Drug Repurposing Guidebook

Building Block I435

This document defines the content of the FACT SHEET to be created for each identified tool, incentives, initiative or practice (the Building Block) introduced by public bodies or used by developers to expedite drug repurposing in Rare Diseases (RDs).

<table>
<thead>
<tr>
<th>ITEM</th>
<th>DESCRIPTION</th>
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</thead>
<tbody>
<tr>
<td>Building Block (BB) Title</td>
<td>CURE Drug Repurposing Collaboratory (CDRC)</td>
</tr>
<tr>
<td>References</td>
<td><a href="https://c-path.org/programs/cdrc/">https://c-path.org/programs/cdrc/</a></td>
</tr>
<tr>
<td>Description</td>
<td>CDRC, convened by the Critical Path Institute (C-Path), in partnership with the FDA-NCATS CURE ID* platform, is a dedicated initiative designed to capture real-world clinical outcome data to advance drug repurposing and inform future clinical trials for diseases of high unmet medical need.</td>
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<tr>
<td>Category</td>
<td>Availability of data</td>
</tr>
<tr>
<td>Type of BB</td>
<td>Development resource</td>
</tr>
<tr>
<td>Geographical scope</td>
<td>International</td>
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<tr>
<td>Availability</td>
<td>App Download: “Download the CURE ID app at (<a href="https://cure.ncats.io/">https://cure.ncats.io/</a>) and begin submitting cases today. It takes a couple of minutes and every case report counts.” Any interested party is welcome to join the public-private partnership by participating in the CDRC Advisory Committee, Therapeutic Area Coordinating Committees, or disease/group of disease-specific working groups. There are also groups focused on automated extraction of EHR data, conduct of pragmatic platform randomized controlled trials to test repurposed drugs, and groups focused on policy, regulatory and legislative issues.</td>
</tr>
<tr>
<td>Scope of use</td>
<td>Identifying new clinical efficacy of known drugs for diseases with high unmet medical need. Covers the spectrum of drug repurposing from disease prioritization, preclinical to clinical translation, real-world clinical data, randomized controlled trials, policy, and legislation.</td>
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<tr>
<td>Stakeholders involved</td>
<td>Physicians, Drug Developers, Clinical Researchers, Scientists, Regulators, Policymakers, Non-profit organizations, Patient and patient advocacy groups</td>
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<tr>
<td>Enablers/ Requirements</td>
<td>Participation in the public-private partnership activities. The Advisory Committee meets every 3-6 months, the Therapeutic Area Coordinating Committees (e.g., Infectious diseases, Rare diseases, Special Populations, etc.) meet once a month, and the disease-specific working groups or other specific projects typically meet every 1-4 weeks. Any qualified party is welcome to participate in these groups. To participate, they must sign a simple non-disclosure agreement (NDA) to protect the confidentiality of internal discussions, in order to participate.</td>
</tr>
<tr>
<td>Output</td>
<td>Movement of drug repurposing candidates from initial efficacy signal identification through the development process of real-world data collection and randomized trials or other robust study designs. Activities to try to facilitate drug repurposing, including legislative and policy initiatives to specifically facilitate repurposing of off-patent drugs.</td>
</tr>
<tr>
<td>Best time to apply and time window</td>
<td>Any time, no formal application, just reach out to <a href="mailto:mschito@c-path.org">mschito@c-path.org</a> and <a href="mailto:heather.stone@fda.hhs.gov">heather.stone@fda.hhs.gov</a></td>
</tr>
<tr>
<td>Expert tips</td>
<td>Reach out to Marco Schito, CDRC Executive Director (<a href="mailto:mschito@c-path.org">mschito@c-path.org</a>) for general information and participation in working groups on rare diseases (including rare cancers and rare non-oncologic diseases); Smitty Heavner, CDRC Scientific Director (<a href="mailto:sheavner@c-path.org">sheavner@c-path.org</a>) about EHR activities; Heather Stone, FDA Liaison to CDRC (<a href="mailto:heather.stone@fda.hhs.gov">heather.stone@fda.hhs.gov</a>) about regulatory and policy topics and infectious diseases; Mili Duggal, Special Populations Coordinating Committee co-chair on pregnancy and neonates (<a href="mailto:mili.duggal@fda.hhs.gov">mili.duggal@fda.hhs.gov</a>).</td>
</tr>
</tbody>
</table>
Developing partnerships and infrastructure to provide sustainable resources to impact patient treatments globally
Long-term Vision for CDRC

