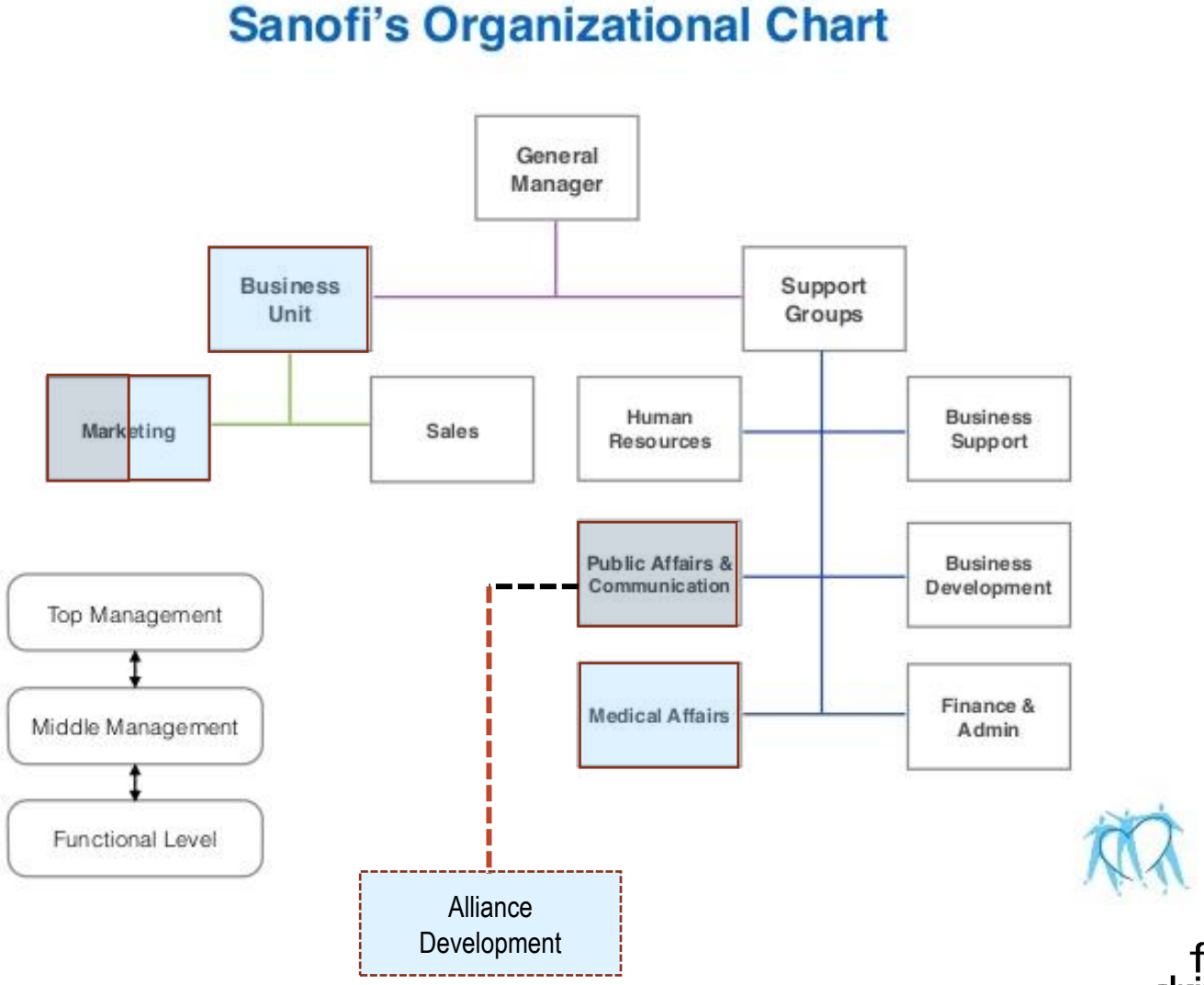
Understand Functions in the Organization that Relate to the Area of Interest for your Collaboration

