Drug Repurposing Guidebook

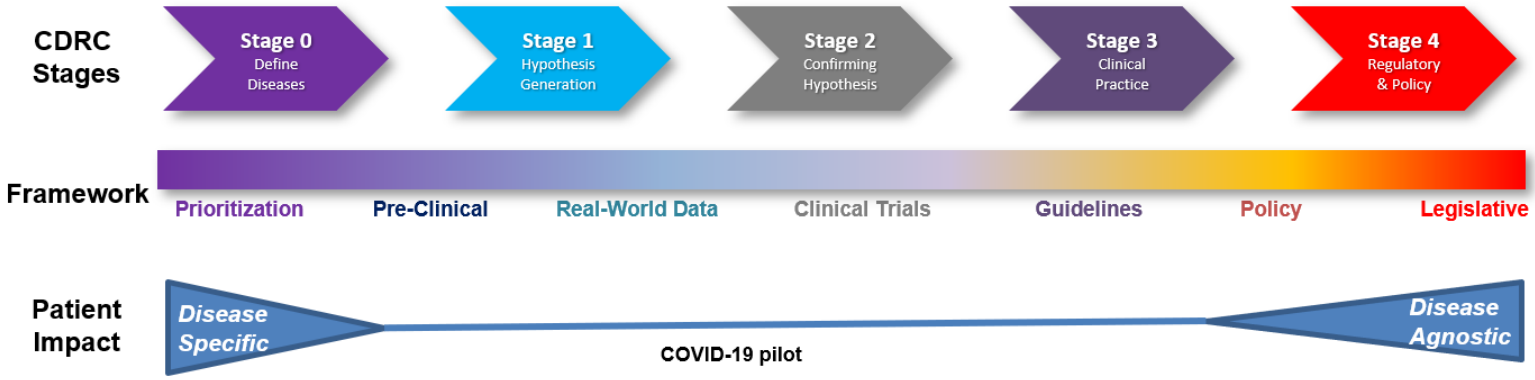
Building Block I435

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).

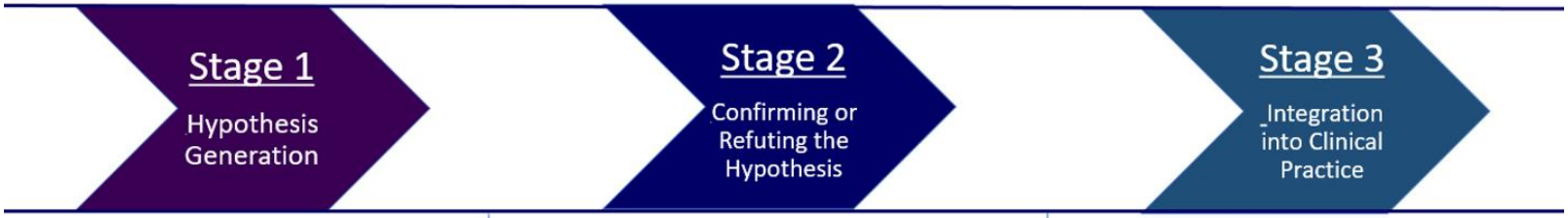
ITEM	DESCRIPTION
Building Block (BB) Title	CURE Drug Repurposing Collaboratory (CDRC)
References	https://c-path.org/programs/cdrc/
Description	CDRC, convened by the Critical Path Institute (C-Path), in partnership with the FDA-NCATS CURE ID* platform, is a dedicated initiative designed to capture real-world clinical outcome data to advance drug repurposing and inform future clinical trials for diseases of high unmet medical need.
Category	Availability of data
Type of BB	Development resource
Geographical scope	International
Availability	App Download: "Download the CURE ID app at (https://cure.ncats.io/) 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.
Scope of use	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.

