BmDR- Biomarker Data Repository

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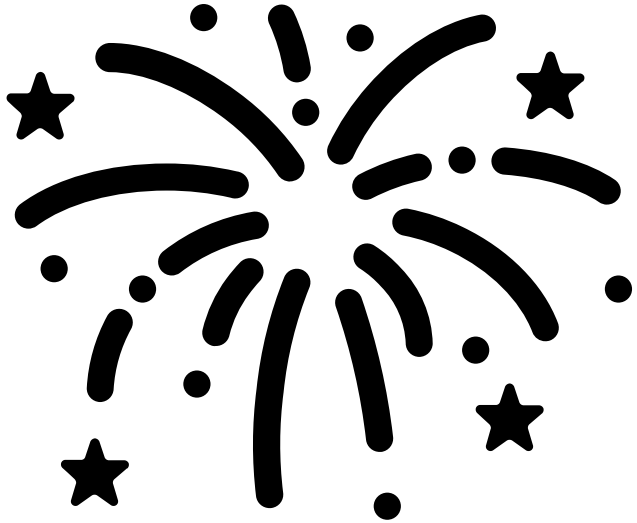
Data: what is it good for?

- Models
- Initiatives
- Registries
- Design of trials
- Qualifications
- Etc., etc., etc.,…

But…. What if it could do even more?



PSTC / FNIH BC –Urinary Kidney Injury Biomarker Composite Measure

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Renal Injury Biomarkers Qualified by US FDA for Use in Phase 1 Clinical Trials

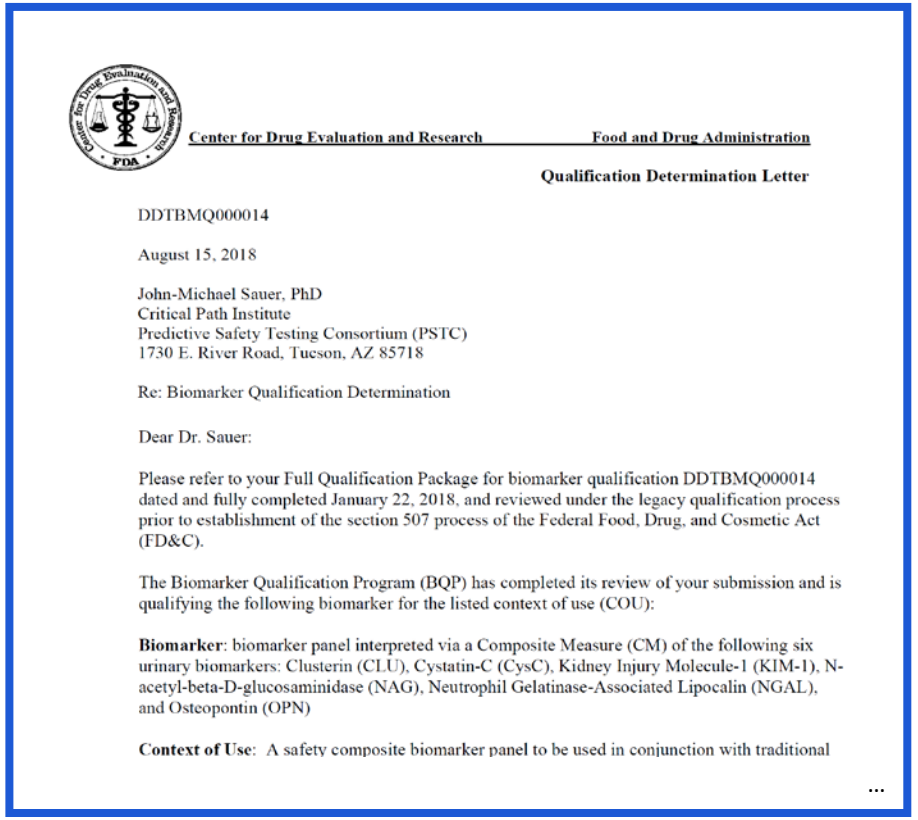
Biomarker

A biomarker panel interpreted via a Composite Measure (CM) of the following six urinary biomarkers:

- Clusterin (CLU)
- Cystatin-C (CysC)
- Osteopontin (OPN)
- N-acetyl-β-D-glucosaminidase (NAG)
- Neutrophil Gelatinase-Associated Lipocalin (NGAL)
- Kidney Injury Molecule-1 (KIM-1)

Context of Use:

A safety composite biomarker panel to be used in conjunction with traditional measures to aid in the detection of kidney tubular injury in phase 1 trials in healthy volunteers when there is an a priori concern that a drug may cause renal tubular injury in humans.



Center for Drug Evaluation and Research — Food and Drug Administration

Qualification Determination Letter

DDTBMQ000014

August 15, 2018

John-Michael Sauer, PhD
Critical Path Institute
Predictive Safety Testing Consortium (PSTC)
1730 E. River Road, Tucson, AZ 85718

Re: Biomarker Qualification Determination

Dear Dr. Sauer:

Please refer to your Full Qualification Package for biomarker qualification DDTBMQ000014 dated and fully completed January 22, 2018, and reviewed under the legacy qualification process prior to establishment of the section 507 process of the Federal Food, Drug, and Cosmetic Act (FD&C).