Grants

- Charitable giving
- Unrestricted or targeted
- May have limit based on percentage of nonprofit's annual revenues

Sponsorships

- Investment not gift
- Consortia
- Role in governance



Engagement of Patient Organizations Across the R&D Continuum

- Input regarding interest of research question to patient community
- Providing data on unmet need & therapeutic burden
- Fundraising and direct funding for research to identify target molecules
- Facilitating collaboration with NIH
- Characterizing the disease and relevant mechanisms of action

- Fundraising & direct funding for research, trial operations support
- Assistance in selecting & recruiting optimum clinical sites
- Clinical infrastructure support
- Helping educate/motivate patient community and recruit for trials
- Providing patient feedback on participant experience
- Serving on Data & Safety Monitoring Board
- Input for any trial adaptations or modifications
- Performing or participating in benefit-risk and patient preference studies

- Serving on postmarket surveillance initiatives
- Helping return study results to participants
- Co-presenting results
- Publications/communications re: results
- Feedback on how patient community views results
- Natural history database & registry support
- Working with payers on reimbursement

Prediscovery → **Preclinical** → **Phase I/II/III** → **FDA Review & Approval** → **PAS/ Outcomes**

- Fundraising and direct funding for research
- Providing translational tools (assays, cell & animal models, biosamples, biomarkers, etc.)
- Helping define study's eligibility crisis
- Natural history database & patient registry support
- Input on meaningful clinical endpoints/PROs
- Assistance on informed consent form/process
- Working with FDA on benefit-risk and draft guidance
- Accompanying sponsor to pre-IND FDA mtg to advocate for study

- Providing public testimony at the FDA Advisory Committee and other FDA hearings
- Preparing submission for newborn screening when appropriate

Source: Society for Clinical Research Sites

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PhRMA: RESPECTING THE VALUES AND INDEPENDENCE OF PATIENT ORGANIZATIONS

All interactions with patient organizations must be consistent with the patient organization's mission and adhere to high ethical standards.

The independence of patient organizations must be respected. When working with patient organizations, companies should ensure that both the involvement of the company and the nature of that involvement are clear from the outset.

No company should require that it be the sole funder of the patient organization or any of its programs.

BIO: FOSTERING PARTNERSHIP AND VALUING INDEPENDENCE

Partnerships between BIO member companies and the patient community should be based on our shared objectives of developing and ensuring access to treatments that improve patient health outcomes.

To that end, BIO and its member companies value and embrace the autonomy of patient advocacy organizations and recognize the importance of their maintained integrity to ensure that they are an independent and trusted voice of patients.

We encourage this and recognize that partners in the patient community independently develop public policy and scientific agendas. These may, in some cases, differ from those of BIO and its members but should not impact the relationship between the patient advocacy organization and BIO or its members.

BIO member companies should not attempt to compel a stakeholder in the patient advocacy community to adopt a specific policy position.

Some Best Practices

✓ **Identify and Engage Fairly. Clarify Shared Value.**	• **Be proactive in seeking contact with companies. Do outreach to many companies but be thoughtful about engagement and value statement. Discuss goals and expectations in engagement conversations.** • **Reserve the right to disengage at any point.**
✓ **Set the Terms. Be Transparent. Protect Patient Privacy.**	• **Clearly define purpose.** • **Focus on pre-competitive space. Expect learnings and outcomes to be shared openly for mutual benefit (avoid IP, gag clauses). Collective learning should be a principle to operate under.**
✓ **Manage Financial Contributions w/ Care.**	• **Maintain proper documentation of all requests for financial support on donor's letterhead. Request unrestricted funding as much as possible. If funding is restricted, maintain total control over program.** • **Be transparent and think about how to show where your funding is going and who you're receiving it from.**
✓ **Advance Clinical Trial (and other areas) Engagement Equally.**	• **Avoid perceptions of exclusive sponsorship.** • **Don't advocate for only one trial.** • **Disseminate accurate and fair-balanced information about clinical trials without adding commentary or opinion that may influence an individual's decision in any way**

