Speaking of Value: Continuing the Evolution of Evidence Communication

Avalere Health | An Inovalon Company
March 2017

Presentation Roadmap

1. ***Context:*** The history of FDAMA 114 and other safe harbors for evidence communication
    a. Biopharmaceutical industry perspective
2. ***Update:*** FDA's guidance on evidence communication
3. ***Impacts:*** The importance of evidence in the shift to value
4. ***Q&A***

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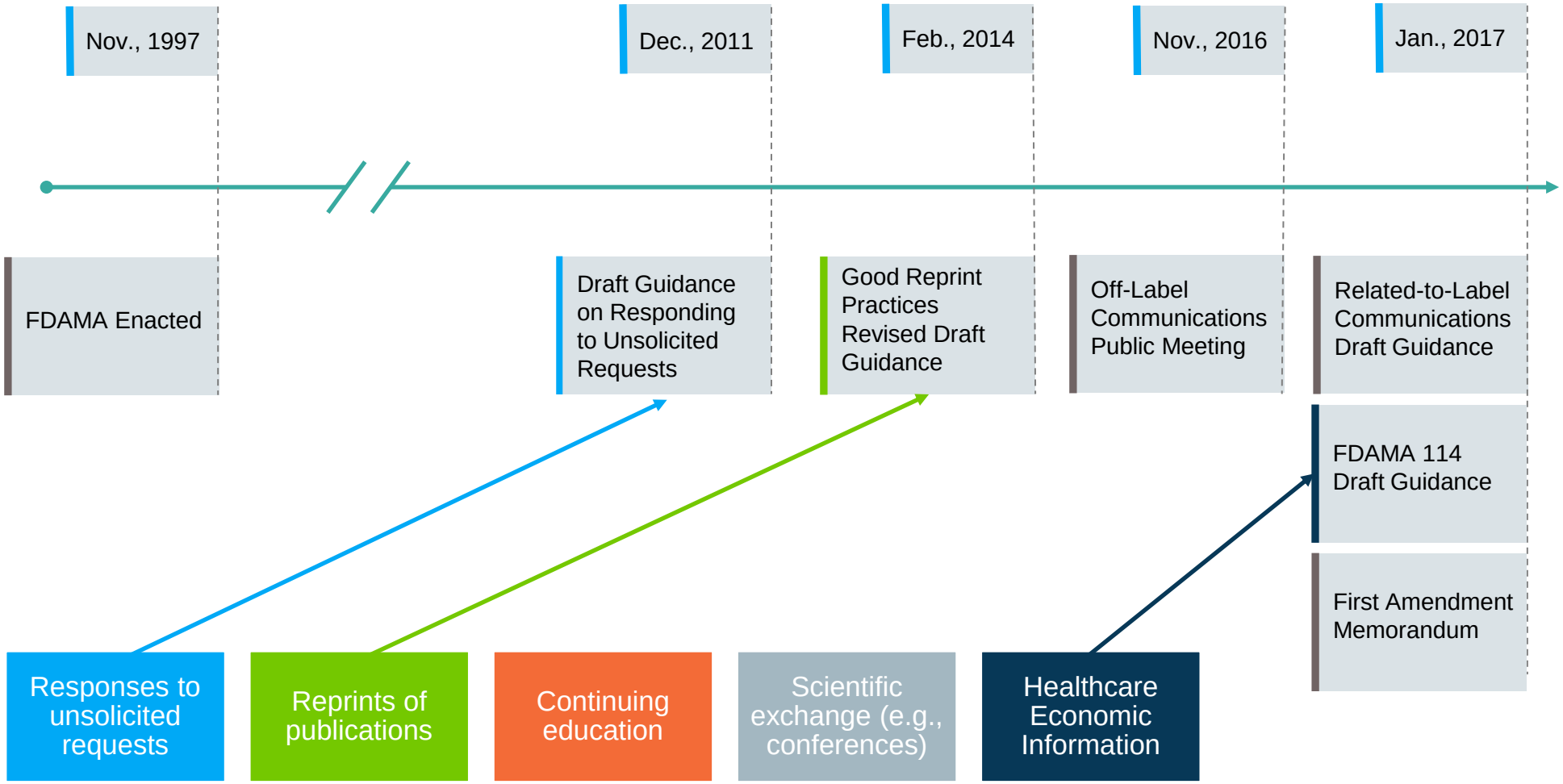
Context: Safe Harbors for Evidence Communication

There are Currently Certain Limited Safe Harbors for Scientific Communication

- Responses to unsolicited requests
- Reprints of publications
- Continuing education
- Scientific exchange (e.g., conferences)
- Healthcare Economic Information

FDA Has Begun Providing More Clarity on its Communications Safe Harbors Recently

While the safe harbors have been known and understood to varying degrees, there was a lack of regulatory clarity until relatively recently



FDA: Food and Drug Administration; FDAMA: FDA Modernization Act

Elements of FDAMA Section 114

Section 114 of the FDA Modernization Act (FDAMA 114) provides safe harbor for communication of economic information related to a drug label; however, FDA had been largely silent on its viewpoint of the statute

Areas of uncertainty within FDAMA 114 include:

- Definition of Health Care Economic Information (HCEI)
- "Competent and Reliable" Evidence Requirements
- Specific Audience: "Formulary Committee or Similar Entity"
- Direct Relation to an FDA-Approved Indication

FDA: Food and Drug Administration

Congress Updated FDAMA 114 in 21st Century Cures

Area of Uncertainty	Change Codified in Cures
Relation to Label HCEI "directly relates" to approved indication	Expands relation by removing "directly": HCEI "relates" to approved indication
Specific Audience "Formulary Committee or Similar Entity"	Expands audience: "a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis…for the selection of drugs for coverage or reimbursement"
Evidentiary Requirement "Competent and reliable scientific evidence"	Includes clinical outcomes in evidentiary standard; requires conspicuous disclaimer

HCEI: Healthcare Economic Information; FDAMA 114: Food and Drug Modernization Act Section 114