The Biomarker Qualification Program (BQP) has completed its review of your submission and is qualifying the following biomarker for the listed context of use (COU):

Biomarker: biomarker panel interpreted via a Composite Measure (CM) of the following six urinary biomarkers: Clusterin (CLU), Cystatin-C (CysC), Kidney Injury Molecule-1 (KIM-1), N-acetyl-beta-D-glucosaminidase (NAG), Neutrophil Gelatinase-Associated Lipocalin (NGAL), and Osteopontin (OPN)

Context of Use: A safety composite biomarker panel to be used in conjunction with traditional

...

Kidney Safety biomarkers

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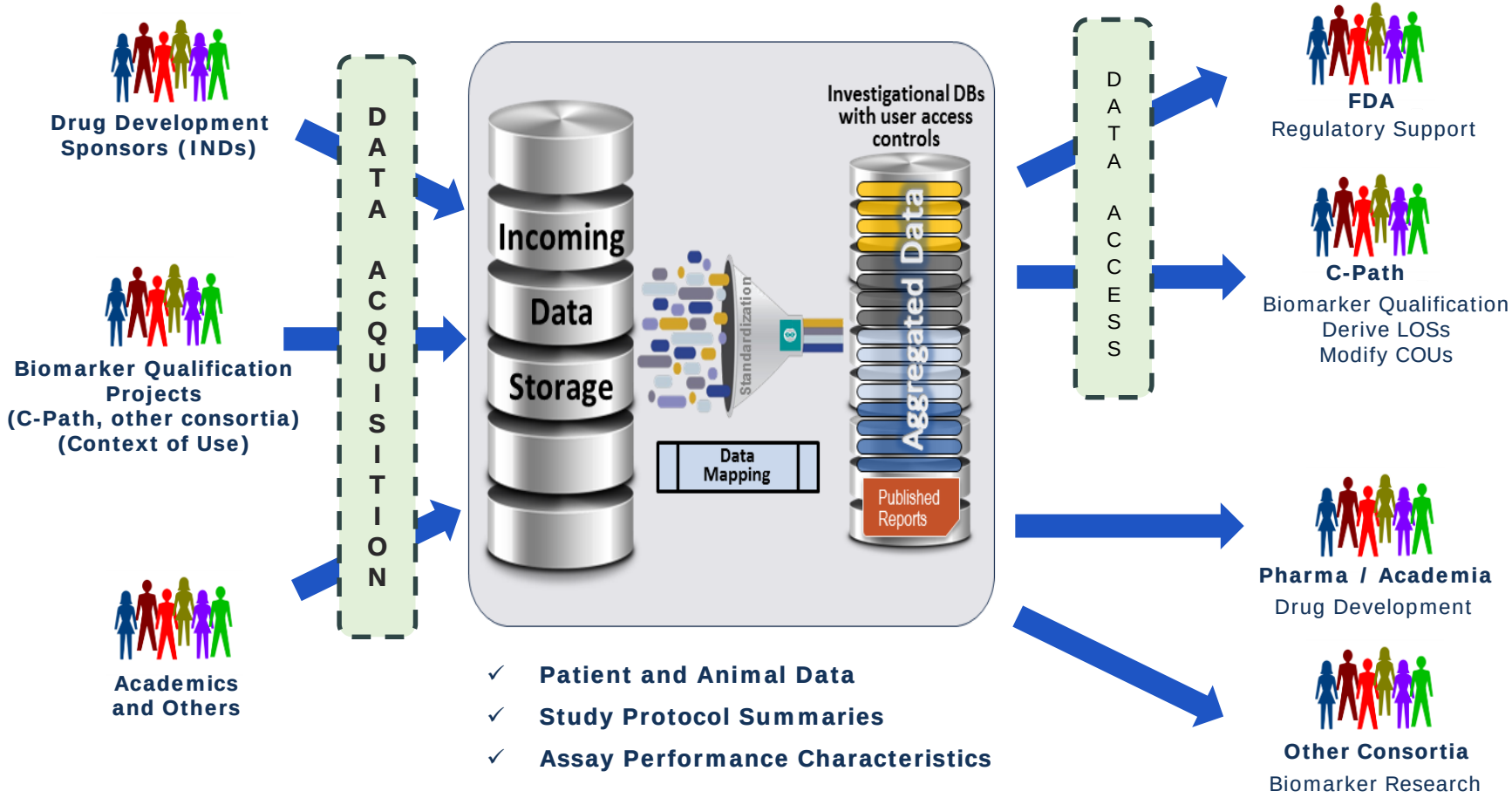
- Qualified and being used in clinical studies now
- All the benefits and advantages that means
  - Kidney injury predicted early
  - No concerns if biomarker data acceptable
  - No need to review biomarker data acceptability
  - Risks mitigated
  - Money saved
- But what if a question arises that the clinical protocol didn't anticipate?

What if….

- Different gender?
- Different population?
- Different genetic background?
- More people?
- Anything?

- Wouldn’t it be great if there was a database of patient data available to ask those questions? Acceptable to the FDA?