Example: UsAgainst Alzheimer's AD PACE A-LIST Operating Principles

1. **The A-LIST conducts research projects in accordance with the A-LIST's IRB approved protocol, The A-LIST What Matter Most Insights Series.**
2. **A-LIST will strive to assure that all of its research projects are free from bias or undue influence.**
3. **Decisions to undertake an A-LIST research project will be made taking into consideration multiple factors:**
    1. Will the research project advance the interests of persons living with the disease?
    2. Will the information generated by the research add to the base of knowledge being developed by the A-LIST?
    3. Will the research project build the credibility of the A-LIST, engender trust, and deliver a sense of contribution among the A-LIST participants?
    4. Is the area of interest a priority for the A-LIST and UsA2?
    5. Is the information sought duplicative of prior research?
    6. Does undertaking the research project pose any risk to the reputation of A-LIST, AD PACE, or UsA2, and has due diligence been undertaken to assure against any such risk?
    7. Is there capacity and adequate funding to conduct the work? Consideration will be given to staff availability based on current survey commitments, as well as balance of funding for new and existing expenses related to a proposed project.
4. **Results from any A-LIST research project will be made public in poster, manuscript form, or otherwise, not later than 12 months following completion of the research project.**
5. **All underlying de-identified data will be deposited in the AD PACE Data Commons within 12 months of research study completion or upon publication, whichever shall first occur.**
6. **A-LIST researchers will be co-authors on any publication of results from an A-LIST research project, in accordance with ICMJE guidelines.**
7. **When A-LIST is working with an industry sponsor of a research project, and before the project findings are published, A-LIST will work to achieve an appropriate balance of transparency and confidentiality.**
8. **The Operating Principles will be included as an Addendum to and incorporated in all contracts for A-LIST services.**
9. **As A-LIST grows, these Operating Principles may be amended from time to time, with review and approval of the Executive Steering Committee of AD PACE.**

2. The Role of Patient Experience Data and How Can Patient Advocacy Groups Influence it's Use in FDA Decision-making

21st Century Cures Act (2016)

Patient Experience Data (Section 3001):

Data that are collected by any persons and are intended to provide information about patients' experiences with a disease or condition

