



# US and UK policy responses to the challenges of repurposing approved drugs for new indications

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- Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.
- There is considerable interest in using RWD to generate RWE to support regulatory decisions about the effectiveness of drug products.
- Regulators have used RWD primarily in its evaluation of safety and only in limited circumstances to inform decisions about effectiveness.
- How can the scientific community move from the collection of anecdotal reports to informing clinical trials, and potentially supplementing drug labels?

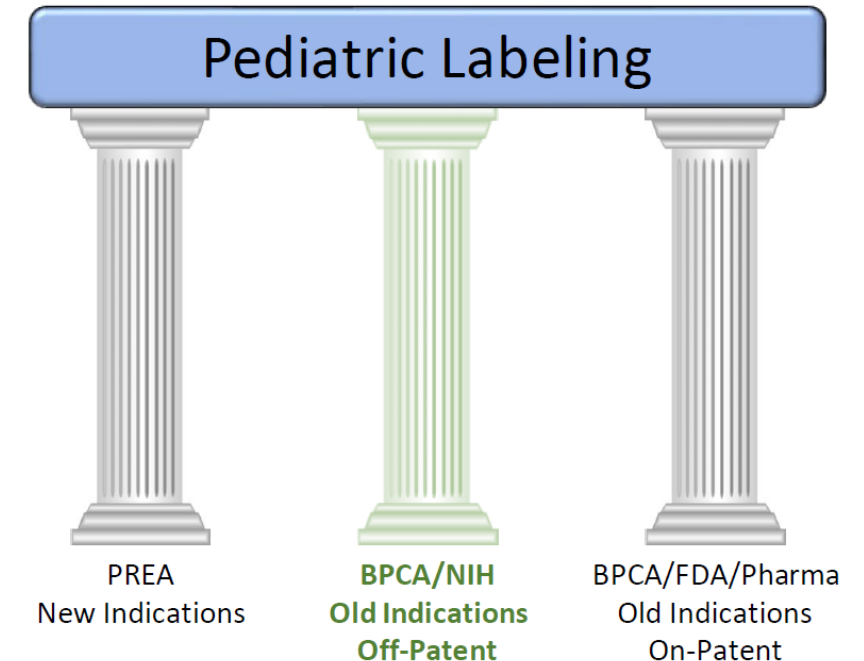
- A significant percentage of the world's population suffers from diseases where no approved therapy exists
- For regulatory drug approval and marketing, a sponsor must submit a new drug application
- The commercial incentives for drug development may not work for all diseases and in all places...
  - Diseases are often neglected
  - No ROI despite evidence of drug efficacy
  - Unlikely to pursue additional indications for generic drugs

## OBJECTIVE

- Can the collection of real-world data regarding off-label prescriptions be used to advance drug repurposing?

# US FDA BPCA/PREA: Why the need?

- Best Pharmaceuticals for Children Act / Pediatric Research Equity Act (2002)
- Historically, inclusion of kids was avoided in drug development and were studied later through extrapolation with limited RCTs
- New approach needed because kids are protected through research not from research
- Advances made in improving health and knowledge through pediatric research



## HOWEVER:

- **On-patent** licensed drugs (FDA) provide narrow indications and limited information for use in children
- **Off-patent** licensed drugs (NIH) have limited PK, PD, and safety information for kids despite having indications

