# Communicating Emerging Drug Therapies Prior to FDA Approval

May 4, 2017

FDLI

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# Communicating Emerging Drug Therapies Prior to FDA Approval

## The Legal and Regulatory Landscape

Michael S. Labson

May 4, 2017

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# Barriers to Communications Under Current FDA Regulations

- Pre-approval communications

***21 C.F.R. § 312.7 Promotion of investigational drugs.***

(a) *Promotion of an investigational new drug.* A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.

# Barriers to Communications Under Current FDA Regulations

- Information on unapproved new uses of approved drugs

***21 C.F.R. § 201.100(c)***

(c)(1) Labeling on or within the package from which the drug is to be dispensed bears adequate information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all purposes for which it is advertised or represented; and
(2) If the article is subject to section 505 of the act, the labeling bearing such information is the labeling authorized by the approved new drug application . . . .

*See also 21 C.F.R. § 201.100(d).*

# Evolving First Amendment Case Law

- Rise of commercial speech doctrine
  - *Valentine v. Chrestensen*
  - *Virginia State Board of Pharmacy*
  - *Central Hudson*
- Emerging shifts in case law
  - *Washington Legal Found.* (D.DC 1999)
  - *Western States* (US 2002)
  - *IMS v. Sorrell* (US 2011)
- New cases
  - *United States v. Caronia* (2d Cir. 2012)
  - *Amarin v. FDA* (SDNY 2015)
  - *Town of Gilbert* (US 2015)
  - *Pacira v. FDA* (SDNY 2015)
  - *United States v. Vascular Solutions* (W.D.Tx 2016)

# FDA Responses

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

(Draft Jan. 2017)

"Medical Product Communications That Are Consistent with the FDA-Required Labeling – Questions and Answers"

(Draft Jan. 2017)

*Part 15 Hearing and Docket:*

"Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Request for Comments"

(Hearing November 2016)"

*"Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products"*

[Scientific Exchange?]

*Pre-Approval Information on Investigational Drugs*

- "FDA does not intend to object …."
- … to:
  - Product information (e.g., drug class)
  - Indication sought, including endpoints and populations studied
  - "Factual presentations of results from clinical or preclinical studies (i.e., no characterizations or conclusions should be made regarding the safety or effectiveness of the product"
  - Anticipated timeline for FDA action
  - Product pricing information
  - Targeting/marketing strategies (e.g., planned outreach strategies)
  - Product-related programs/services (e.g., patient support programs)

*Pre-Approval Information on Investigational Drugs*

- Clear statement that product is under investigation
- Provide information on stage of product development
- Follow up when information becomes outdated

- <u>Some questions/issues</u>:
  - New indications
  - Relationship to regulations?
  - Including HCEI in pre-approval communication?
  - Who can deliver?
  - Any rules/limits on timing?

# "Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers"

*Audience:*

- Includes payors, formulary committees, drug information centers, technology assessment panels, pharmacy benefit managers, and "other multidisciiplinary entities that review scientific and technology assessments to make drug selection, formulary management, and/or coverage and reimbursement decisions on a population basis for health care organizations"
  - Health care organizations may include integrated health care delivery networks, hospitals, hospital systems
- Key criteria:
  - Deliberative process
  - Population-based
  - Expertise
- Some questions
  - Financial risk?
  - Pathway organizations?
  - Group practices?

# Select Additional Remaining Pre-Approval Issues

- Non-payor audiences
- Non-promotional scientific exchange
- Clarity in overall legal framework

# Recent FDA Enforcement on Pre-Approval Communications

OPDP Untitled & Warning Letters, 2016 thru April 2017

- Chiasma – octreotide capsules (12/2016)
- Zydus – saroglitazar tablets (12/2016)
- DURECT & Pain Therapeutics – Remoxy/PTI-821 (9/2016)
- Celator – CPX-351 (8/2016)

*4 of 11 letters on pre-approval*

# Thank You!

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PhRMA
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# Communications with Health Care Professionals and Payers