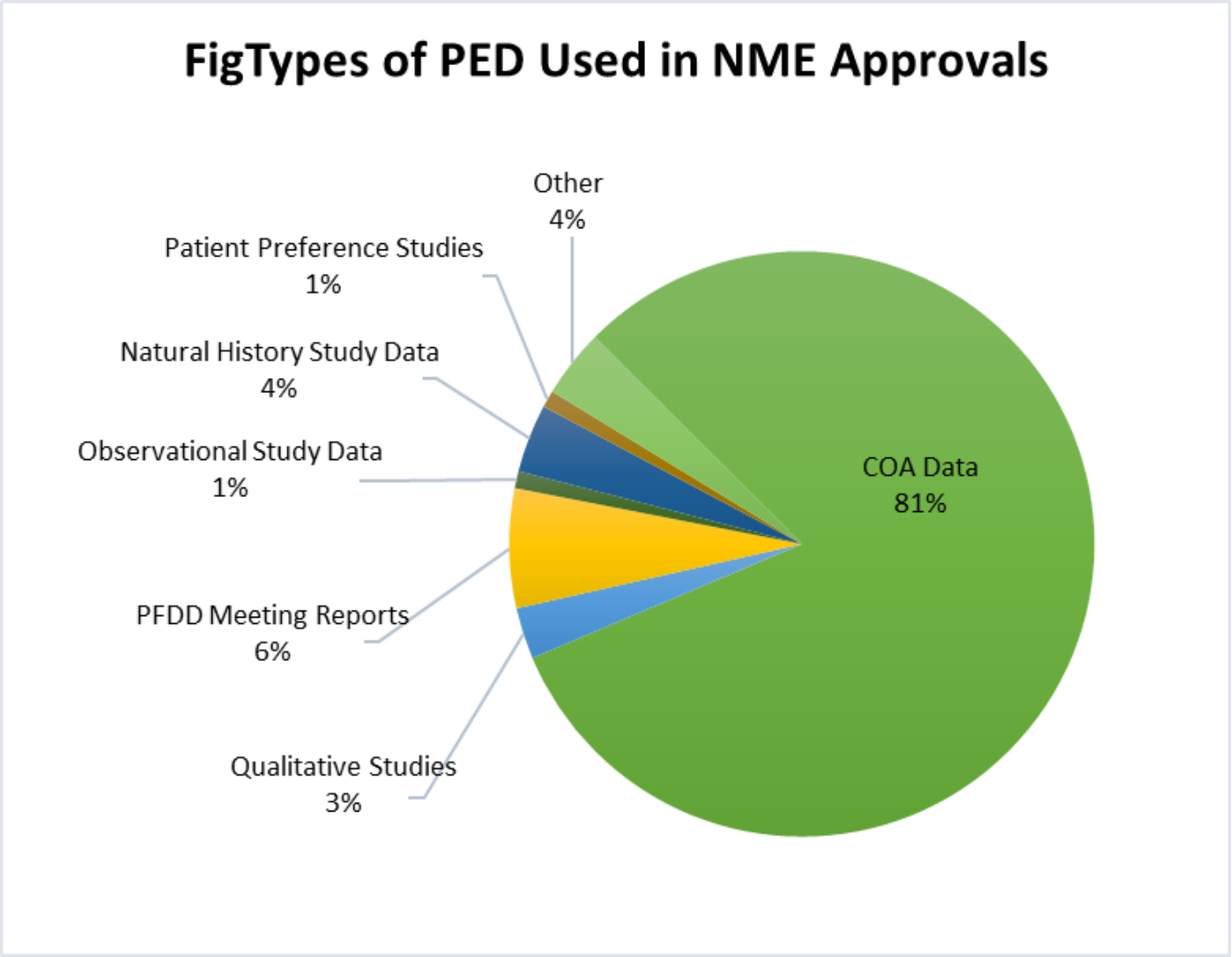
Includes the experiences, perspectives, needs and priorities of patients related to (but not limited to):

- symptoms of their condition and its natural history
- Impact of the conditions on their functioning and quality of life
- Experience with treatments
- Input on which outcomes are important to them
- Patient preferences for outcomes and treatments
- Relative importance of any issue as defined by patients

The Role of Patient Experience Data and How Can Patient Advocacy Groups Influence it's Use in FDA Decision-making: FDA Guidances

