Drug Repurposing Guidebook

Building Block I438

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	Engaging with Market Authorisation holders (MAH)
References	The Article 57 data base list product names /active substances and marketing authorisation holder's and give a contact email address and telephone number for pharmacovigilance enquiries. (QP PV) https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/public-data-article-57-database Helpful background reading: Drug repurposing from the perspective of pharmaceutical companies - PMC Drug repurposing: a systematic review on root causes, barriers and facilitators On-Label or Off-Label? Overcoming Regulatory and Financial Barriers to Bring Repurposed Medicines to Cancer Patients Current Drug Repurposing Strategies for Rare Neurodegenerative Disorders
Description	There are two main reason to engage with a MAH • engage with the originator who owns the original license to get access to development history, data and regulatory files

	• identify the future MAH to guide the development for the repurposed indication As per the EMA definition, the Marketing Authorisation Holder (MAH) is a legal entity that has the authorization to market a medicine in a given market and will fulfill the legally binding requirements to maintain that authorisation. Marketing authorisation holders are responsible for ensuring that they and any parties working for them comply with all relevant standards set out in the research and development, marketing authorisation and post authorisation stages. To inform the regulatory strategy for a new indication with an "available" product it is most logical to first engage with the pharmaceutical company who maintains the original marketing authorisation. The originator will have a full understanding of the development history of the molecule, the IP rights and access to the regulatory master file. It is also recommended to identify early or during the process if other entities beside the originator could be the future Marketing Authorisation Holder for the repurposed indication and under which circumstances (resources, regulatory and IP status). There is no single defined process to engage with a MAH and part of the challenge will be to identify the right decision maker within a company and to convince them of the strategic importance of this new indication.
Category	Engagement with MA
Type of BB	Development practice
Geographical scope	International
Availability	This is a must to bring on label a new clinical use for any product or active substance.
Scope of use	This BB is for approved chemical entities that have reached or will soon reach the end of their IP and regulatory exclusivities. The engagement with the MAH and the level of support the MAH will demonstrate for the new indication development will impact development timelines and shape the regulatory strategy. If the original MAH doesn't intend to develop the additional indication, then you need to have access not only to the MAA modules of the regulatory dossier, but also to ALL the raw data (basis of the MAA

	dossier). To this extent the repurposing champion will have to engage multiple times with the "originator" with a solid argumentation. The case of a redevelopment of an active substance that has never obtained a marketing authorisation or the case of a medicine still well within intellectual property or regulatory data protection periods, are considered out of scope for this BB as the freedom to operate is significantly different. It is still relevant to contact the originator MAH to confirm the exclusivity rights and signal interest in a new indication.
Stakeholders involved	Principal investigator leading on the new clinical use, marketing authorisation holder and IP holders. Of note IP holders can be a different entity from the marketing authorisation holder, they will receive royalties without necessarily being involved in the development plan or carry the liability which is with the MAH. Within the context of a collaborative framework more stakeholders can be represented in the engagement: physicians, academics, hospitals and not-for-profit organizations, patient organizations, pharmaceutical industry, health technology assessment bodies, payers, and regulators
Enablers/ Requirements	Convincing pharmaceutical industry to join forces can be challenging, fulfilling requirements from the list below will increase your chances of success to find an interested MAH - Project supported by a mature and robust data set - Documented scientific advice from regional authorities (EMA, FDA,...) with scientific and regulatory guidance - Evidence generated according to GxP and meeting the regulatory standards expected from the MAH (see also definition of MAH above). - Natural history data and other data to fit an economic model supporting cost-effectiveness. - Being aware of the competitive landscape and the strategic fit for the company portfolio and pipeline - Repurposing undertaken within a multi-partner project involving collaborators who are respected, knowledgeable, and experienced in getting repurposed drugs approved for new indications.

Output	1. Access to important information like the development history, data and the regulatory master file 2. A defined regulatory strategy and path to patient access 3. Identify the future MAH that will carry the risks and meet legal obligations linked to MA.
Best time to apply and time window	At the time it is decided to bring a new clinical use on label Each time a new milestone is reached in the development process Till a MAH is identified for the repurposed indication
Expert tips	Often the original MAH will already have evaluated whether to develop the drug in that indication and has not prioritized that development program. You will have to work to reverse that decision. Understanding why the program wasn't considered in the first place can be very useful to build a convincing case (see also enablers). Be aware that beyond the costs for the MA holder to submit a regulatory dossier and to maintain the product on the market (life-cycle management), repurposing will require the MAH to dedicate skilled staff to the project. If the repurposed program doesn't have a high a strategic fit with the MA holder activities - the dossier might experience significant delays as other priorities take precedence. Consider generic companies interested in value-added medicine as MAH for out of patent products Show a good understanding of PV and adverse event reporting standards. Companies are liable for the products they commercialize. Keep in mind it is not all about efficacy. Pharmacovigilance and the risk brought by a new clinical use to an existing on label indication might be a deterrent for a company to support a label update. Persistence will be key, start with your contacts within the industry and make sure your support for the repurposed indication has a direct influence on decision-making in portfolio reviews. Multi-partner collaborations between pharmaceutical companies, academic institutions, non-profit organizations and biotechnology

	companies was the most commonly discussed facilitator for drug repurposing cited in the literature.