ITEM	DESCRIPTION
Stakeholders involved	Physicians, Drug Developers, Clinical Researchers, Scientists, Regulators, Policymakers, Non-profit organizations, Patient and patient advocacy groups
Enablers/ Requirements	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.
Output	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.
Best time to apply and time window	Any time, no formal application, just reach out to mschito@c-path.org and heather.stone@fda.hhs.gov
Expert tips	Reach out to Marco Schito, CDRC Executive Director (mschito@c-path.org) for general information and participation in working groups on rare diseases (including rare cancers and rare non-oncologic diseases); Smitty Heavner, CDRC Scientific Director (sheavner@c-path.org) about EHR activities; Heather Stone, FDA Liaison to CDRC (heather.stone@fda.hhs.gov) about regulatory and policy topics and infectious diseases; Mili Duggal, Special Populations Coordinating Committee co-chair on pregnancy and neonates (mili.duggal@fda.hhs.gov).

Developing partnerships and infrastructure to provide sustainable resources to impact patient treatments globally



Long-term Vision for CDRC



Methods of Generating Hypotheses

a. Learning from Clinical Care Experience
- Clinical Care Data (from off-label use)
  - CURE ID – clinician case reports
  - Registries
  - EHRs and automated extraction
  - Claims Data
  - Published literature
  - Clinical trials & observational studies

b. Pre-clinical Signal Identification
- High Throughput Screening
- Biological studies of drug targets, mechanisms and disease pathways
- AI literature and record mining to identify targets or associations

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

Translating Real-world Data Hypotheses into Evidence

a. Generate a prioritized list of which drug-disease combinations look the most promising

b. Determine the Type of Study Needed to Generate Confirmatory Evidence of Safety and Efficacy
- Is randomization needed? Is it ethical and feasible?
- What patient population will be included? How large does it need to be? How will the outcome be measured?
- Is it intended for regulatory purposes (IND required) or is it exempt? Consult with FDA on study design.

c. Address the practical considerations
- Who will fund the trial? What will it cost?
- Who will conduct the 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 Dissemination and/or Regulatory Approval

3(a) Regulatory Approval Route
- Is there a pathway for regulatory submission?
- If a normal pathway is not available, is there a less traditional pathway that could be used (e.g. BPCA)?
- Need to determine:
  - Who will serve as the sponsor?
  - What level of evidence will be required?

3(b) Non-Regulatory Route

If there is no available or feasible route to US regulatory approval, consider other means of review and dissemination:
- Approval by other Stringent Regulatory Authorities/WHO
- Recommended by CDC or Professional Societies
- Publication in Peer-reviewed Literature

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 CURE DRUG REPURPOSING COLLABORATORY CRITICAL PATH INSTITUTE | CURE ID Challenging cases... New approaches