Michelle Drozd | Deputy Vice President

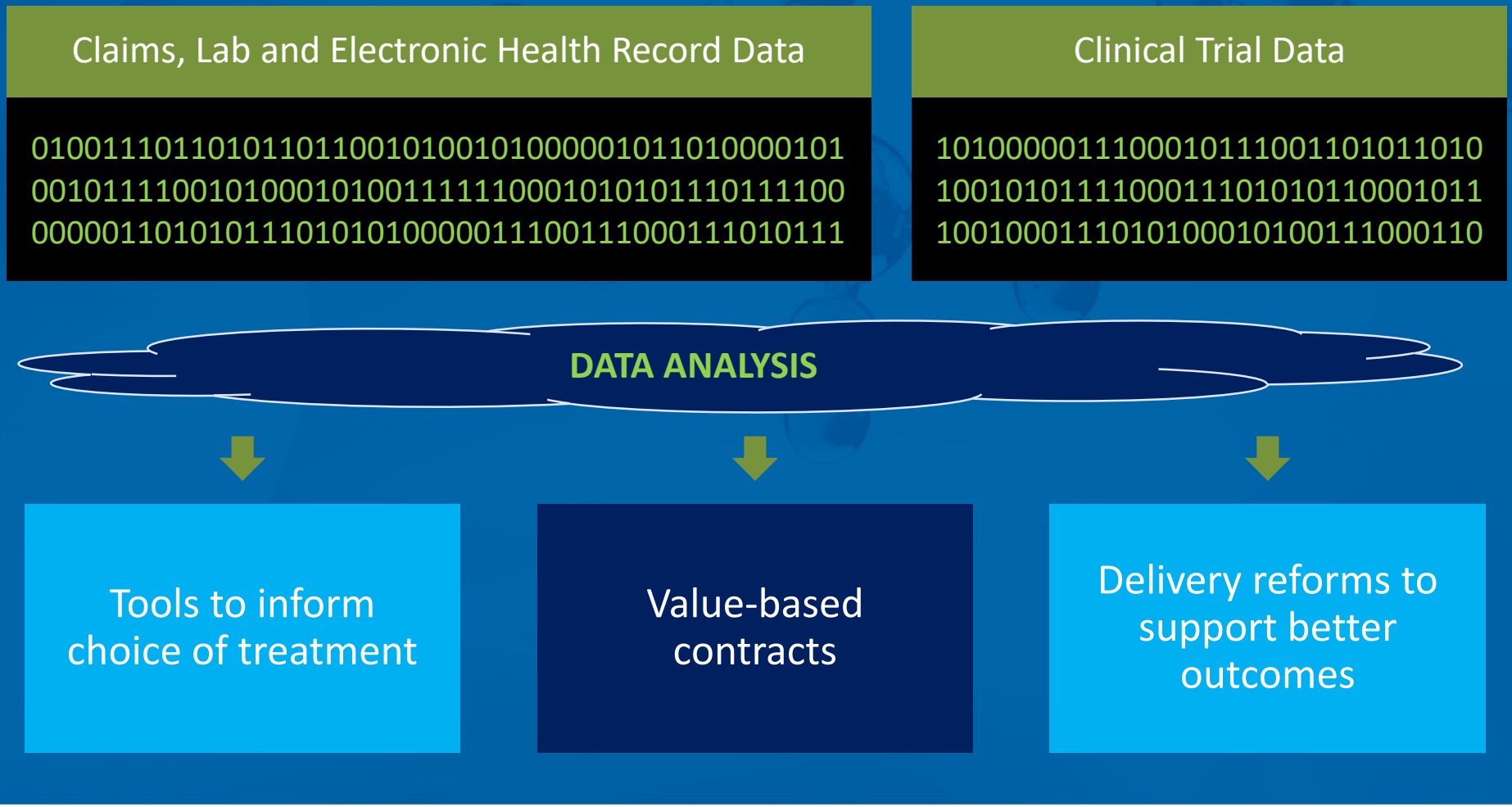
FDLI

# Challenge in Medicine's Information Age

In the era of data-driven medicine, health care professionals and payers seek more, not less, information about the safety, effectiveness, and value of treatments

Today, the wealth of information about medicines is more comprehensive and complex than ever before, and a modernized regulatory framework would support more effective sharing of important data

# Payers, Providers, and Patients Are Using Real World Data to Inform Treatment Choices



# Ongoing Research and Use of a Medicine Over Time Improves Our Understanding

FDA approval and introduction of a new therapy is a significant milestone for patients but it is ***only the beginning***.

