Drug Repurposing Guidebook

Building Block U231

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	**Initiative updating old labels – Project Renewal**
References	https://aacrjournals.org/clincancerres/article/27/4/916/125031/FDA-Oncology-Center-of-Excellence-Project-Renewal https://www.fda.gov/about-fda/oncology-center-excellence/project-renewal https://www.fda.gov/about-fda/oncology-center-excellence/project-renewal-faq https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-updated-drug-labeling-including-new-indications-and-dosing-regimens-capecitabine https://www.fda.gov/drugs/resources-information-approved-drugs/fda-disco-burst-edition-fda-approves-updated-drug-labeling-including-new-indications-and-dosing
Description	This building block describes the Project Renewal pilot initiative established by the U.S. Food and Drug Administration (FDA) Oncology Center of Excellence (OCE) by which FDA drug labels can be updated. Project Renewal is a collaborative program that leverages external oncology experts to review publicly available data in the literature to update certain older oncology drug prescribing information to ensure this information is clinically meaningful and scientifically up to date.
Category	Regulatory and HTA engagement

Type of BB	Regulatory
Geographical scope	US
Availability	Project Renewal is focused on the evaluation of long-standing oncology drugs with decades of clinical experience and use.
Scope of use	Oncology drugs on the market for over 20 years that are important components of standard multi-agent chemotherapy regimens, some of which have curative potential, but have standard of care uses that are not included in the labeling or have outdated information Project Renewal will not be used to modify FDA-approved product labeling for drugs initially approved in the past 15 years.
Stakeholders involved	External Scientific Expert Teams, Hematology and oncology fellows from academic training programs, FDA, Reference listed drug (RLD) holders
Enablers/ Requirements	The Project Renewal process is initiated and directed by the OCE in the following steps: - Identify and prioritize oncology products into a Candidate drug list (CDL) - Engage RLDs to confirm participation in Project Renewal - Identify and select potential off-label uses for each product - Identify and onboard research team members (RTMs) to evaluate evidence and discuss clinical use - Identify and onboard clinical fellow to support identifying and evaluating scientific literature - Identify and evaluate publicly available literature on selected off-label use(s), summarized in a draft product report - Discuss clinical use and the evidence to support potential labeling updates through a series of labeling evidence evaluation process (LEEP) meetings - Finalize the product report, summarizing available evidence and labeling considerations - Deliver final product report and draft labeling considerations to FDA for independent review - Document labeling considerations and decisions in a repository - Capture lessons learned about Project Renewal process for continual process improvement

	- Publish finding from labeling updates, as appropriate
Output	- Updated labeling information - Prescribing information in Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) format. - Project Renewal is intended to help inform the provider community responsible for caring for cancer patients. This includes oncologists, advanced practice providers, registered nurses, and pharmacists at community and specialty pharmacies who use FDA prescribing information to inform clinical decisions and patient care. When applicable, revisions made to the prescribing information are also included in Patient Information, using nontechnical language to ensure safe and effective use.
Best time to apply and time window	Project Renewal does not accept external applications, it makes its own choices about what drugs to put through the process. The process takes several years. However, may speed up as they gain more experience and work out the issues with the process.
Expert tips	Project Renewal is limited to updating labeling of older oncology drugs with decades of use, multiple supportive clinical studies, and substantial post-marketing experience. The focus of Project Renewal is not to update product labeling with all possible or reported uses, but rather to identify currently unlabeled uses, which could be supported by published studies meeting FDA's regulatory standard of substantial evidence of effectiveness There is flexibility in the type and quantity of data used to conduct the benefit–risk assessment supporting a recommendation for inclusion of new uses and dosing regimens. The product report produced by project renewal is just one resource that the FDA will use during their independent labeling review, and FDA may include additional evidence when creating their final recommendations to ensure product labeling contains essential scientific information, is not misleading, and provides adequate directions for use.

	Drugs selected for Project Renewal have decades of safety and other clinical data Several factors increase the acceptability of relying on published reports to support approval of a new use, including having multiple studies conducted by different investigators with consistent findings across studies, a high level of detail in the published reports (including statistical methods and analysis plans), appropriate endpoints that can be objectively assessed, robust results achieved by protocol-specified analyses, and studies conducted by research groups with a history of implementing high quality studies. After FDA independent review, FDA-reviewed draft labeling is sent to the reference listed drug company along with a letter requesting submission of a supplemental application. The company is encouraged to submit the FDA-reviewed product labeling, with or without further modifications, in their supplemental marketing application(s). The Project Renewal process is intended to facilitate submissions by companies, with a goal to reduce burden and maximize the efficiency of review of supplemental applications submitted to update older oncology product labeling. FDA OCE Project Renewal Lead: Dr. Sundeep Agrawal: Sundeep.Agrawal@fda.hhs.gov