# NICHD/NIH: Pediatric Trials Network (PTN)



  
**>12,500**  
participants enrolled

  
**26**  
products submitted  
to the FDA

  
**301**  
sites in

**45**  
states and



**4**  
foreign countries

**20**  
therapeutic areas  
studied

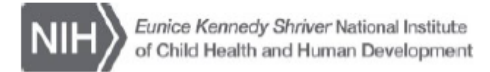


  
**46**  
studies

  
**18**  
label changes

  
**>100**  
publications

  
**>200**  
methods developed



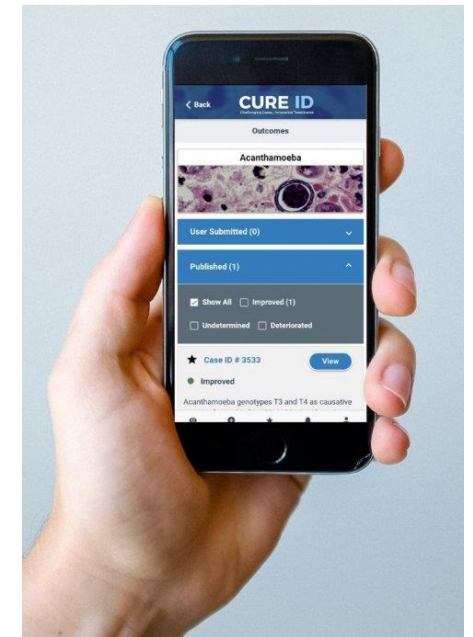
A project of the Best Pharmaceuticals for Children Act



- **Rifampin** was relabeled in February 2023 to include clinical pharmacology and adverse reactions for infants.
- Pending final review: **fluconazole** dosing and safety in preterm neonates

# US FDA CURE ID concept

- Internet-based repository that lets the clinical community report novel uses of existing drugs for difficult-to-treat infectious diseases through a website, a smartphone or other mobile device.
- Focuses on the use of repurposed drugs (approved but used for a new indication)
- Designed to demonstrate where real-world data can be of value
  - Rare diseases with poor investment return
  - Sporadic diseases that are hard to study
  - Emerging diseases with no time for discovery/development
  - Provides opportunity for clinicians to enter cases on any infectious disease where a repurposed drug is being used
  - Currently includes ~380 infectious diseases and a global forum to discuss challenging cases with limited treatment options and seek advice

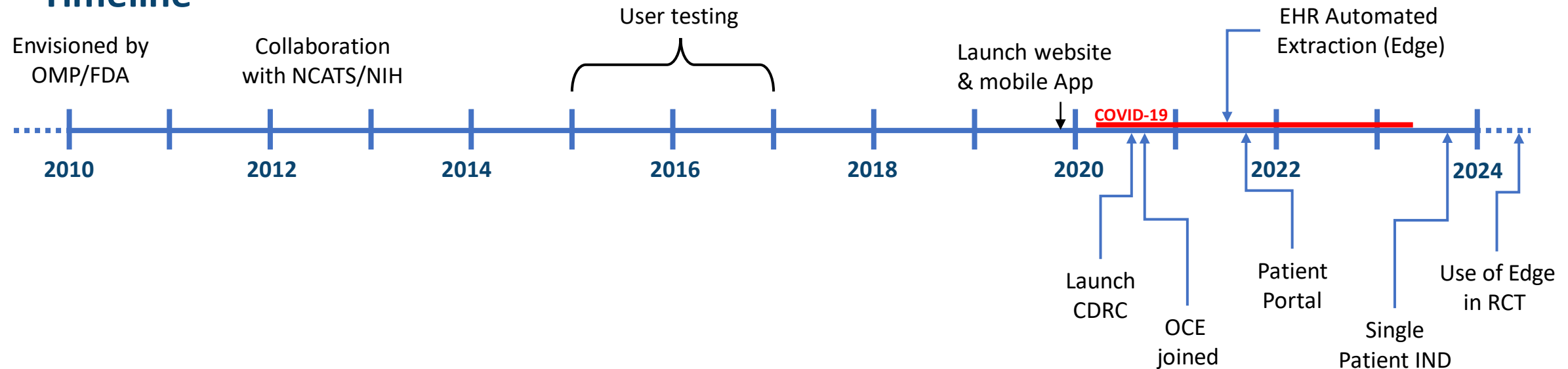


# US FDA CURE ID and Cure Drug Repurposing Collaboratory (CDRC)



- **Goal:** To identify new uses of approved medical products for areas of unmet medical need, including facilitating clinical trials and further drug development
- **Strategy:** Use of a web-based case report form for clinicians to share how they repurposed drugs for difficult-to-treat infectious diseases

## Timeline



- A public health initiative (October 2018) to update older oncology drug labels
  - Off-patent drugs that have been used to treat cancer for decades
- Goal is to provide prescribers the most accurate labeling information to inform treatment decisions
- Close collaboration with oncology community to obtain clinical SMEs
- Close collaboration with companies
  - Agreement to voluntarily participate in Project Renewal
  - May provide additional information used to update labeling
  - Submit application to update their labeling to FDA
- User fees not required for supplements → removes important barrier for voluntary label submissions by referenced licensed drug holders
- Aims to reduce burden for companies that may have little incentive to update labels



## 1. Evaluate drug compendia for off-label uses

- Lexicomp, Micromedex, NCCN, etc.
- Prioritize by level of evidence (Level 1, Category A, etc.)