**Additional value may be realized over time through:**[1]

- ✓ Earlier use
- ✓ Use in combination with other agents
- ✓ Use in specific sub-populations of patients using diagnostics
- ✓ Use in other disease indications

*"The relative value of a given cancer treatment is likely to change over its lifetime… the assessment of the value of any treatment must be dynamic and adapt to new medical information that may better inform its use, mitigate its toxicity, or modify its place in the treatment landscape."*

— American Society of Clinical Oncology[2]



Source: 1) Boston Healthcare Associates, "The Value of Innovation in Oncology: Recognizing Emerging Benefits Over Time," Boston Healthcare Associates, Inc., May 2015. 2) ASCO. ASCO Publishes Conceptual Framework to Assess the Value of New Cancer Treatment Options. June 22, 2015;

# A Responsible Path Forward

FDA should define clear standards governing *responsible, truthful and non-misleading communications* to inform health care professionals and payers about the safe and effective use of medicines

**Key principles should include:**

- Science-based communication
- Provide appropriate context about data
- Tailoring communications to the intended audience

The PhRMA-BIO Principles pertain primarily to data and information outside of FDA-approved labeling, such as additional clinical trials or analysis of real-world patient outcomes


PRINCIPLES ON RESPONSIBLE SHARING OF TRUTHFUL AND NON-MISLEADING INFORMATION ABOUT MEDICINES WITH HEALTH CARE PROFESSIONALS AND PAYERS

PhRMA

INTRODUCTION

KEY CONCEPTS OF THE PRINCIPLES INCLUDE OUR MEMBERS':

- **Commitment to Science-based Communication.**
- **Commitment to Provide Appropriate Context about Data.**
- **Commitment to Accurate Representation of Data.**

# Three Part Approach to Regulatory Reform: Categories of Communication

| **Communications with Payers / Population Health Decision Makers** | **Communications with HCPs (*Consistent w/ Approved Indication*)** | **Communications with HCPs (*Medically Accepted Alternative Uses*)** |
|---|---|---|
| • Pharmacoeconomic information<br>• Pipeline information (pre-approval)<br>• Broad clinical information to payers | • Real-World Evidence<br>• Subpopulation information<br>• Other information from clinical trials | • Real-World Evidence<br>• Subpopulation information<br>• Other information from clinical trials |

# Recent FDA Activity on Manufacturer Communications

| Audience | Investigational products | Approved Products | |
|---|---|---|---|
| | | Approved Uses | Unapproved Uses |
| **Payers & Population Health Decision Makers** | **Draft Guidance:** Drug And Device Manufacturer Communications With Payers, Formulary Committees Or Similar Entities | | • **Final Rule:** Amendments to Regulations Regarding "Intended Uses"<br>• **Open Docket:** Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products<br>• **Memorandum:** Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products |
| **Health Care Professionals** | No Recent Changes | **Draft Guidance:** Medical Product Communications that are Consistent with the FDA-Required Labeling | |

