Why Medical Product Development Has Special Requirements

Raymond L. Woosley, MD, PhD
President and CEO
Critical Path Institute
Medical Products are Different

Human Health – Life & Death Outcomes
Regulated by FDA/EMA

Human Diversity Affects Product
Objective of Precompetitive Sharing

Develop a scientific consensus on which methods are “qualified for use” in drug development among......

1) those who will **use the methods** (industry),

AND

2) those who will **accept the methods** (FDA).
What Can Be Shared

- Work to Define:
  - Common Data Elements
  - Define Performance Standards
- Methods
  - Safety Testing
  - Efficacy Testing
- Knowledge of Diseases
- Applied Science Research
- Regulatory Science Research
Industry R&D Rising, but...

New Approvals

17 in 2007
21 in 2008
25 in 2009
A Global Issue – A call for collaboration

Centre for Medications Research International Ltd. Pharmaceutical R & D Factbook

![Graph showing trends in R&D expenditure, development times, and NME output from 1995 to 2004.](image)
C-Path’s Consortia Model

Multiple Companies

Formal Legal Agreement

Precompetitive Neutral ground

C-Path

FDA

EMEA

Patients

NIH

Academia
C-Path’s Neutral Funding

- FDA and AHRQ
- Foundations
- Philanthropy

- Foundation for NIH
- Innovative Med. Initiative
- Regulated Industry

Critical Path Institute

Research Grants

Consortia fees for Research
Participants in C-Path’s Consortia

- 28 Major Pharmaceutical Companies
- FDA and EMEA
- NIA, NINDS, NCI, NHLBI
- Six Patient Advocacy Organizations
- Over 600 Scientists
A Global Endeavor
>600 Scientists

Consortia Members and Advisor Locations

Spans 17 Time Zones!
C-Path’s Consortia
Addressing Regulatory Science

- Predictive Safety Testing Consortium (PSTC)
  DRUG SAFETY
- Patient-Reported Outcomes (PRO)
  DRUG EFFICACY
- Coalition Against Major Diseases (CAMD)
  SHARING CLINICAL DATA (Placebo/control)
Qualification of New Tools

A new pathway.....

Planning Phase
- Legal Agreement, Coordinating Committee, Planning etc
- Work Scope Document
- Working Groups
  1. ...
  2. ...
  3. ...
  4. ...

Execution Phase
- Methods & Results Sharing

FDA/EMA Review Phase
- FDA/EMA Submission
- FDA/EMA Review
- BQRT
- Qualified Methods

Scientific Consensus

Greater Efficiency & Safety
Predictive Safety Testing Consortium (PSTC) Members

Advisors: FDA, EMEA
Kidney Working Group Progress

Creatinine & BUN do not detect subtle drug injury
Tests Are 105 Years Old

Twenty-three new kidney biomarkers:

- Extremely Sensitive
- Seven: excellent data for submission to FDA and EMEA
Biomarker Qualification Submission

Data for 7 renal injury biomarkers

**First** FDA submission of its kind – for a process change
**First** to create a Biomarker Review process
**First** joint submission to both US FDA and EMEA
(June 15, 2007)

**First trilateral** (US- Europe-Japan) review meeting
**First** FDA-EMEA (US-Europe) regulatory decision

April 7, 2008 - First joint approval of Renal biomarkers qualified for use in drug development
April 14, 2008

RE: Review Submission of the Qualification of Seven Biomarkers of Drug-Induced Nephrotoxicity in rats.

Dear Drs. Dieterle, Mattes, and Sistare:

This letter provides the conclusions from our review of your submission supporting the qualification of seven biomarkers of drug-induced nephrotoxicity in rats. We conclude that:

The urinary kidney biomarkers (KIM-1, Albumin, Total Protein, β2-Microglobulin, Cystatin C, Clusterin and Trefoil factor-3) are acceptable biomarkers for the detection of acute drug-induced nephrotoxicity in rats and can be included along with traditional clinical chemistry markers and histopathology in toxicology studies.
EMEA Decision: “Biomarkers Qualified”

London, 3 July 2008
Doc. Ref. EMEA/250885/2008 Rev. 1

COMMITTEE FOR HUMAN MEDICINAL PRODUCTS

FINAL REPORT ON THE PILOT JOINT EMEA/FDA VXDS EXPERIENCE ON QUALIFICATION OF NEPHROTOXICITY BIOMARKERS.

<table>
<thead>
<tr>
<th>Event</th>
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<tbody>
<tr>
<td>Adoption by CHMP</td>
<td>April 2008</td>
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<tr>
<td>For Release for Consultation</td>
<td>May 2008</td>
</tr>
<tr>
<td>End of Consultation (Deadline for Comments)</td>
<td>Extended to July 2008</td>
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Summary: Needed for Innovative Drug Development

- Common data elements in development
- Biomarkers “qualified for use”
- Independent certification that the biomarker assays perform as intended (Analytic Validity in the Field)
- Innovative tools/methods for trial design
  - Adaptive clinical trial design
  - Trial simulation using disease models
- Innovative Business Models