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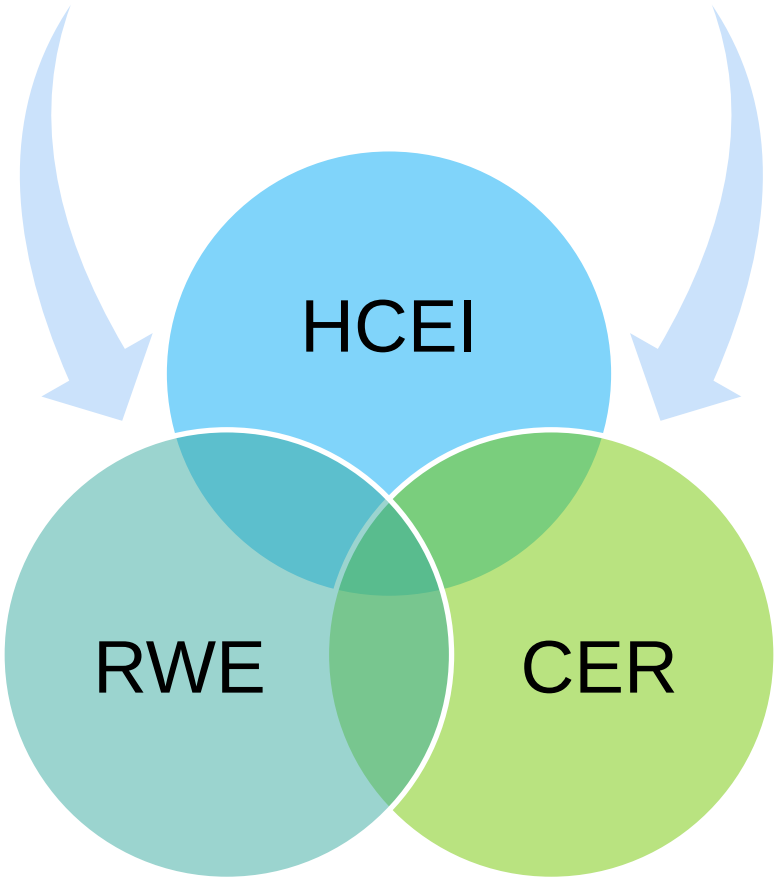
Biopharma Industry Perspective

Avalere Assessed the Biopharma Perspective on Evidence Communication

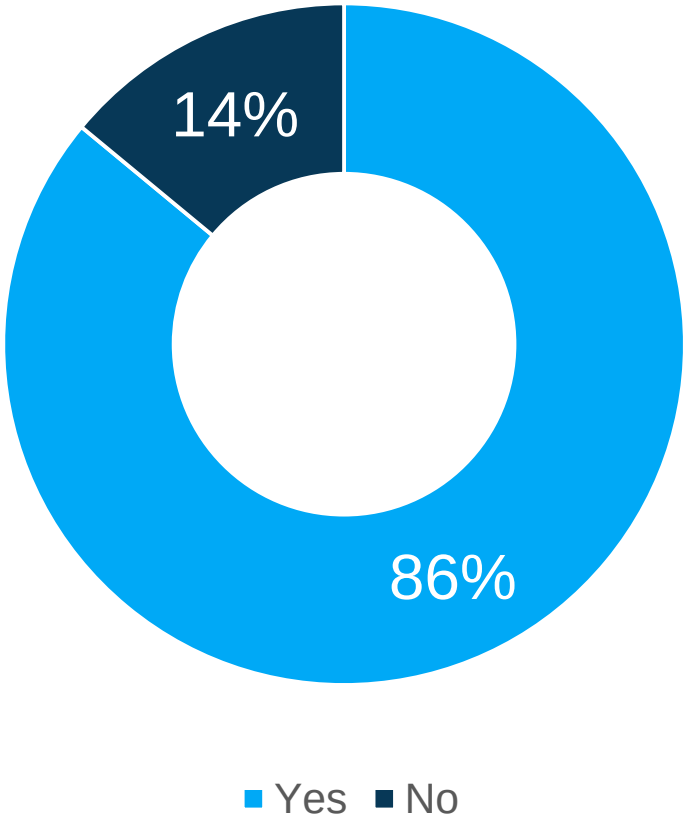
14 manufacturers surveyed



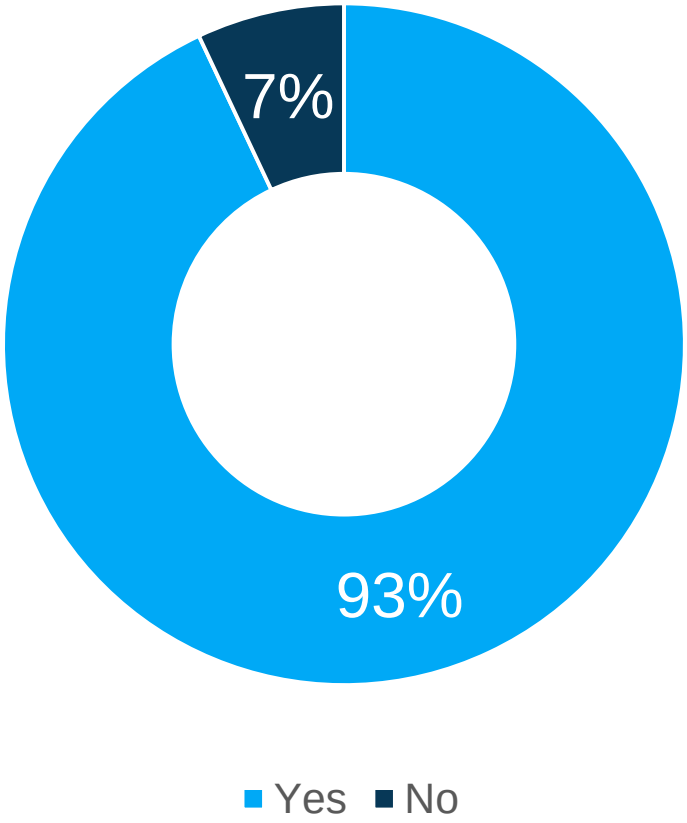
1 Using Evidence to Support Value-Based Decision-Making: Understanding Challenges to Manufacturer Communications. Avalere Health. May 2015. Available at: http://avalere-health-production.s3.amazonaws.com/uploads/pdfs/1432214912_052015_EvidenceComm_WhitePaper_LP_041.pdf

Lack of Guidance Prevented the **Development** and **Dissemination** of Economic and Comparative Evidence

Has lack of guidance from FDA inhibited your organization's dissemination or development of HCEI?