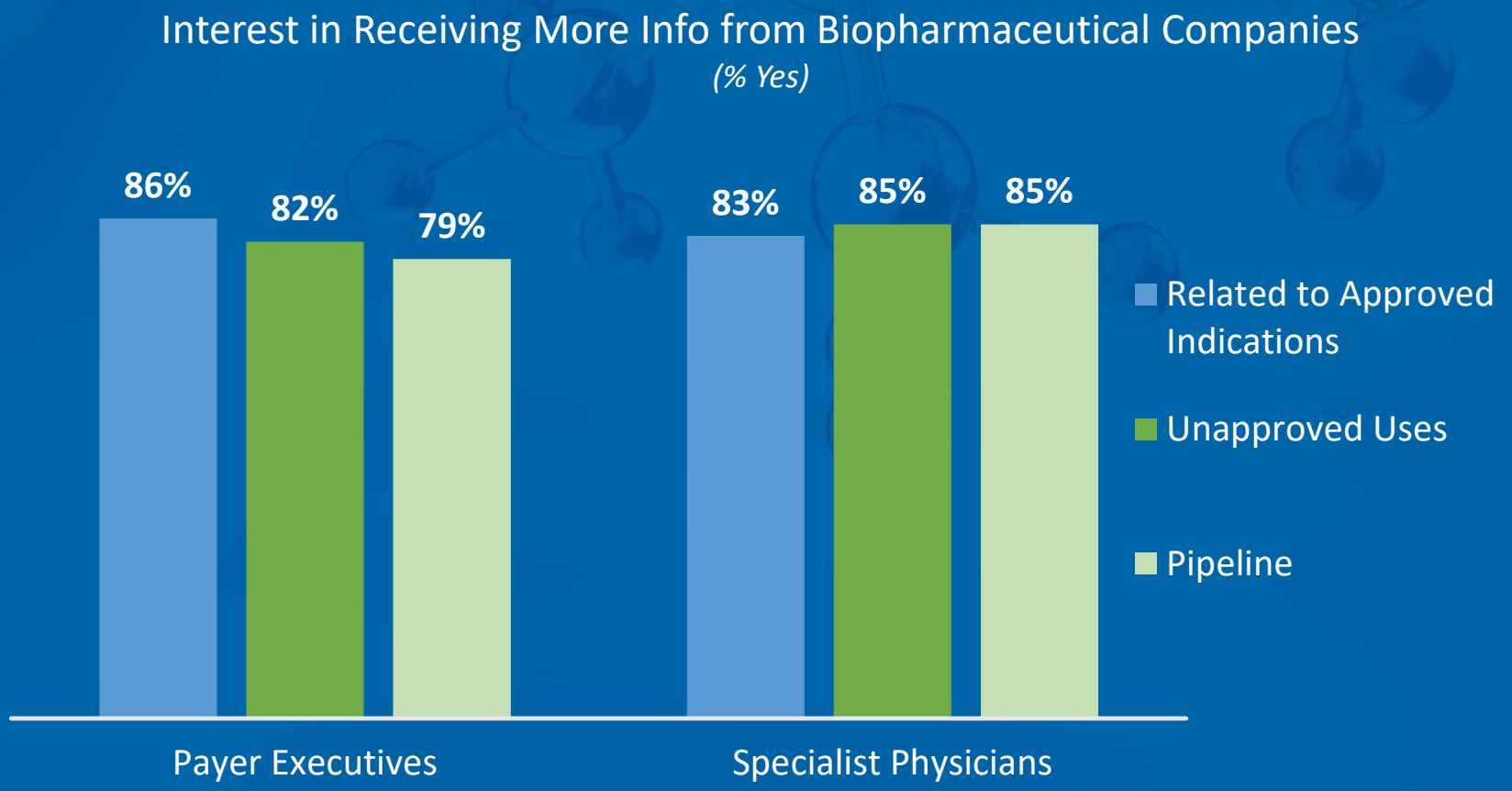
# Many Unapproved Uses of Medicines are Medically-Accepted

**Examination of medically accepted unapproved uses for 46 branded medicines from CMS-recognized compendia used for Medicare or Medicaid payment purposes**

| | NCCN Compendium | DRUGDEX Compendium |
|---|---|---|
| Medicines with Any Recommendation for Unapproved Use | 31 (67%) | 15 (33%) |
| Types of Unapproved Use* | | |
| Additional Combinations Not Included on the Label | 27 (59%) | 7 (15%) |
| Subpopulations not Included in the Main Indication | 8 (17%) | 0 |
| Use in Alternative Disease Progression (e.g. Lines of Therapy) | 29 (63%) | 1 (2%) |
| Recommendations on Other Aspects Considered for Diagnosis (e.g. pregnancy, diagnostic test results, or genetic test results) | 13 (28%) | 0 |

*Medicines, on average, had 1.71 (NCCN) and 1.53 (DRUGDEX) recommendations for an unapproved indication. As a result, the numbers for "Types of Unapproved Use" do not sum to the number displayed in the first row.