BmDR – a solution that does exist



Data for both novel and current standard biomarkers (sCR, BUN, eGFR) would be included

BmDR – a solution that does exist

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What is it?

A repository for data on novel translational biomarkers (animal and human) evaluated during drug development studies.

Why? A database of robust data can

1) facilitate qualification of biomarkers (with existing and new data),
2) support the implementation of exploratory biomarkers in drug development
3) help inform determinations about the value of biomarkers in the clinical space
4) act as a multiplier of data
5) can be queried for questions your study did not ask, and
6) may provide data on populations you did not study

How?

- Map blinded, de-identified data from multiple sponsors to CDISC standards and store in secure repository;
- Majority of data are likely to be contained in regulatory submissions, and thus not new disclosures, and/or captured in studies sponsored by granting agencies.

FDA Endorsement

U.S. FOOD & DRUG ADMINISTRATION

From the Desk of Janet Woodcock

New drugs—and new uses for existing drugs—save lives, reduce suffering, and improve the quality of life for millions of Americans. I am continually challenged to make sure that FDA's regulatory process remains the world's gold standard for drug approval and safety. As part of my role as the director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA), I have led many of FDA's drug initiatives, including the introduction of FDA's "Critical Path" Initiative in 2004, which is designed to move medical discoveries from the laboratory to patients more efficiently.

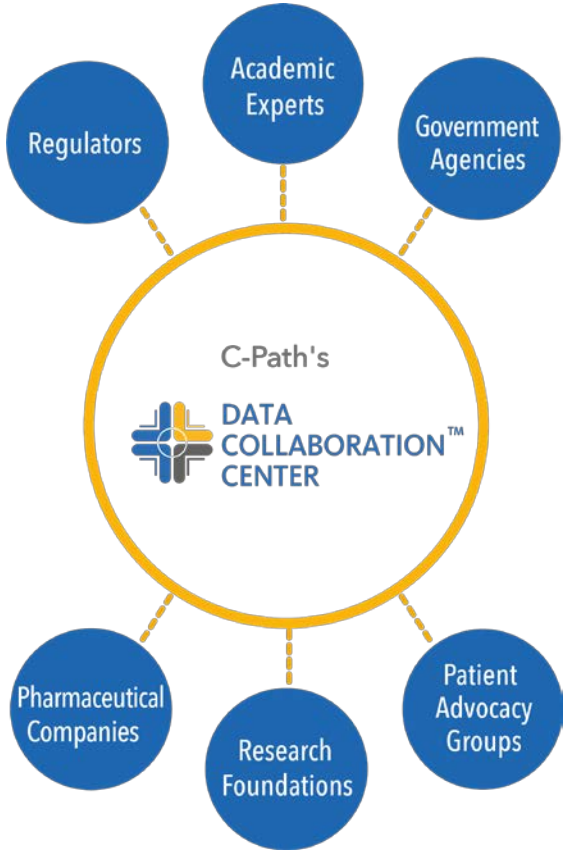
The Critical Path Institute (C-Path), formed in 2006 as a response to that initiative, is actively seeking to make that vision a reality. This non-profit organization brings worldwide regulatory agencies (such as the FDA) and pharmaceutical companies together to further the science and collaboration necessary to accelerate rapid and safe drug development.

The Predictive Safety Testing Consortium (PSTC), one of many consortium within C-Path, is currently reaching out to industry partners in Pharmaceutical and Biotech sectors to contribute to a Biomarker Data Repository as part of a pilot project aimed at new and modified context of use (COUs) for kidney safety biomarkers. C-Path has a long history of data management in a controlled, de-identified manner that protects the data and contributors. Additional information on the Kidney Safety Biomarker Data Repository Pilot program is available on the C-Path website(www.c-path.org).

I support this effort and hope our industry colleagues will contribute. I look forward to the output of the pilot and hopefully in the future, the expanded repository.

Janet Woodcock

Leveraging C-Path's Data Collaboration Center



- ✓ Provides large-scale data solutions for scientific research
- ✓ Develops customized data platforms for improved collaborations
- ✓ Multisource data aggregation and standardization
- ✓ Curation and administration of data and its storage
- ✓ Robust security policies and framework
- ✓ Application of current regulations to ensure compliance

As of February 2018, the DCC's data platform securely hosts data from 107 clinical trials and 119 nonclinical studies, representing over 60,000 subjects, over 200 million data points, and six different therapeutic areas.

Overcoming the barriers;
How Does BmDR work for you?

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- FDA endorsed; will FDA accept this?
- Neutral space; C-path has experience in data storage and curation
- Common Format; Data in actionable form
- Acceptable biomarkers; Qualified and utilized

What remains is to collect the data that is being generated NOW!

How does this work? Data contribution! And then…..

- What if that database included data on other biomarkers?
- Other COUs could be qualified… data is here.
- Recalibrate normal value ranges and cut point ranges.
- Other phases of clinical development (exploratory development)?
- Data available to learn and confirm!
- help inform determinations about the value of biomarkers in the clinical space.

What else could a data base of de-identified biomarker data do? What barriers could this overcome? What other solutions could this provide?

Panel discussion