**Stage 1**
Hypothesis Generation

<table>
<thead>
<tr>
<th>Methods of Generating Hypotheses</th>
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<tbody>
<tr>
<td>a. Learning from Clinical Care Experience</td>
</tr>
<tr>
<td>- Clinical Care Data (from off-label use)</td>
</tr>
<tr>
<td>- CURE ID – clinician case reports</td>
</tr>
<tr>
<td>- Registries</td>
</tr>
<tr>
<td>- EHRs and automated extraction</td>
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<tr>
<td>- Claims Data</td>
</tr>
<tr>
<td>- Published literature</td>
</tr>
<tr>
<td>- Clinical trials &amp; observational studies</td>
</tr>
<tr>
<td>b. Pre-clinical Signal Identification</td>
</tr>
<tr>
<td>- High Throughput Screening</td>
</tr>
<tr>
<td>- Biological studies of drug targets, mechanisms and disease pathways</td>
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<tr>
<td>- AI literature and record mining to identify targets or associations</td>
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**Stage 2**
Confirming or Refuting the Hypothesis

<table>
<thead>
<tr>
<th>Translating Real-world Data Hypotheses into Evidence</th>
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<tbody>
<tr>
<td>a. Generate a prioritized list of which drug-disease combinations look the most promising</td>
</tr>
<tr>
<td>b. Determine the Type of Study Needed to Generate Confirmatory Evidence of Safety and Efficacy</td>
</tr>
<tr>
<td>- Is randomization needed? Is it ethical and feasible?</td>
</tr>
<tr>
<td>- What patient population will be included? How large does it need to be? How will the outcome be measured?</td>
</tr>
<tr>
<td>- Is it intended for regulatory purposes (IND required) or is it exempt? Consult with FDA on study design.</td>
</tr>
<tr>
<td>c. Address the practical considerations</td>
</tr>
<tr>
<td>- Who will fund the trial? What will it cost?</td>
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<tr>
<td>- Who will conduct the trial?</td>
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**Stage 3**
Integration into Clinical Practice

<table>
<thead>
<tr>
<th>Result Dissemination and/or Regulatory Approval</th>
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<tbody>
<tr>
<td>3(a) Regulatory Approval Route</td>
</tr>
<tr>
<td>- Is there a pathway for regulatory submission?</td>
</tr>
<tr>
<td>- If a normal pathway is not available, is there a less traditional pathway that could be used (e.g. BPCA)?</td>
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<tr>
<td>- Need to determine:</td>
</tr>
<tr>
<td>- Who will serve as the sponsor?</td>
</tr>
<tr>
<td>- What level of evidence will be required?</td>
</tr>
<tr>
<td>3(b) Non-Regulatory Route</td>
</tr>
<tr>
<td>If there is no available or feasible route to US regulatory approval, consider other means of review and dissemination:</td>
</tr>
<tr>
<td>- Approval by other Stringent Regulatory Authorities/WHO</td>
</tr>
<tr>
<td>- Recommended by CDC or Professional Societies</td>
</tr>
<tr>
<td>- Publication in Peer-reviewed Literature</td>
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**Result**
- Identification of a Safety or Efficacy Signal

**Next Steps**
- Determine the strength of the signal and whether it merits further study
- Determine if additional data (pre-clinical, animal studies, RWE, etc.) are needed prior to trial

**Result**
- Execution of clinical trial(s) or other robust research methods to provide confirmatory evidence

**Next Steps**
- Determine if trial or other evidence will be submitted for regulatory approval (IND required)
- Determine how the results of the trial(s) may be disseminated if regulatory approval is not an option

**Result**
- FDA Review/labeling change and/or other Evidence dissemination

**Next Steps**
- Explore new legislative/policy opportunities that would create pathways for others to submit data to FDA
- Ensure patients have access to affordable treatment with sustained manufacturing of high-quality product
CDRC Sources of Data for Each Therapeutic Area
CDRC Partnership Coordinating Center (PCC) Organizational Structure

Primary Institutional Partners
- **Johns Hopkins School of Medicine**
- **SCCM/Mayo VIRUS Registry**
- **Emory School of Medicine**
- **IDDO Oxford University**

Secondary Institutional Partners
- **VIRUS Sites**
  - 250 Existing Sites (mostly manual entry)
  - 37 Newly Automated Sites using EDGE tool (including Wellspan Health and International Institutions)
- **Emory Healthcare - 7 Hospital System**
- **ISARIC Other Global Partners**

Getting Cases from EHRs and Registries

SCCM VIRUS Registry
Partner institutions sharing their EHR or registry data in VIRUS CRF
- Manual VIRUS sites
- EDGE tool VIRUS sites
- Emory
- JHU
- SCCM VIRUS
  - Mayo Clinic Site De-identification
  - Merged data extracted by the EDGE tool
  - EDGE tool data 180 variables
- Viral data 180 variables
- Legacy VIRUS Data 40 variables
- Data in VIRUS (REDCap) CRF
- Data access to VIRUS dataset
- CDISC/SDTM
- CDISC/CDASH
- CURE ID CRF
- IDDO platform
- Data access to ISARIC + VIRUS dataset
- ISARIC
- NCATS Data Harmonization
- CURE ID