# Payers and Providers Want More Information From Manufacturers

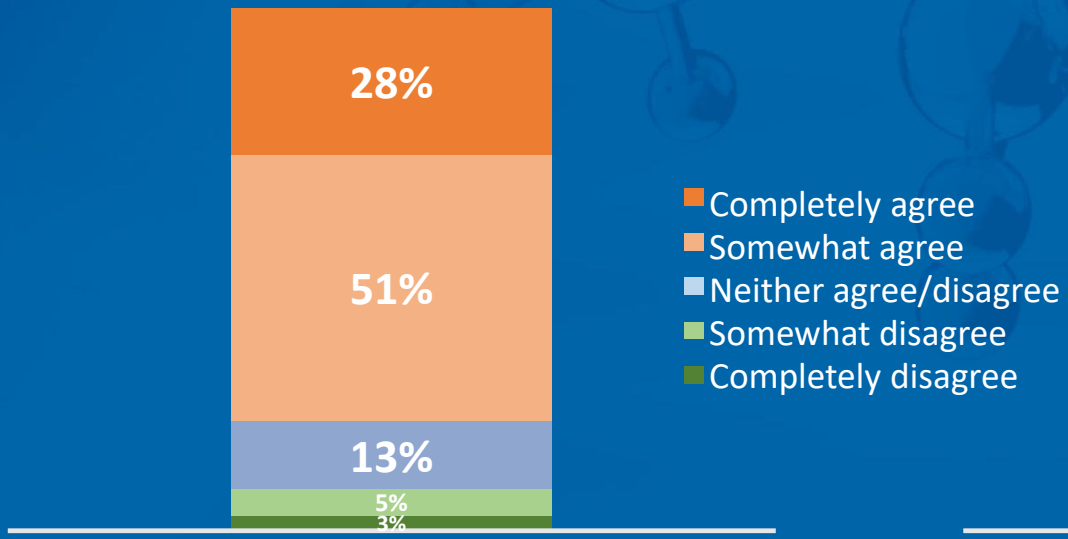



n=39 executives, n=178 physicians.
Source: Health Strategies Group, Custom Research, December 2016.

# FDA Approval Will Remain the Gold Standard for Stakeholders

## *Payer Executives*

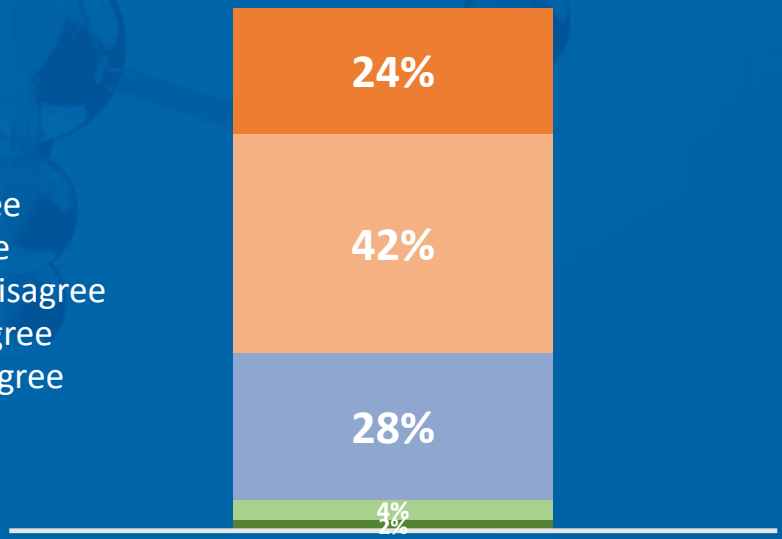
*If companies were able to proactively share more information regarding unapproved uses of a product, I would…*




Still want to see the manufacturer take steps to have the use approved as an indication in the product labeling

## *Physicians*

*If I had more information about unapproved uses, I would…*




More often refer patients to clinical trials that seek to develop evidence about the benefits of these uses

n=39 executives, n=178 physicians.
Source: Health Strategies Group, Custom Research, December 2016.

# Conclusion

- FDA guidance documents are a significant step forward, further clarification would be helpful in some cases

- Manufacturers should have additional flexibility to communicate with payers and health care professionals about unapproved uses – particularly medically accepted alternative uses

# Population Health Decision Maker Perspective on Preapproval Communications

Soumi Saha, PharmD, JD
Director of Pharmacy & Regulatory Affairs

AMCP Academy of Managed Care Pharmacy®

# Academy of Managed Care Pharmacy

## Vision

Managed care pharmacy - improving health care for all

## Mission

To empower its members to serve society by using sound medication management principles and strategies to improve health care for all