Has lack of guidance from FDA inhibited your organization's dissemination or development of CER?



FDA: Food and Drug Administration; HCEI: Healthcare Economic Information; CER: Comparative Effectiveness Research

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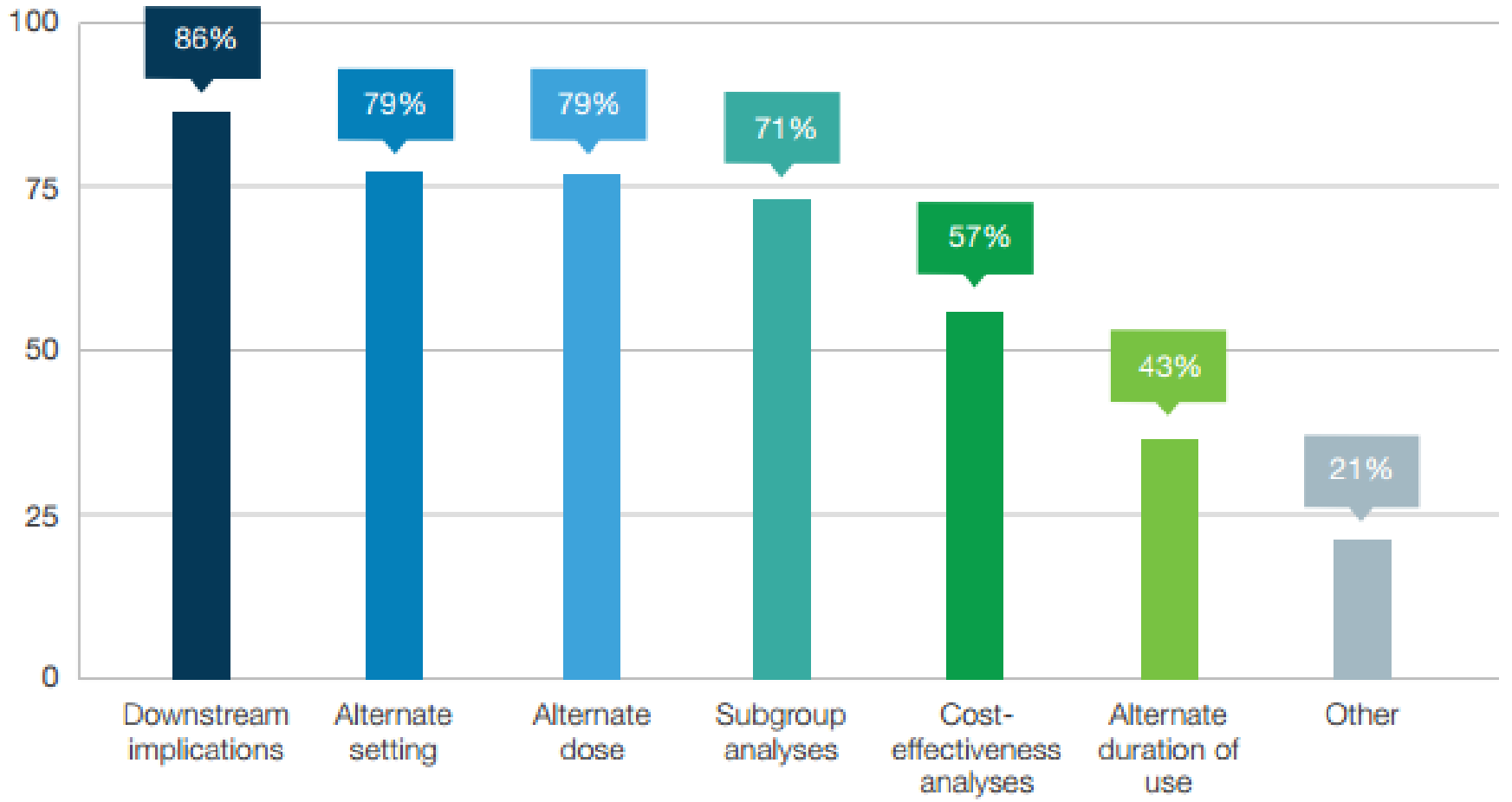
Lack of Guidance Was Seen as Stymying Related-to-Label Communications

Has your organization faced uncertainties as to the appropriateness of proactively disseminating the following types of economic information?



Other: patient registries; real-world utilization patterns that are the standard of care even if off-label; comparative analyses

