Commentary

Data Sharing in the Pharmaceutical Enterprise: The Genie's Out of the Bottle

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ABSTRACT

Objective: This Commentary shows that the present emphasis on the sharing of data from clinical trials can be extended to the entire pharmaceutical enterprise.

Methods: The authors constructed a Data Sharing Dashboard that shows the relationship between all of the life-cycle domains of the pharmaceutical enterprise from discovery to obsolescence and the domain-bridging disciplines, such as target credentialing, structure-activity relationships, and exposure-effect relationships.

Findings: The published literature encompassing the pharmaceutical enterprise is expansive, covering the major domains of discovery, translation, clinical development, and post-marketing outcomes research, all of which have even larger, though generally inaccessible, troves of legacy data bases. Notable exceptions include the fields of genomics and bioinformatics.

Implications: We have the opportunity to broaden the present momentum of interest in data sharing to the entire pharmaceutical enterprise, beginning with discovery and extending into health technology assessment and post-patent expiry generic use with the plan of integrating new levels and disciplines of knowledge and with the ultimate goal of improving the care of our patients. (*Clin Ther*. 2017;39:1890–1894)

Key words: data sharing, exposure effect relationship, outcomes research, pharmaceutical enterprise, structure activity relationship, target discovery.

Since the passage of the US Food and Drug Administration's Modernization Act in 2002, with its provision for ClinicalTrials.gov,[1] momentum has been building to make the case for an ethical basis and scientific need for the sharing of data from clinical trials conducted by the pharmaceutical research and development enterprise.[2,3] Authors have emphasized the importance of verifying the original analyses and the potential for providing insight into new lines of research. The National Institutes of Health have further proposed a policy on the dissemination of National Institutes of Health–funded clinical trial information, beginning from Phase I,[4] and the European Medicines Agency established a policy on the publication of clinical reports that are submitted as part of marketing authorization applications, beginning in January 2015.[5] ClinicalTrials.gov and clinicaltrialsregister.eu include advanced searching capabilities for finding individual, patient-level and grouped, study arm-level information, and ClinicalTrials.gov has created a public–private partnership, the Clinical Trials Transformation Initiative, for the development of a relational database to facilitate aggregated analyses.[6]

However, this is really only the beginning. As presented in the **Figure**, the pharmaceutical research and development enterprise spans the entire range of domain processes, including: (1) discovery (target identification[21] and molecule development[14]); (2) translation (experience in animal models,[22] first-in-human Phase I tolerability, pharmacokinetics and pharmacodynamics,[23,24] and proof-of-principle Phase II dose-ranging studies); and Phase III large-scale clinical trials. The focus and emphasis of much of the published literature on sharing data have been

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Domain - Bridging Disciplines	Life -Cycle Domains	Data Sharing Dashboard
Target Credentialing	Target	Advaita,[7] DiscoverX,[8] Drug Bank,[9] GenScript[10]
Structure Activity Relationship	Molecule	SAR, [11-13] Computer-aided Drug Design[14]
Exposure – Effect Relationship	Animal Model	Interconnectivity of disparate data silos[15]
Clinical Pharmacology	First In Humans	Bioinformatics[16]
Outcomes Research	Clinical Trials	ClinTrials.gov[1] Europeana Linked Open Data[17]
Cost -Benefit Cost - Effectiveness	Commerce	Patient -Centered Outcomes Research Institute (PCORI)[18]
	Generic	Potentially new uses[19,20]

Figure. Data-sharing dashboard of life-cycle domains and domain-bridging disciplines.

overwhelmingly on clinical trials. However, the arguments that support the application of the principle of data sharing to the ultimate benefit of patients apply equally well to the other domains of discovery and translation. Furthermore, this concept can be extended to the full spectrum of a molecule's life-cycle activities, including those involved in the commercialization of a patented product (outcomes research[18]). These domains may also be considered in this same arena of interest in the sharing of data. Furthermore, after patent expiry, when drugs find greater marketability as generics, they may also find new markets following screening for repurpose, as recently reported on treatments for Zika virus,[19] or as outdated drugs that are considered for new indications.[20]

In addition, the Figure includes *domain-bridging disciplines,* which are well-established scientific models of correlative analysis that serve to deepen our understanding of the "how" in the mechanisms of action at each level. These disciplines are as follows.

Target discovery and credentialing strive to understand the effect of the molecule on the target site. Pathway analysis related to pathology is addressed at a very early stage of the concept validation process to avoid a more costly failure at a later stage of development. The goals are to identify potential nodes of importance that clarify disease pathways and to identify sensitive targets (eg, nuclear receptors, immune checkpoints, kinases, G protein–coupled receptors, biochemical pathways of drug effects). A number of bioinformatics tools are now available to contribute to the credentialing process.[7–10,25]

Structure–activity relationship clarifies the 3-dimensional structure of a molecule and its relationship to biological activity. Molecular property modifications and spatial relationship of functional groups characterize *quantitative SAR*. The intensity of effect and the nature of the pharmacologic outcome in relationship to a specific pharmacophore are dictated by SAR.[11–13]

Exposure–effect relationship focuses on understanding the concentration—pharmacologic effects of a drug as they are observed over the whole range of studies, from the in vitro relationship through the in vivo models and finally to clinical proof of principle. Typical pharmacokinetic-pharmacodynamic modeling helps to project the concentration–effect relationship from the preclinical to the clinical setting and to validate the concept and dose selection. All of the changes in the interfering and contributing factors are captured as they occur at each step in the process.

Clinical pharmacology determines the tolerability window of doses, maximum tolerated dose, and parametric values for pharmacokinetics and pharmacodynamics and begins to set the statistical brackets on the frequency and the characterization of adverse events as a drug is studied in larger numbers of patients.

Outcomes research describes the usage parameters as a drug moves from the research clinic to clinical practice. The measures of interest are focused on functionality and quality of life, often in the context