## AMCP

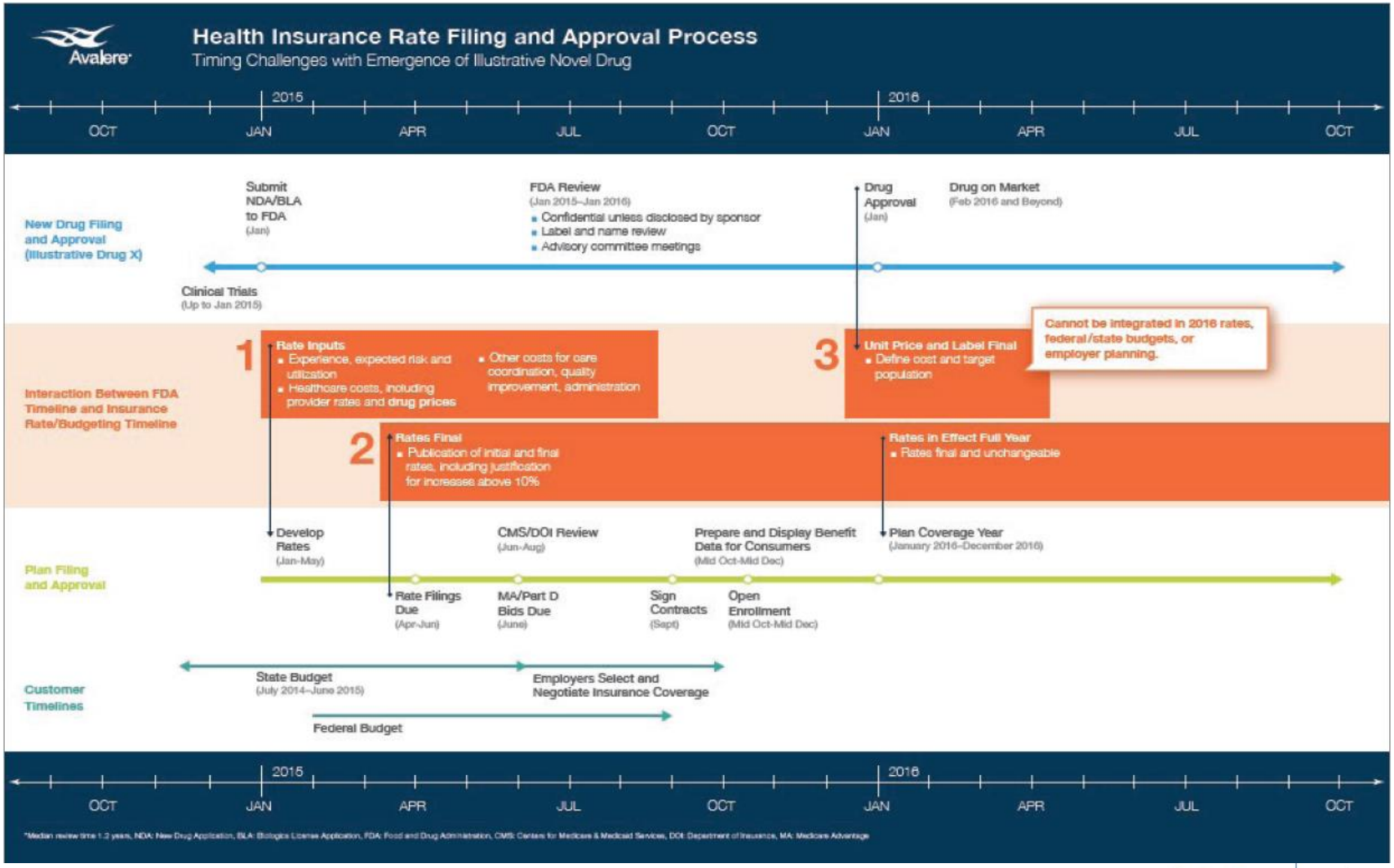
Nation's leading professional association dedicated to increasing patient access to affordable medicines, improving health outcomes and ensuring the wise use of health care dollars

AMCP Academy of Managed Care Pharmacy®

# Three Main Imperatives

Proper planning, budgeting, and forecasting

# Health Insurance Rate Filing and Approval Process




Eli Lilly and Company and Anthem. Facilitating Open Communication About Emerging Therapies. January 29, 2016. (pg 6-9) https://lillypad.lilly.com/WP/wp content/uploads/LillyAnthemWP2.pdf

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# Three Main Imperatives

Proper planning, budgeting, and forecasting

Value-based payment models

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Proper planning, budgeting, and forecasting

Value-based payment models

FDA breakthrough designation

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# Three Main Imperatives

- Proper planning, budgeting, and forecasting
- Value-based payment models
- FDA breakthrough designation

# AMCP Partnership Forum

**Objective**: To convene a Partnership Forum for stakeholders to define AMCP's role in meeting the needs of managed care pharmacy with respect to dissemination of health care economic information (HCEI) pre-approval

**Key Stakeholders**: Pharmaceutical industry, managed care industry, health care providers, pharmacoeconomic experts, health policy experts, and patient advocates