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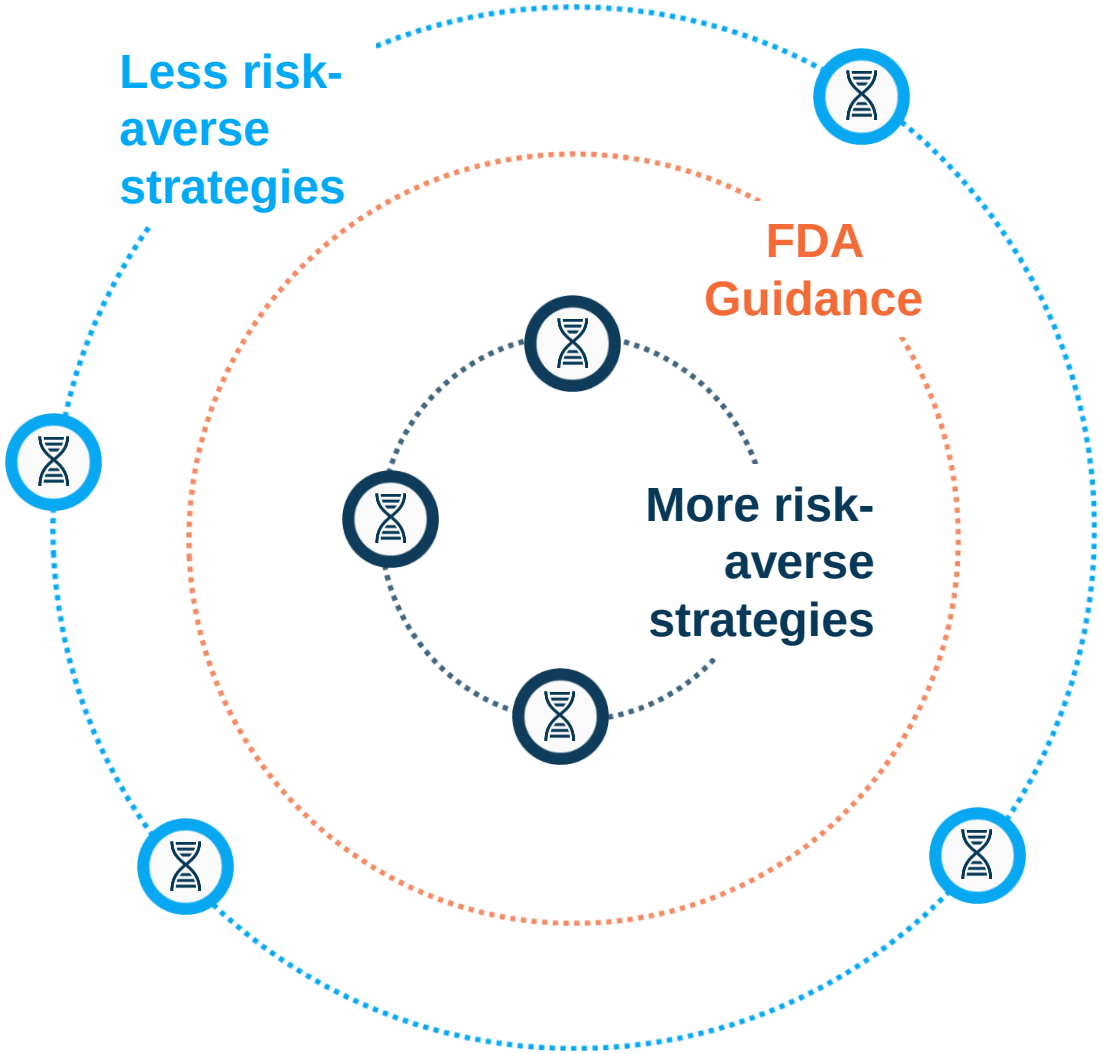
Guidance, However, May Not Always Be the Best Option



Biopharma manufacturer

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Update: Recent Clarity on Evidence Communication

FDA Has Provided Recent Clarity on Evidence Communication

Guidance/ Document	**Content**
Medical Product Communications Consistent with Labeling Draft Guidance	Q&A about communicating product information **consistent with label**
HCEI Draft Guidance	FAQs on **HCEI** communication to payers
First Amendment Memorandum	Discussion white paper on balance of **commercial free speech** and public health considerations

HCEI: Healthcare Economic Information

FDA Has Outlined a Test for Allowing Related-to-Label Communication

In order to promote a product for a use not strictly included in a label, the promotion must meet several criteria:

Condition for Use	Potential for Harm	Safe and Effective Use
Information regarding indication, patient population, dosage & administration, etc., must be consistent with the label	The promotion must not increase the potential for harm relative to the risk-benefit profile of the labeled indication	The promotion must allow for safe and effective use as directed by the label

Communications that promote different indications, populations, dosage & administration, disease course, continue to not be allowed

Consistent with 21st Century Cures, FDA Clarified Several Aspects of FDAMA 114

Defining the Audience

- "Payor": Any entity "responsible for the financing or reimbursement of costs associated with health care services"
- Formulary committee: "multidisciplinary committees [responsible] for the selection of drugs and the management of a drug formulary."