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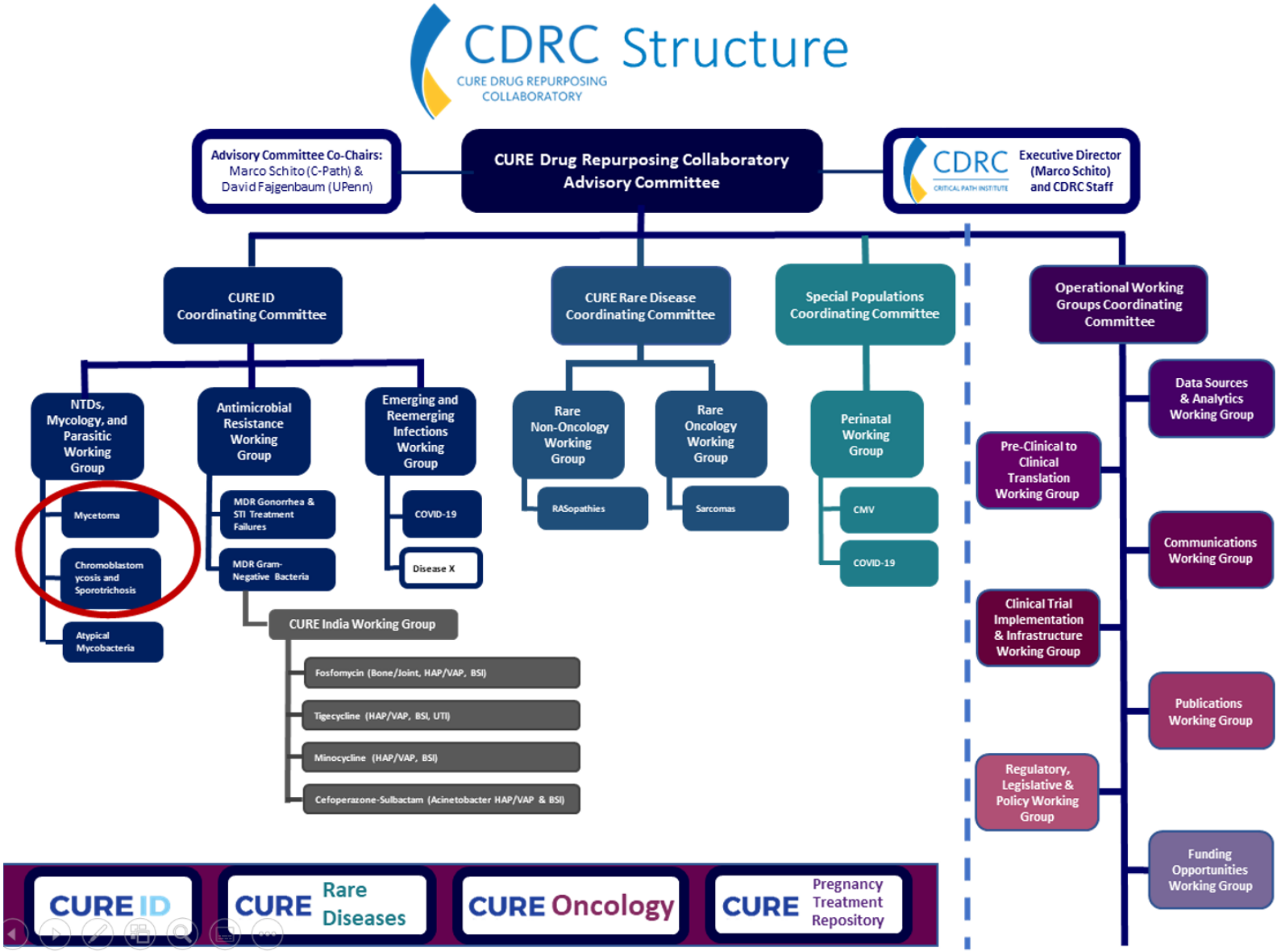
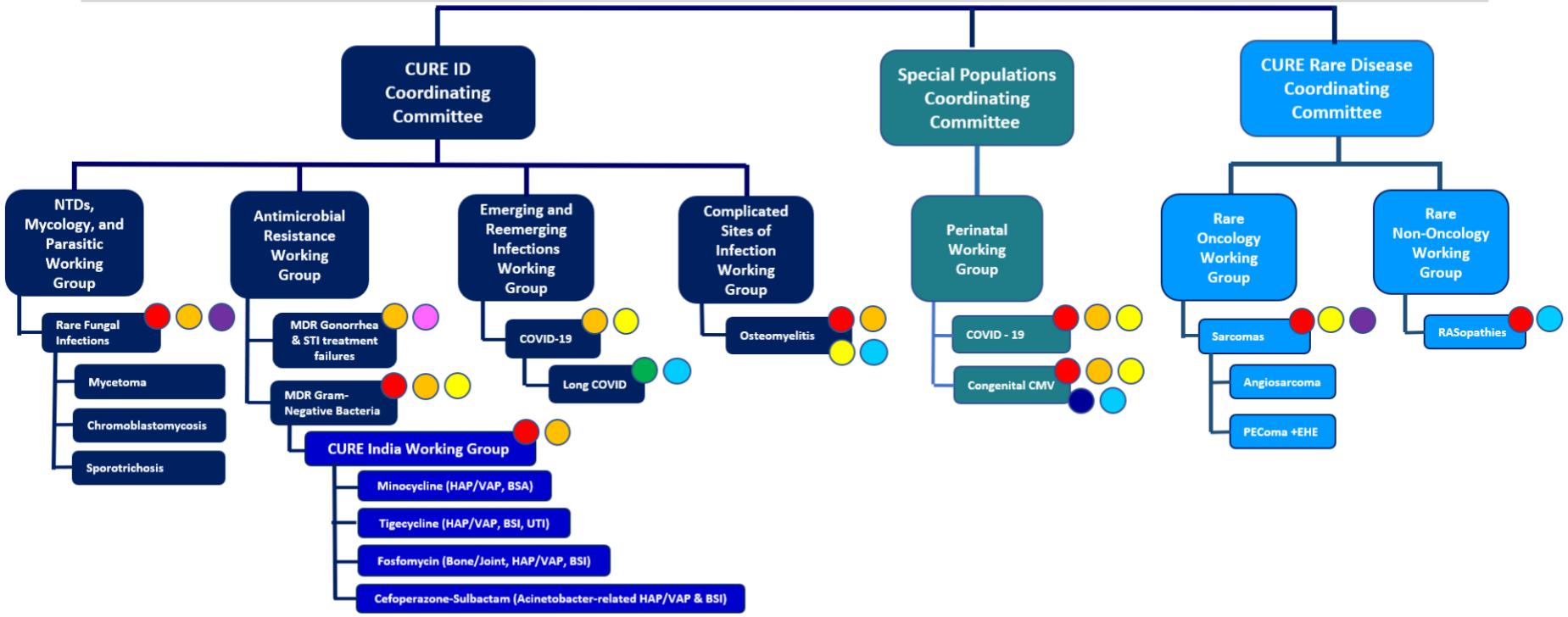