Guidance/Workshop Title	21CC?	Estimated Date of Next Action	Status / Notes
Submitting Documents Using Real-World Data and Real-World Evidence to the Food and Drug Administration for Drugs and Biologics		Original estimate: First half of 2020 (final guidance)	Draft guidance published in May 2019
PFDD Guidance 3: Select, Develop, or Modify Fit-for-Purpose Clinical Outcome Assessments	✓	Original estimate: Q2 2020 (draft guidance)	Workshop held in October 2018 (in conjunction with workshop for Guidance 2)
Characterizing FDA's Approach to Benefit-Risk Assessment Throughout the Medical Product Life Cycle		Original estimate: June 2020 (draft guidance)	Workshop held in May 2019.
PFDD Guidance 4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making	✓	Second half of 2020 (draft guidance)	Workshop held in December 2019. This guidance may revise or supplement the 2009 Guidance for Industry on Patient-Reported Outcome Measures.
Developing and Submitting Proposed Draft Guidance Relating to Patient Experience Data (a.k.a. the "Guidance on Guidances")	✓	Original estimate: September 2020 (final guidance)	Draft guidance posted in December 2018.
PFDD Guidance 2: Methods to Identify What is Important to Patients	✓	Late 2020 (final guidance)	Draft guidance published in September 2019.
Enhancing the Diversity of Clinical Trials Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs		None planned	Final guidance published in November 2020.
PFDD Guidance 1: Collecting Comprehensive and Representative Input	✓	None planned	Final guidance published in June 2020
Framework for a Real-World Evidence Program	✓	None announced	FDA published draft framework in December 2018. Webinar held in March 2019.
Enhancing the Incorporation of Patient Perspectives on Clinical Trials		None planned	Workshop held in March 2019, workshop summary published in June 2019
Patient Perspectives on the Impact of Rare Diseases: Bridging the Commonalities		None announced	Public meeting held in April 2019.
Characterizing the Food and Drug Administration's Approach to Benefit-Risk Assessment Throughout the Medical Product Life Cycle		None announced	Public meeting held in May 2019.
Leveraging Randomized Clinical Trials to Generate Real-World Evidence for Regulatory Purposes		None announced	Public workshop held in July 2019.
Developing Real-World Data and Evidence to Support Regulatory Decision-Making	✓	None announced	Public workshop held in October 2019.
Establishing a High-Quality Real-World Data Ecosystem		None announced	Public meeting held July 13-14, 2020
Prescription Drug User Fee Act VI Benefit-Risk Implementation Plan		None announced	In April 2018, FDA published a draft five-year plan on the agency's planned approach for implementing a structured benefit-risk assessment.

The Role of Patient Experience Data and How Can Patient Advocacy Groups Influence it's Use in FDA Decision-making



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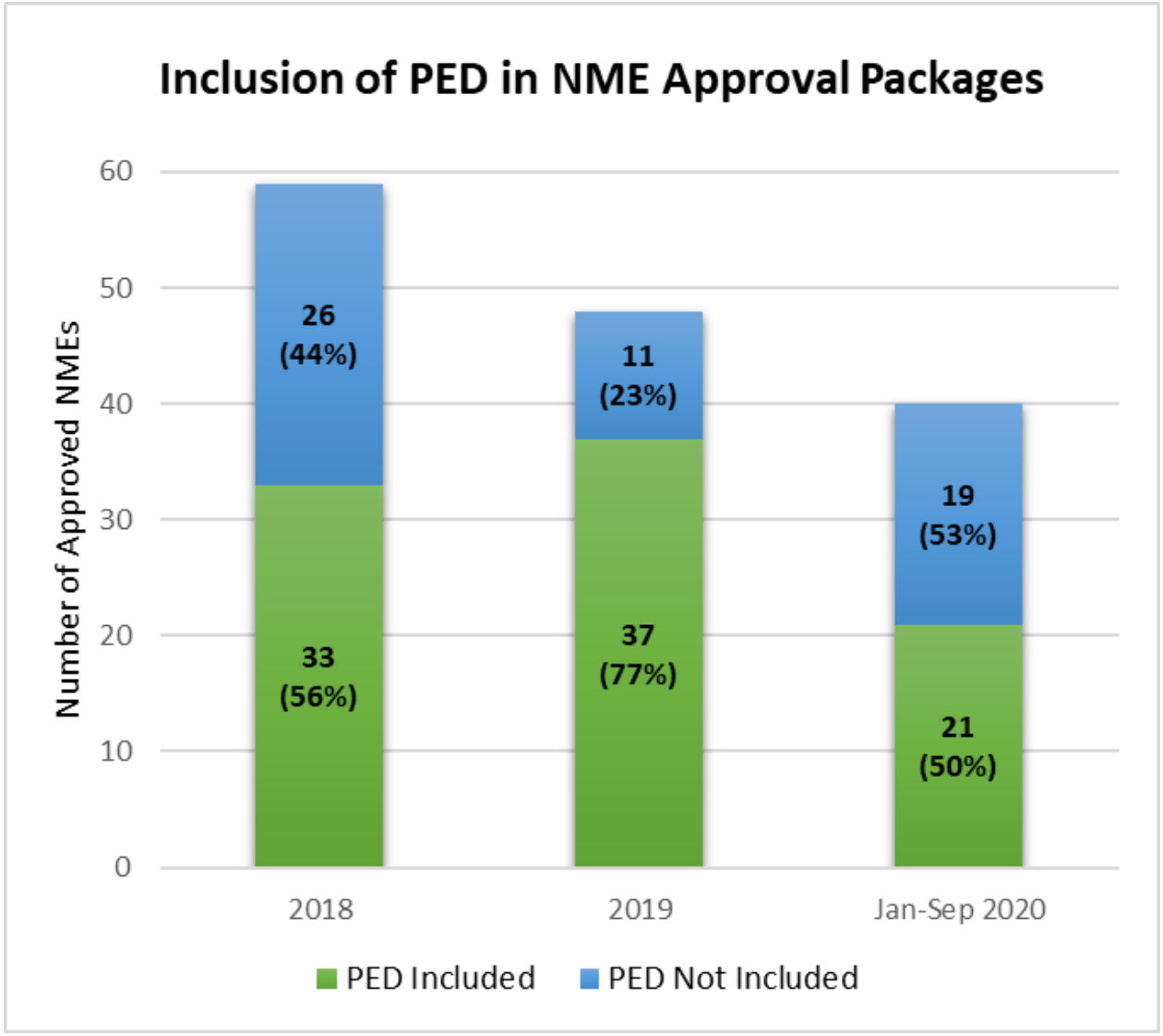