Relation to Label

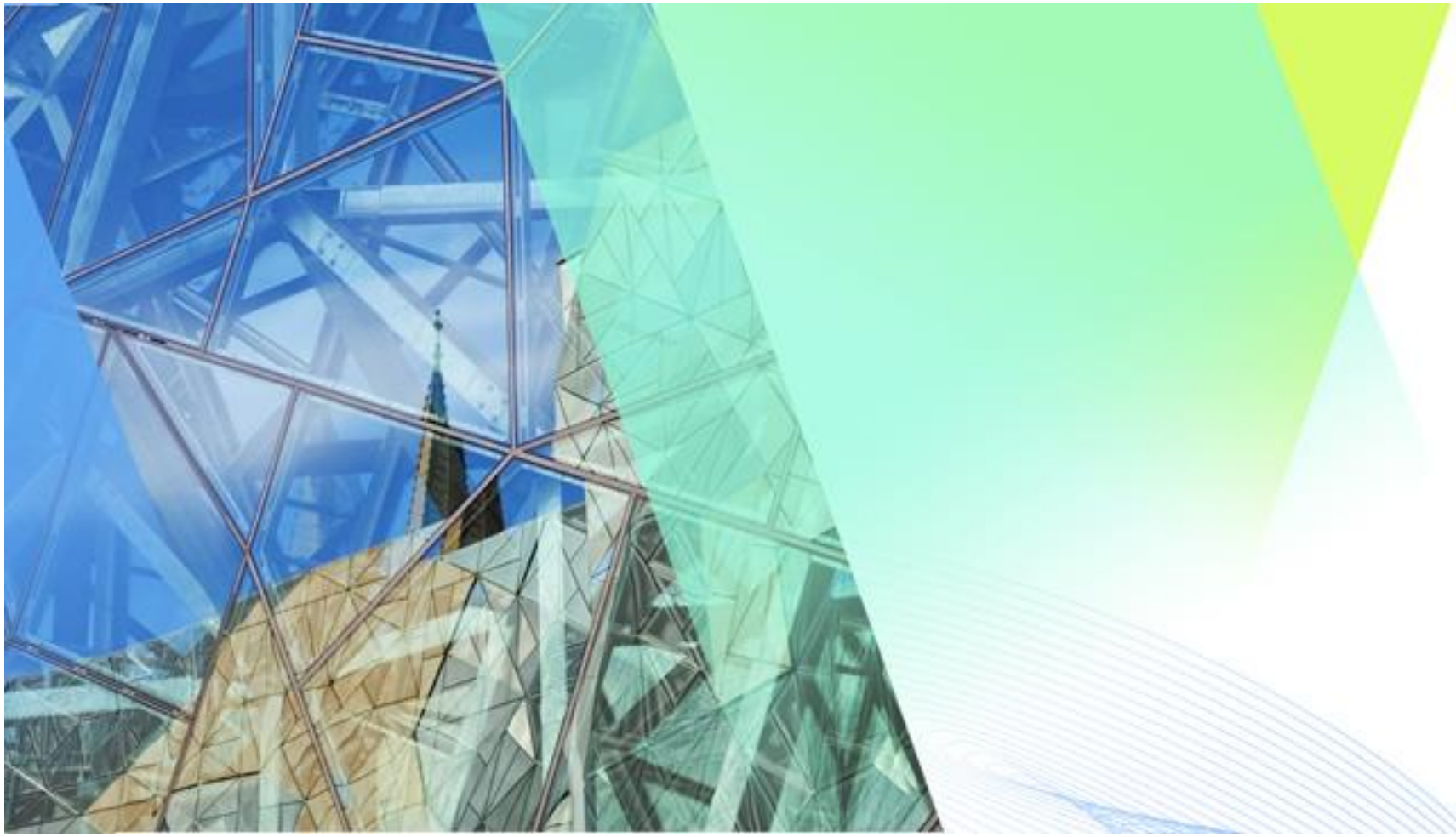
- HCEI may be protected if it does not *only* relate to off-label indication
- Can address BOI, LoS, RWE related to setting, dosing, subgroups, COAs

Pre-Approval Communication

- Allows factual and non-misleading communication of pre-approval information, e.g., pricing, approval timeline, trial results

Clinical outcomes associated with HCEI are to be held to "competent and reliable" evidentiary standard

HCEI: Healthcare Economic Information; FDAMA 114: Food and Drug Modernization Act Section 114; BOI: Burden of Illness; LoS: Length of Stay; RWE: Real World Evidence; COAs: Clinical Outcome Assessments



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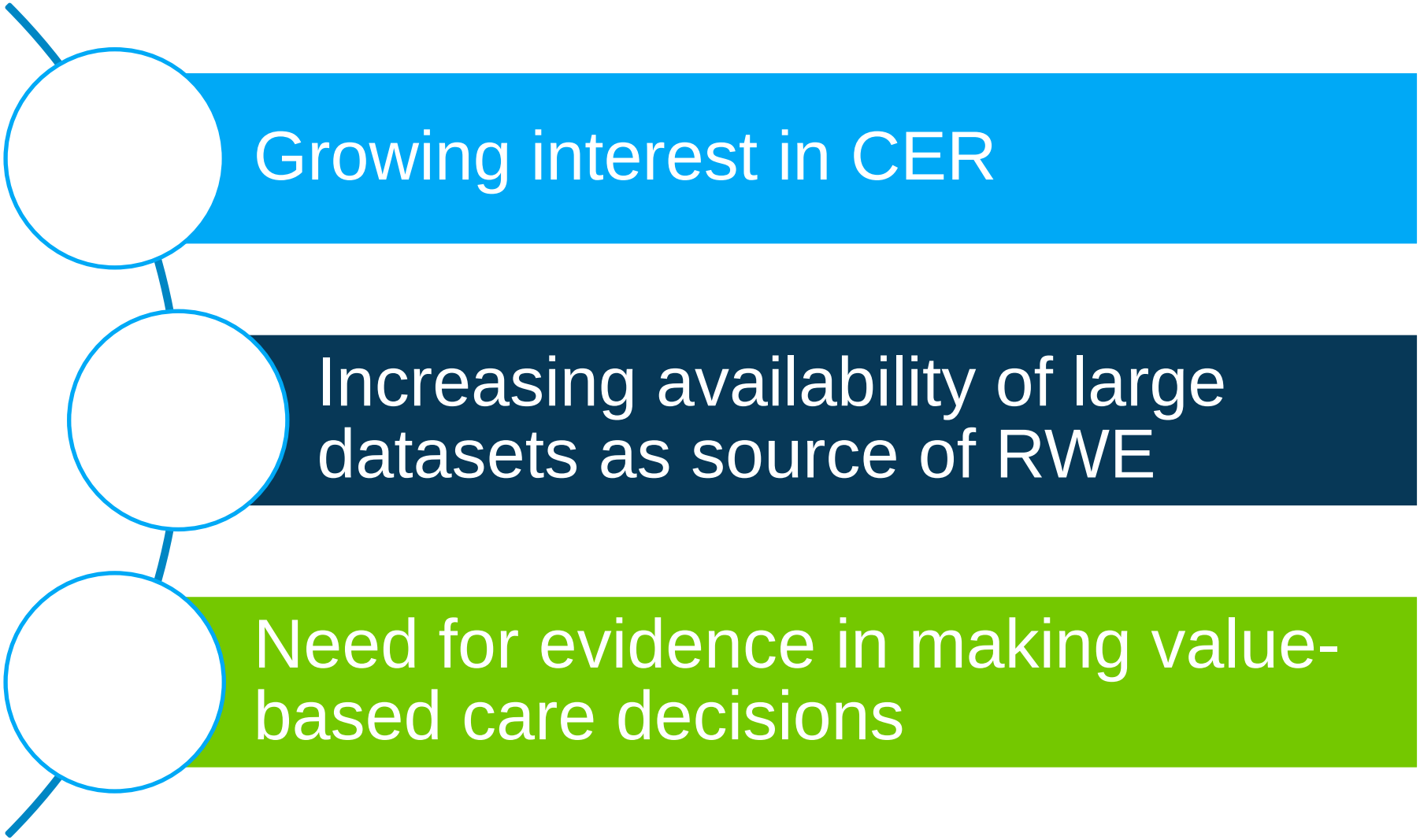
Impacts: The Importance of Evidence in the Shift to Value-based Care