CDRC Structure
CURE DRUG REPURPOSING COLLABORATORY
Advisory Committee Co-Chairs: Marco Schito (C-Path) & David Fajgenbaum (UPenn)
CURE Drug Repurposing Collaboratory Advisory Committee
CDRC CRITICAL PATH INSTITUTE
Executive Director (Marco Schito) and CDRC Staff
CURE ID Coordinating Committee
CURE Rare Disease Coordinating Committee
Special Populations Coordinating Committee
Operational Working Groups Coordinating Committee
NTDs, Mycology, and Parasitic Working Group
Mycetoma
Chromoblastomycosis and Sporotrichosis
Atypical Mycobacteria
Antimicrobial Resistance Working Group
MDR Gonorrhea & STI Treatment Failures
MDR Gram-Negative Bacteria
CURE India Working Group
Fosfomycin (Bone/Joint, HAP/VAP, BSI)
Tigecycline (HAP/VAP, BSI, UTI)
Minocycline (HAP/VAP, BSI)
Cefoperazone-Sulbactam (Acinetobacter HAP/VAP & BSI)
Emerging and Reemerging Infections Working Group
COVID-19
Disease X
Rare Non-Oncology Working Group
RASopathies
Rare Oncology Working Group
Sarcomas
Perinatal Working Group
CMV
COVID-19
Data Sources & Analytics Working Group
Pre-Clinical to Clinical Translation Working Group
Communications Working Group
Clinical Trial Implementation & Infrastructure Working Group
Publications Working Group
Regulatory, Legislative & Policy Working Group
Funding Opportunities Working Group
CURE ID
CURE Rare Diseases
CURE Oncology
CURE Pregnancy Treatment Repository