Examples of Regulatory Utility

PFDD Meetings

* disease burden, current treatments
* Inform B-R Framework

Pre-Competitive, Non-Product Specific Surveys

* What matters most to patient community, subpopulations?

Product-Specific Surveys

* Address key questions, often on specific benefits and risks

3. Ways Patient Groups Can *Effectively* Engage with FDA

Formal

Patient-Focused Drug Development Meetings (internal, external)

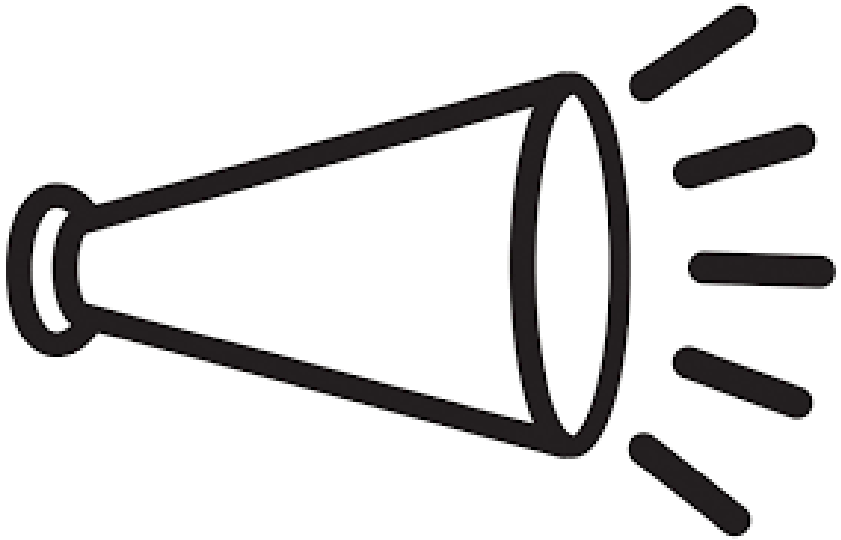
Listening Sessions

Patient Engagement Advisory Committee

Patient Representative Program

Advisory Committees

Type C Meetings



Informal

Leadership

Offices/Divisions

Projects

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4. Payor Communications

- Health decision makers (payors) are required to evaluate their plan designs, formularies, and rates 12-18 months in advance to meet submission deadlines before the beginning of the intended plan year.
- With rates being filed over a year in advance, proper planning, budgeting, and forecasting are integral to accurately account for the effect of new therapies that will enter the market.
- However, restrictions on the sharing of clinical and health economic information on products yet to receive FDA approval do not facilitate such accurate forecasting.
- The unplanned approval of one novel, high priced drug can result in a significant departure from projections on which a given year's premium rates are based.

