Drug Repurposing Guidebook

Building Block I459

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	Safety data across indications
References	A general comprehensive reference on pharmacovigilance and pharmaco-epidemiology (pharm-epi) is: Strom BL, Kimmel SE, Hennessy S (editors). *Pharmacoepidemiology,* 6th edition. Chichester, Wiley, 2019. https://www.wiley.com/en-us/Pharmacoepidemiology%2C+6th+Edition-p-9781119413417 There are many other references, including whole journals and dedicated journal articles.
Description	For marketed medicines, data on safety (or harms) will have been collected in non-clinical research, clinical trials, and post-marketing studies (and/or spontaneous reports). Safety data from some non-clinical work and clinical uses might be relevant to a repurposed therapy being used in new indications or in new ways, helping to define for example the correct dosing strategy and the design of future clinical studies.
Category	Clinical development, including extrapolation of efficacy and safety data
Type of BB	Development resource
Geographical scope	International
Availability	Data should be available from original regulatory assessments (e.g., from FDA or EMA), product information (e.g., summary of product

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	characteristics) prescribing guides (e.g., national formularies) and from publications.
Scope of use	Will vary depending on the relationship between already authorised indications, and new uses. Dose and dose scheduling, route of administration, etc., might make prior data more, or less relevant to the new situation. In general, it seems appropriate to start with the known side effect profile and assume it has relevance to the new situation, then consider what might or might not be relevant, i.e., take a "top-down" approach (rather than assume none is relevant and include data only from a "bottom up" approach).
Stakeholders involved	Patients, carers, treating physicians, regulators.
Enablers/ Requirements	Availability of, and access to, data from publications or from regulatory submissions in other indications.
Output	A first basis for considering potential safety issues of a therapy in a new setting.
Best time to apply and time window	Not applicable in terms of "applying". But data would be relevant for the design of the non-clinical and clinical programmes and ethics and regulatory approvals to start new studies in new therapeutic areas / licensing decisions.
Expert tips	Consider the totality of the data available and determine relevance for extrapolation to the new use to avoid unnecessary duplication and replication. Consider patient *exposure* to medication (e.g., half-life, C_{max}, etc.) rather than just dose and dose frequency. Be cautious of selective reporting and publication of safety data from other sources (e.g., spontaneous reporting typically will under-report events, but high profile/publicly reported safety concerns may result in subsequent over-reporting.