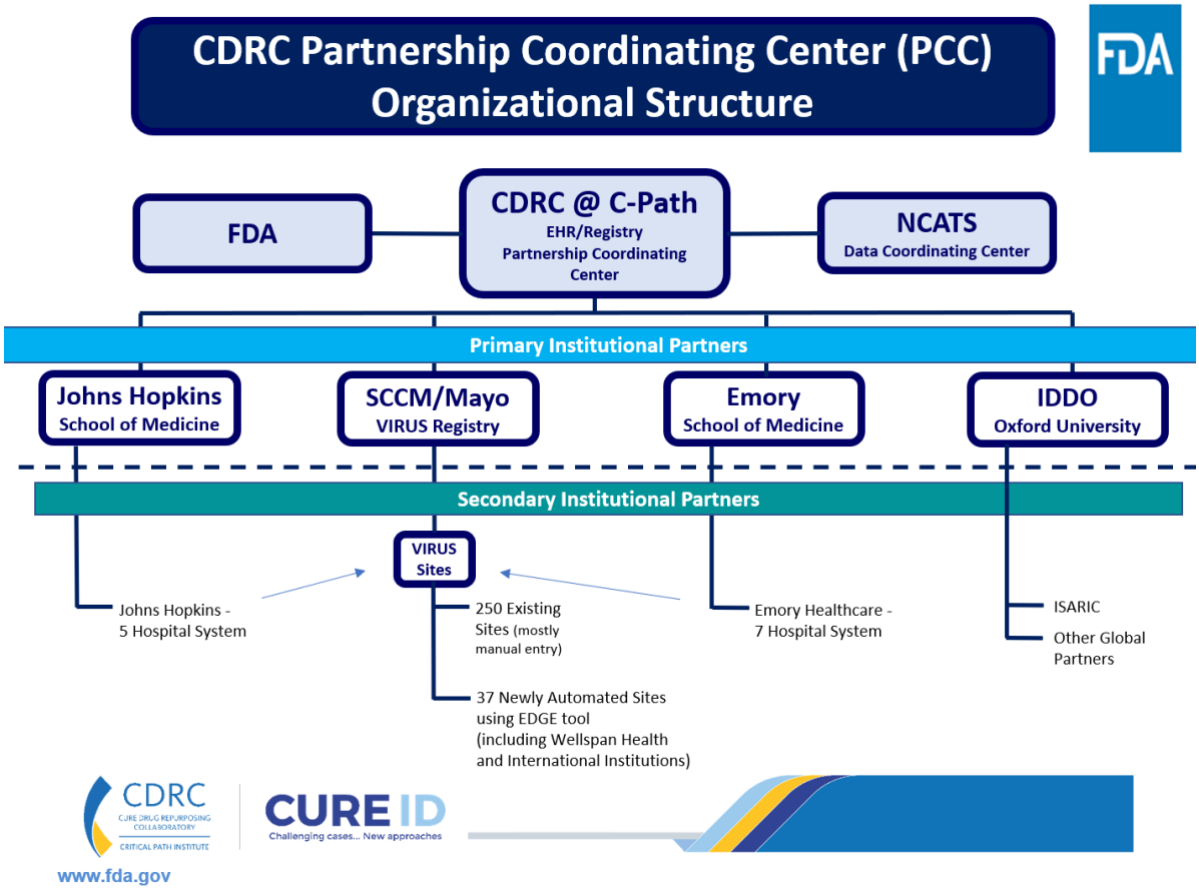
CDRC Sources of Data for Each Therapeutic Area



Legend:

- = Clinician-Submitted Case
- = Published Case Report
- = Case extracted from EHR "EDGE" Tool
- = Government/Health Authority Supplied Case
- = Combined Registries
- = Clinician Survey on Off-Label Use
- = Patient Treatment Survey
- = Patient Portal
- = Patient-Supplied EHRs