**Date**: September 13-14, 2016 in Tysons Corner, VA

**Moderator**: Susan Dentzer, President & CEO of NEHI

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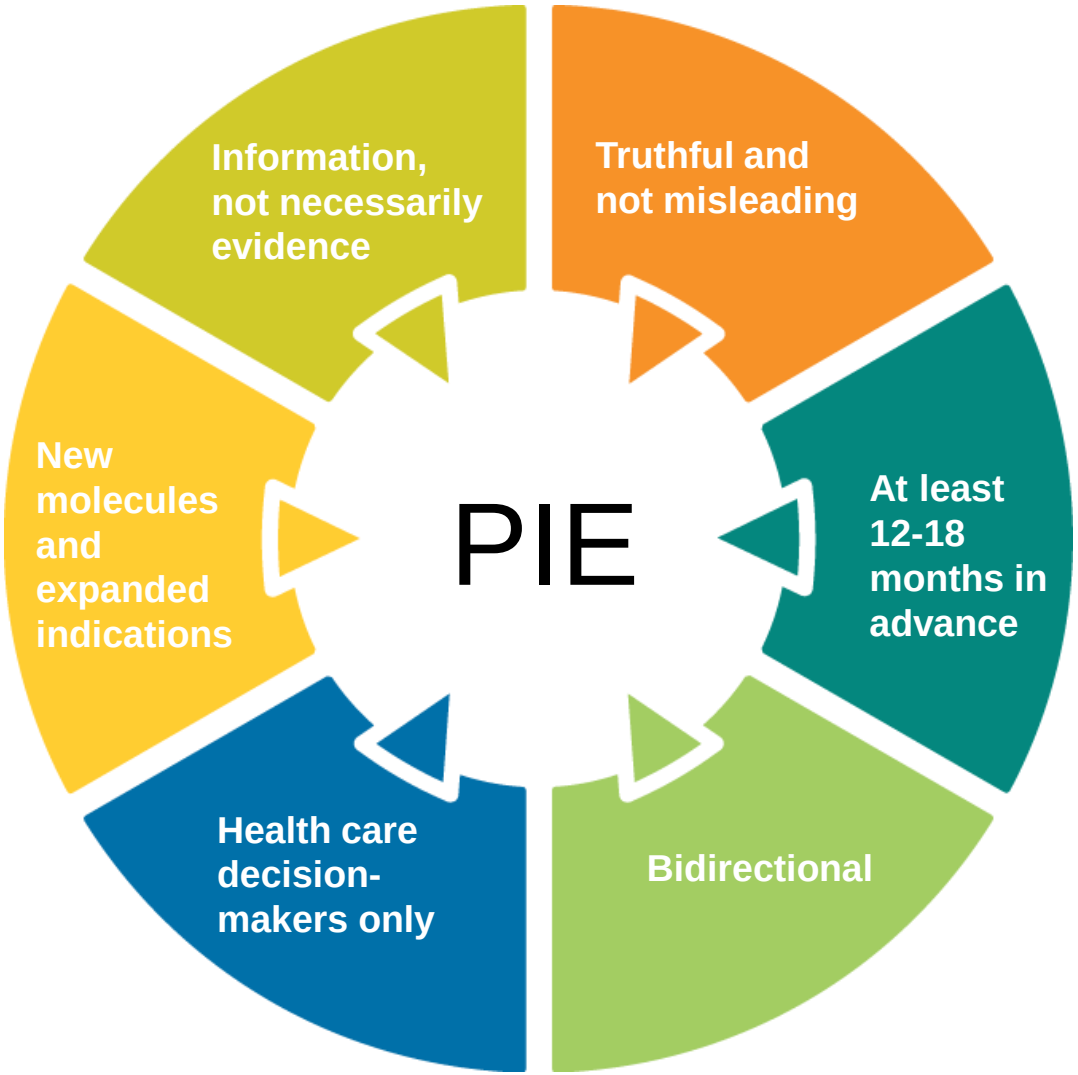
# Consensus Recommendations

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# Legislative Activity

- H.R. 2026 – Pharmaceutical Information Exchange (PIE) Act of 2017
  - To improve patient access to emerging medication therapies by clarifying the scope of permitted health care economic and scientific information communications between biopharmaceutical manufacturers and population health decision makers
  - Referred to the House Committee on Energy and Commerce

# Thank You!

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# Panel Discussion

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# Questions & Answers


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Thank You!

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