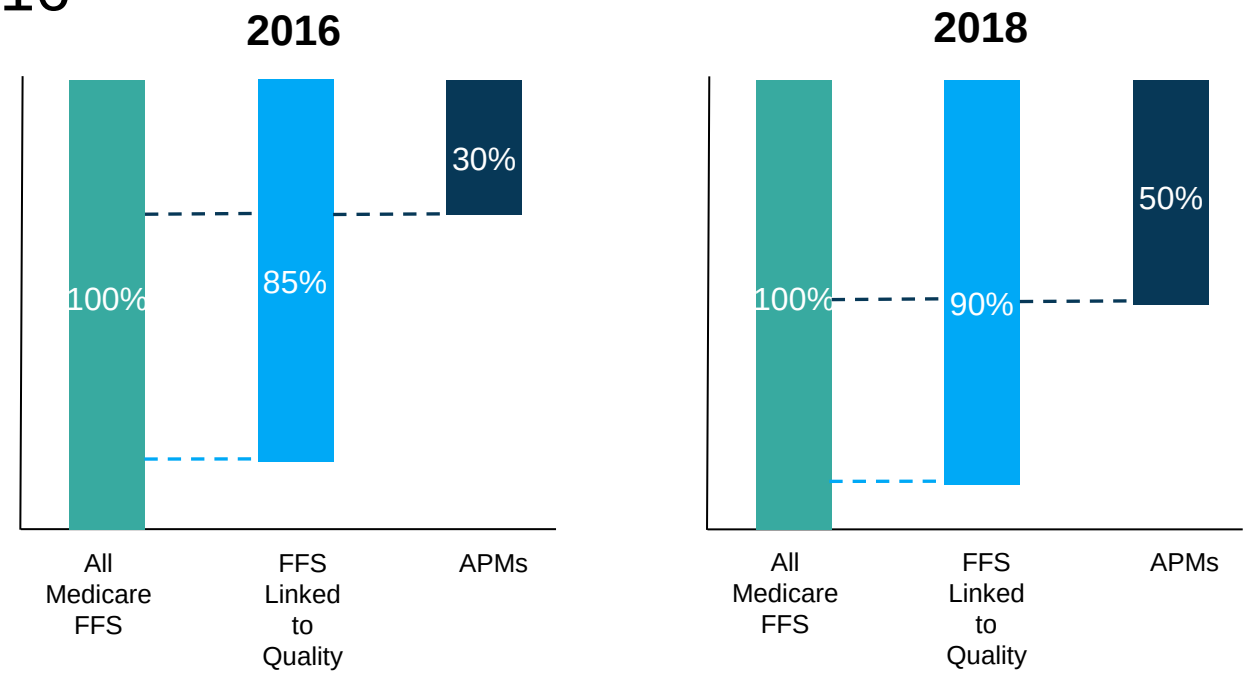
Why Does This Matter?



CER: Comparative Effectiveness Research; RWE: Real World Evidence

Achieving Quality and Value is a Fundamental Goal of Today's Healthcare System

- A high-quality healthcare system is safe, effective, patient-centered, timely, efficient, and equitable
- Value in health is a function of quality and cost
- HHS is migrating FFS payments to APMs and value-based payments
- HHS achieved its 2016 goals but included several upside-only models in its calculation