1


CDRC Partnership Coordinating Center (PCC)
Organizational Structure
FDA
FDA
CDRC @ C-Path
EHR/Registry
Partnership Coordinating
Center
NCATS
Data Coordinating Center
Primary Institutional Partners
Johns Hopkins
School of Medicine
SCCM/Mayo
VIRUS Registry
Emory
School of Medicine
IDDO
Oxford University
Secondary Institutional Partners
VIRUS
Sites
Johns Hopkins -
5 Hospital System
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
CDRC
CURE ID
Challenging cases... New approaches
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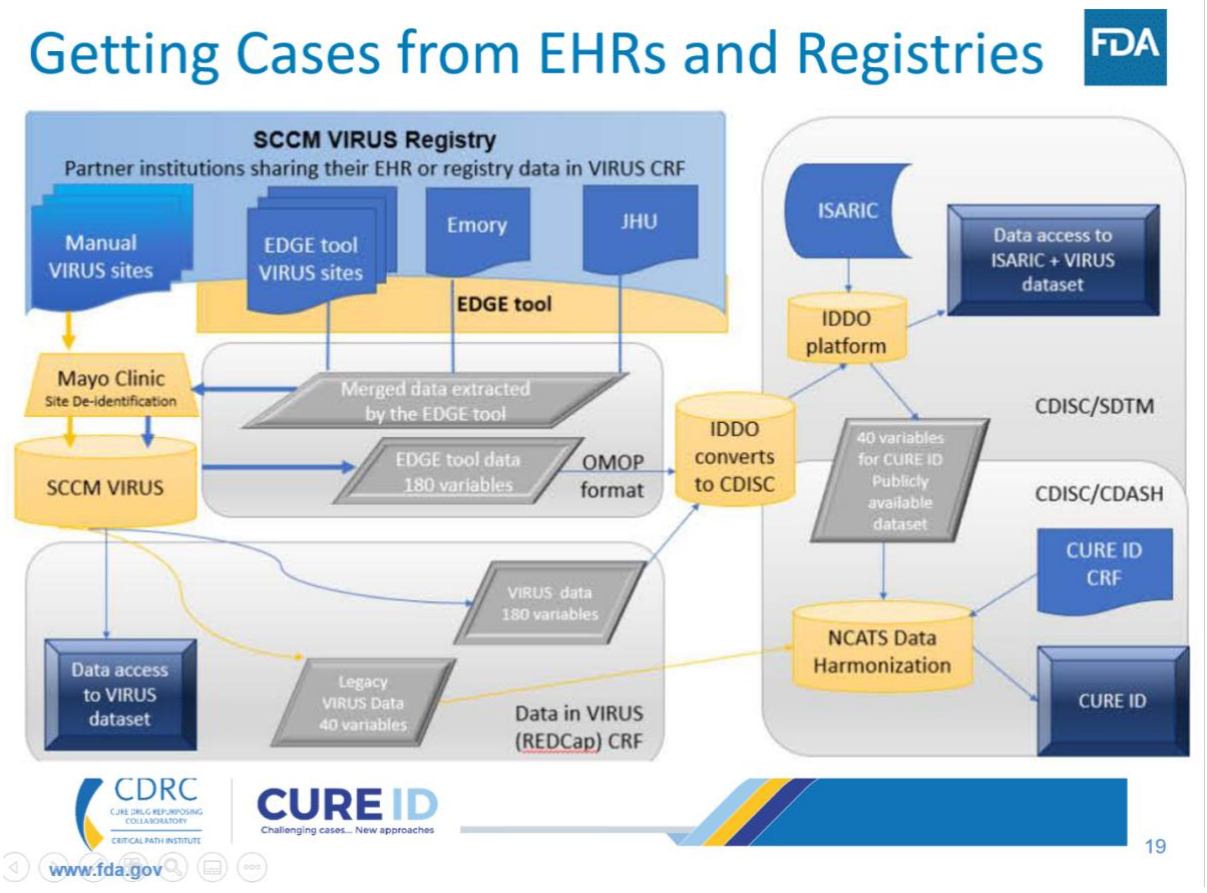
Getting Cases from EHRs and Registries
FDA
SCCM VIRUS Registry
Partner institutions sharing their EHR or registry data in VIRUS CRF
Manual
VIRUS sites
EDGE tool
VIRUS sites
Emory
JHU
EDGE tool
Mayo Clinic
Site De-identification
SCCM VIRUS
Merged data extracted
by the EDGE tool
EDGE tool data
180 variables
OMOP
format
IDDO
converts
to CDISC
ISARIC
Data access to
ISARIC + VIRUS
dataset
IDDO
platform
CDISC/SDTM
40 variables
for CURE ID
Publicly
available
dataset
CDISC/CDASH
CURE ID
CRF
NCATS Data
Harmonization
CURE ID
VIRUS data
180 variables
Data access
to VIRUS
dataset
Legacy
VIRUS Data
40 variables
Data in VIRUS
(REDCap) CRF
CDRC
CURE ID
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19