## 2. Engage external Research Team Members

- Evaluate use in clinical practice
- Identify anecdotal safety concerns

## 3. Literature search

- Identify sources of data to potentially support revisions
- Review data in series of evidence evaluation meetings

## • Approved updated labeling for capecitabine tablets (Dec 2022)

- First-line treatment of patients with metastatic colorectal carcinoma
- Stage III colon cancer, advanced rectal cancer, advanced or metastatic breast cancer, HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, pancreatic adenocarcinoma

### Key Goals



**Develop Repeatable Processes**  
to evaluate scientific evidence and determine whether labeling updates are needed



**Use Published Data**  
to research off-label uses and develop a method to update existing labels



**Engage with Oncology Community**  
to increase transparency of FDA processes and encourage collaboration

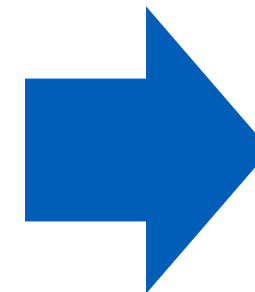
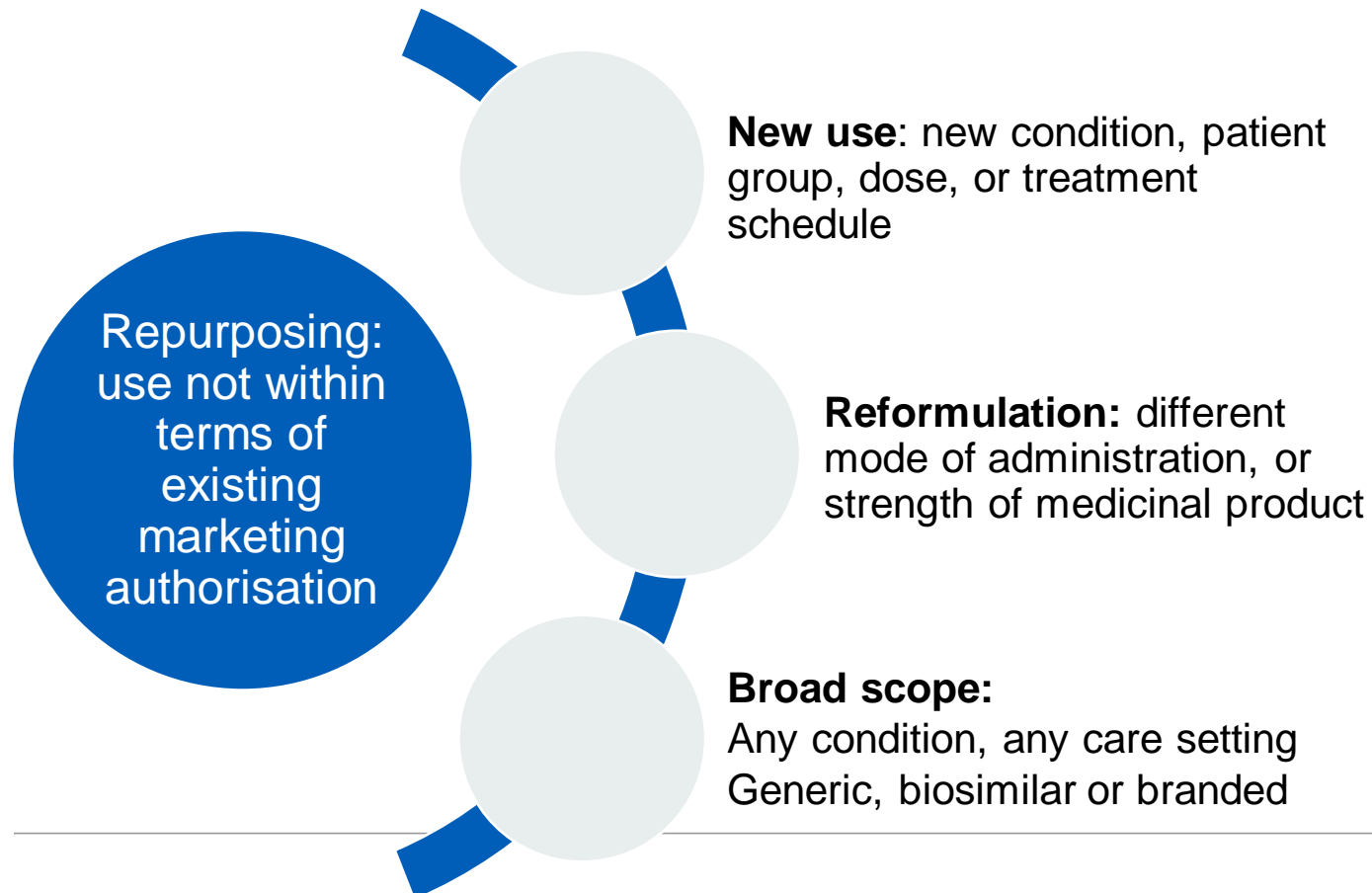
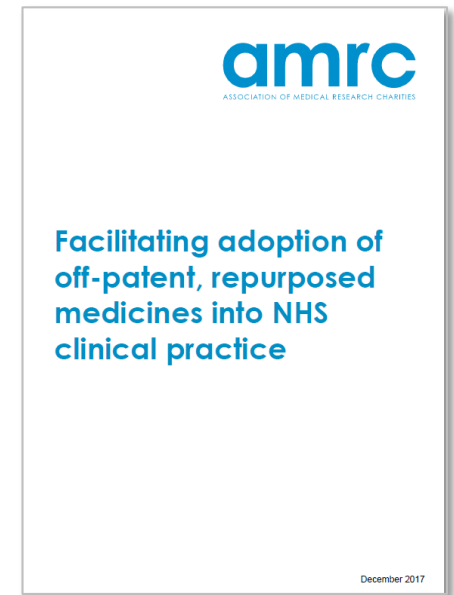