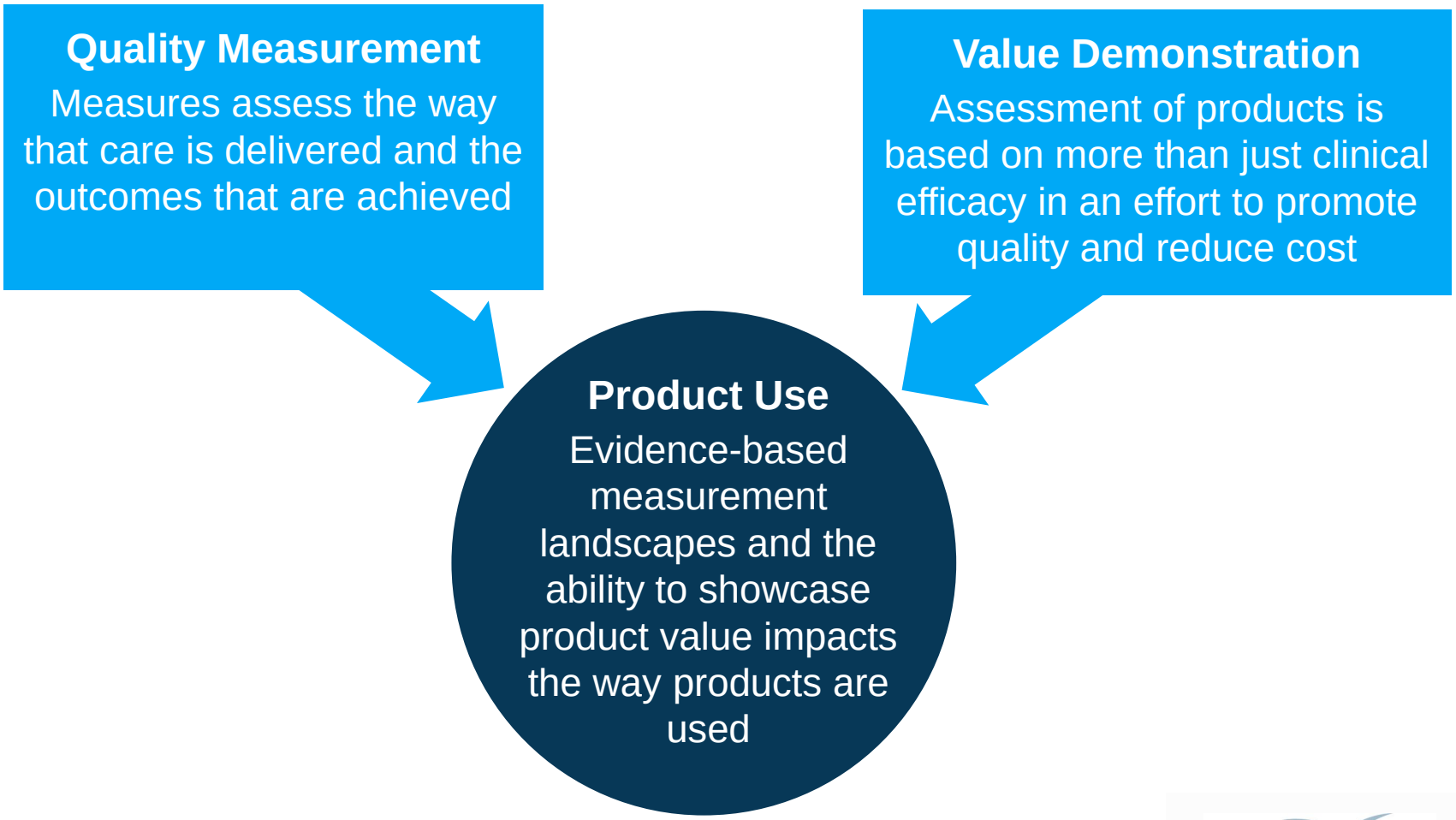


FFS = Fee-for-service; APMs = Alternative payment models

1. Crossing the Quality Chasm. IOM. March 1. 2001
2. Better, Smarter, Healthier: In historic announcement, HHS sets clear goals and timeline for shifting Medicare reimbursements from volume to value. HHS Press Release, Jan. 26, 2015.

Product Use and Commercialization are Increasingly Impacted by Quality and Value

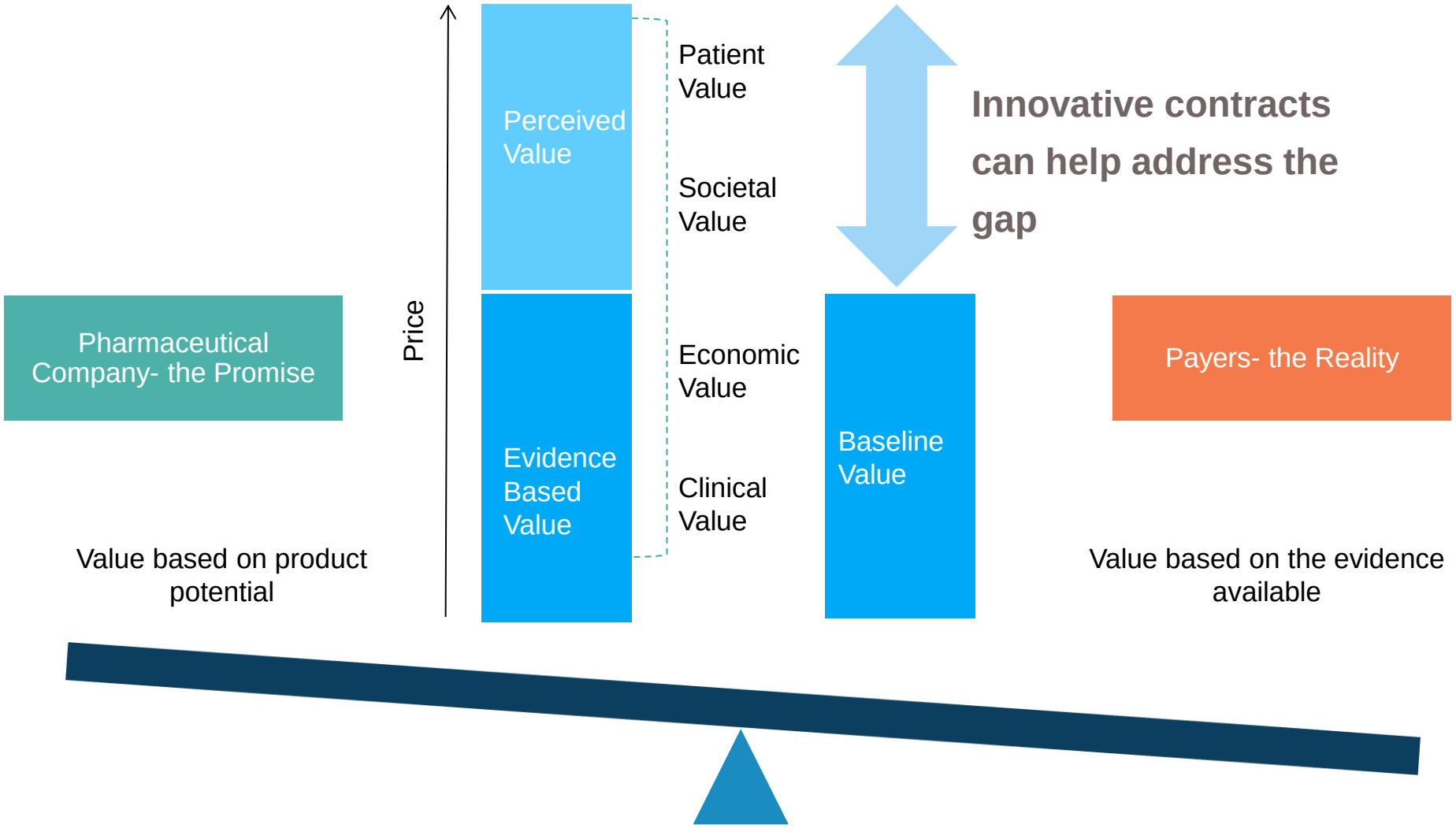
Products that demonstrate high quality and value are preferred relative to alternatives on the market