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Payor Communications: FDAMA 114 - Background

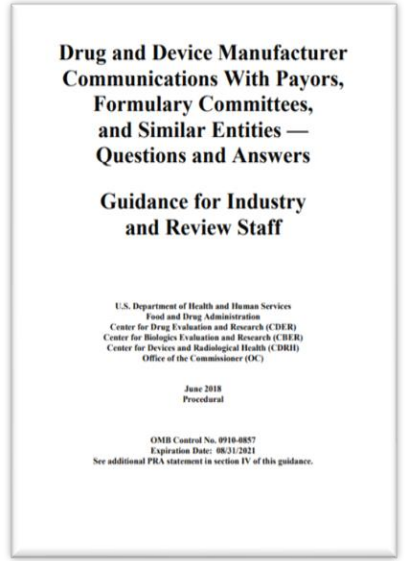
- **In 1997 Congress enacted Section 114 of FDAMA as a regulatory safe harbor with the goal of increasing the dissemination of health care economic information (HCEI) to those responsible for formulary decision making.**
- **Under the statute, such communications did *not* constitute false or misleading promotion *if* the HCEI: (1) directly related to an FDA-approved indication; and (2) was based on competent and reliable scientific evidence.**
- **Out of concern that industry was not taking advantage of FDAMA 114, for fear of pre-approval and off-label communication prosecution, amendments to FDAMA were made in the 21st Century Cures Act in 2016.**
  - **Removal of "directly."** HCEI no longer needs to "directly" relate to an FDA-approved indication, but rather only to relate.
  - **Revised HCEI definition.** Includes analyses that may be comparative to the use of another drug or intervention, or to no intervention.
  - **Expanded audience of who may receive HCEI.** Payors, formulary committees, or other similar entites with knowledge and expertise in the area of health care economic analysis, carrying out responsibilities for the selection of drugs for coverage or reimbursement.
  - **Disclaimer requirements.** conspicuous and prominent statement describing any material differences between the HCEI and the labeling of the approved drug.

Payor Communications: FDA Guidance Documents – Finalized June 2018

- **Following changes to FDAMA 114, FDA announced a shift in policy concerning sponsor communications through the release of two recent guidance documents**

  - “Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers” (Payor Guidance)

  - “Medical Product Communications That Are Consistent With the FDA-Required Labeling—Questions and Answers“ (CFL Guidance)



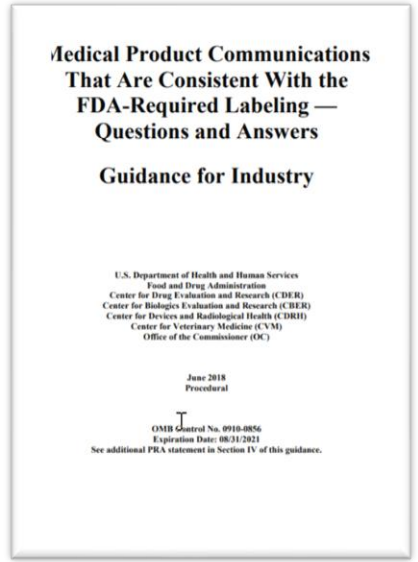
Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities — Questions and Answers

Guidance for Industry and Review Staff

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of the Commissioner (OC)

June 2018
Procedural

OMB Control No. 0910-0857
Expiration Date: 08/31/2021
See additional PRA statement in section IV of this guidance.



Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers

Guidance for Industry

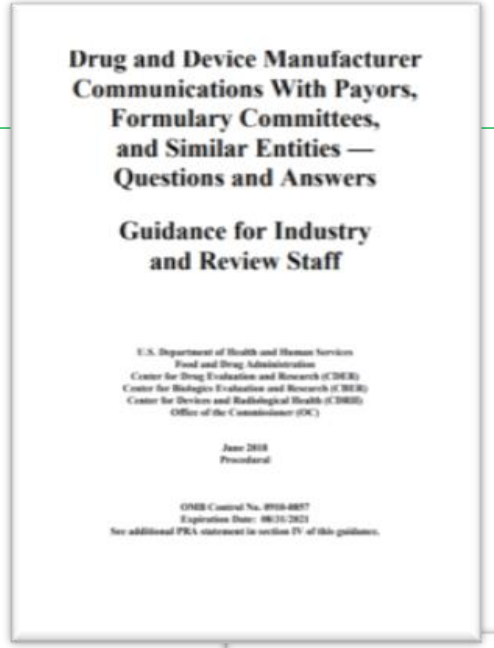
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Veterinary Medicine (CVM)
Office of the Commissioner (OC)

June 2018
Procedural

OMB Control No. 0910-0856
Expiration Date: 08/31/2021
See additional PRA statement in Section IV of this guidance.

Payor Communications: What Does it All Mean?

- **In a press release announcing the final guidance documents, FDA Commissioner Scott Gottlieb emphasized "the importance of linking payments for drugs to their value" and "removing regulatory obstacles to value-based purchasing by payors.“**
- **With respect to the CFL Guidance, Commissioner Gottlieb emphasized that the guidance will facilitate the sharing of information, such as post-market study data, that "may help inform decision-making regarding patient care."**
  - The guidance will likely encourage companies to communicate more data about the “real world” impacts of prescription drugs. That should increase demand for the services of health economics and outcomes departments within drug companies as well as contract researchers and businesses promoting databases (for example, Flatiron and IBM Watson).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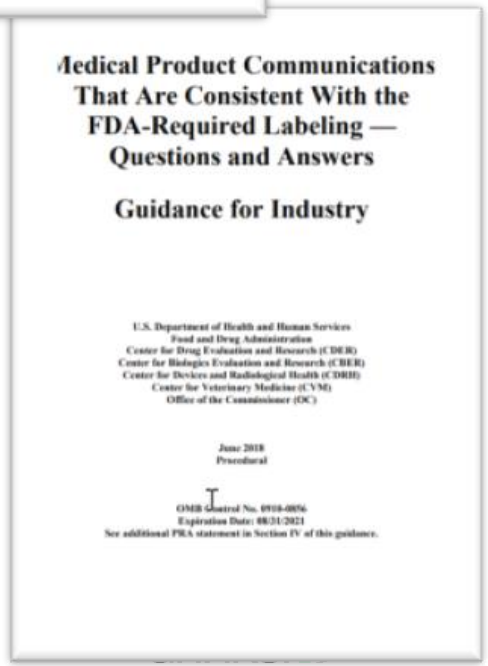
Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers

Guidance for Industry

Payor Communications: Value Assessment

Institute for Clinical and Economic Review

* Private, non-profit
* QALY-based analysis of medical products to align cost with value

Patient-Centered Outcomes Research Institute

* Created in ACA; quasi-governmental
* Reauthorization expanded scope to consider the full range of clinical and patient-centered outcomes, including the potential burdens and economic impacts of various healthcare services, along with the relative health outcomes and clinical effectiveness measures.

Payor Communications: Integration of Regulatory & Reimbursement

2020 Medicare Coverage of Innovative Technology (MCIT) Program

* CMS national coverage simultaneously with FDA approval, for a period of four years, for “breakthrough” medical devices and diagnostics.

* Clarifies CMS’ definition of reasonable and necessary in regulation to give companies a clearer understanding of CMS standards for coverage and payment.

* After that time, CMS may reevaluate the device based on clinical and real-world evidence of improvement in health outcomes among Medicare beneficiaries.

* Will other medical products follow?

Stakeholder Interactions in the Drug Development Community

DISCUSSION

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