**Foster Educational Experiences**  
for Oncology Fellows to learn about FDA's Mission and regulatory process



# NHS Medicines Repurposing Programme

- Established in early 2021 in partnership with other national agencies
- Association of Medical Research Charities (AMRC) 2017 report



- Improved clinical outcomes
- Better experience for patients
- Maintain or improve value for money

## Anastrozole

- Licensed to treat breast cancer in postmenopausal women
- Repurposed use: primary prevention of breast cancer in postmenopausal women at increased risk
- Recommended by NICE, cost saving for those at highest risk, but low uptake
- MHRA: the data could support approval of a variation, subject to a full review
- Contracted company; licence variation application submitted



## Metformin

- Tuberous sclerosis complex: over-activation of mechanistic Target of Rapamycin (mTOR) pathway, causing non-cancerous tumours and epilepsy
- Metformin, a diabetes drug, also inhibits mTOR
- Phase 2 trial: metformin reduced seizure frequency and subependymal giant cell astrocytomas (SEGA) volume
- NIHR considering application(s) for research funding



- Regulators and healthcare commissioners in the US and UK recognize the benefits of using existing approved drugs for new therapeutic uses, but also the need for support
- Increased understanding of the molecular mechanisms of disease pathways coupled with new insights in mechanisms of action has allowed deeper understanding how existing drugs may be used to benefit more patients
- Maximize the use of existing drugs and resources
  - Current process does not incentivize the pharmaceutical industry (generics)
  - There is growing interest in repurposing internationally
  - Moves to create opportunities to explore lessons learned, information, resources and look for chances to collaborate and share data across agencies
- Regulators are piloting initiatives with different tools, resources and approaches
  - Not a one size fits all (legislation, health care systems, reimbursement, prescriber practices...)

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Thank you