Third-Party Entities Have Begun to Make Value Assessments

Initiative	Description
ASCO's Value Framework	Conceptual framework for assessing the value of new cancer drugs based on treatment benefits, toxicities, and drug cost
ICER's Emerging Therapy Assessment and Pricing Program	Value assessment and price benchmark reports focusing on a number of specialty drugs/therapeutic areas. Reports address clinical effectiveness, cost-effectiveness, potential budget impact and propose a "value-based price benchmark" for each therapy evaluated
Memorial Sloan Kettering's DrugAbacus	Calculator intended to be used to assess prices for cancer drugs based on its efficacy, toxicity, novelty, related R&D expense, rarity, and population health burden
NCCN's Evidence Blocks	Visual representation of five measures: efficacy, safety, quality of evidence, consistency of evidence, affordability for evaluation of cancer drugs that builds on its current guidelines

Innovative Payment Solutions Such as Outcomes Based Contracts Require Evidence Communication



New Opportunities for Manufacturer-Payer Communication

Statutory changes, legal challenges, and regulatory clarity allow manufacturers and payers to move more boldly into the shift to value-based care

Expanded Use of CER and RWE

- Comparative/head-to-head studies
- Patient-reported outcomes data when consistent with label
- Competent and reliable evidence – both clinical and economic – not necessarily reaching RCT threshold

Pre-Approval Communication

- Communication regarding products not yet approved for marketing

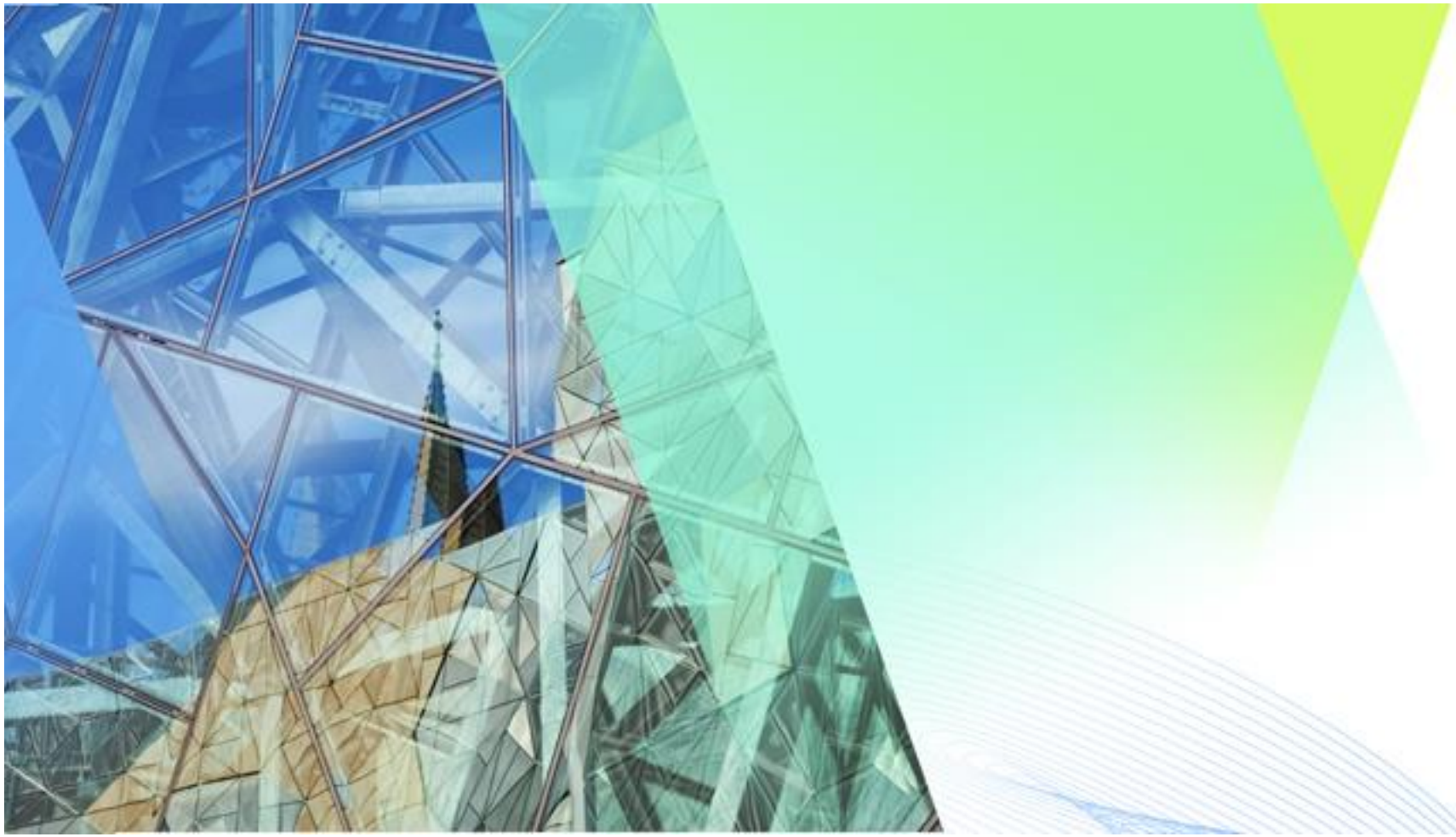
More Specificity

- New subgroup analyses when consistent with label or HCEI-focused
- Longer-duration safety/efficacy studies consistent with label

CER: Comparative Effectiveness Research; RWE: Real World Evidence; RCT: Randomized Controlled Trial; HCEI: Healthcare Economic Information

Next Steps

1. Continued engagement with and clarity from FDA and other regulatory bodies
    a. FDA's evidence communication docket remains open through April
    b. Other issues must be addressed, including modernized regulation regarding price reporting and the anti-kickback statute
2. Proliferation of innovative, value-based arrangements
    a. There are currently relatively few innovative contracting arrangements in the United States
3. Evolved engagement between payers and manufacturers
    a. Use increased statutory and regulatory flexibility to engage in more advanced value-based arrangements
    b. The role of PBMs in this space remains somewhat undefined



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Q & A