Drug Repurposing Guidebook

Building Block I445

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	**Patent Framework of Drug Repurposing**
References	**[1]** *Study to support the evaluation of the EU Orphan Regulation*. (European Commission report; 2019) https://health.ec.europa.eu/system/files/2020-08/orphan-regulation_study_final-report_en_0.pdf **[2]** *Orphan Drugs In The United States: An Examination Of Patents and Orphan Drug Exclusivity* (NORD® Commissioned Report, 2021) available https://rarediseases.org/wp-content/uploads/2021/03/NORD-Avalere-Report-2021_FNL-1.pdf **[3]** Seki K et al., 2022. *Lifecycle management of orphan drugs approved in Japan*. Orphanet J Rare Dis. 17: 299. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9336109/ **[4]** *"Drugs and Orphan Diseases"* issue in Therapies 2020 https://www.sciencedirect.com/journal/therapies/vol/75/issue/2 **[5]** Verbaanderd C et al., 2020. *On-Label or Off-Label? Overcoming Regulatory and Financial Barriers to Bring Repurposed Medicines to Cancer Patients* Front Pharmac. 10:1664 https://www.frontiersin.org/articles/10.3389/fphar.2019.01664 **[6]** Strohbehn G et al. 2021. *Combination therapy patents: a new front in evergreening*. Nat Biotechnol. 39: 1504-1510. https://www.nature.com/articles/s41587-021-01137-6 . **[7]** Krauß J and Kuttenkeuler D, 2021. *When to file for a patent? The scientist's perspective.* N Biotechnol. 60: 124-9. https://www.sciencedirect.com/science/article/pii/S1871678420301849 **[8]** Donald K et al., 2018. *Tips for reading patents: a concise introduction for scientists*. Expert Opin Ther Pat. 28: 277-280. https://www.tandfonline.com/doi/full/10.1080/13543776.2018.1438409 **[9]** Krauß J and Kuttenkeuler D, 2018. *Intellectual property rights from academic research and their role in bioeconomy-A guide for scientists*. N Biotechnol. 40: 133-9. https://www.sciencedirect.com/science/article/pii/S1871678416326450

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	[10] Aboy M et al., 2022. *European patent protection for medical uses of known products and drug repurposing.* Nat Biotechnol. 40: 465–471. https://www.nature.com/articles/s41587-022-01269-3 **[11]** *Drug Prices: The Role of Patents and Regulatory Exclusivities* (Congressional Research Service, US congress 2021). https://sgp.fas.org/crs/misc/R46679.pdf **[12]** Agranat I and Marom H, 2020. *In Defense of Secondary Pharmaceutical Patents in Drug Discovery and Development.* ACS Med Chem Lett. 11: 91-98. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7106985/ . **[13]** EMA (European Medicines Agency) Medicines portal https://www.ema.europa.eu/en/medicines **[14]** FDA (U.S. Food & Drug Administration) Drug Approvals and Databases https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases **[15]** Terrot M et al., 2019 *Overview of Orange Book and Off-Patent/Off-Exclusivity List* at "WIPO conference Standing Committee on Law of Patents, 31st Session" https://www.wipo.int/edocs/mdocs/scp/en/scp_31/scp_31_h_orange.pdf **[16]** Durvasula M et al., 2022. *The NBER Orange Book Dataset: A User's Guide (No. w30628).* National Bureau of Economic Research, Cambridge, USA. https://doi.org/10.3386/w30628 **[17]** Zhou Y et al., 2022. *Therapeutic target database update 2022: facilitating drug discovery with enriched comparative data of targeted agents*. Nucleic Acids Res. gkac95. https://academic.oup.com/nar/article/50/D1/D1398/6413598 **[18]** Avram S et al., 2022. *DrugCentral 2023 extends human clinical data and integrates veterinary drugs*. Nucleic Acids Res. gkac1085. https://doi.org/10.1093/nar/gkac1085 **[19]** Li F et al., 2022. *DrugMAP: molecular atlas and pharma-information of all drugs*. Nucleic Acids Res. gkac813. https://doi.org/10.1093/nar/gkac813 **[20]** Kim S et al., 2022. *PubChem 2023 update*. Nucleic Acids Res. gkac956. https://doi.org/10.1093/nar/gkac956 **[21]** Masoudi-Sobhanzadeh Y et al., 2020. *Drug databases and their contributions to drug repurposing.* Genomics. 112: 1087-1095, https://www.sciencedirect.com/science/article/pii/S0888754319301284?
Description	Patent-related policies play a fundamental role in drug development and approval, and even more when the objective is to evaluate how giving access to drugs that are potentially available but not to target patient populations with specific needs and expectations such as those affected by a rare disease. There is a wide literature explaining the main requirements for obtaining the official authorization of a drug to be prescribed in a rare disease with respect to legislation related to Orphan Medicinal Product Designation and drug life cycle management in various geographical areas[1-4], and the identified factors acting barriers or facilitators to

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	translate research into repurposed orphan drugs for specific indications, as in cancer-related ones [5,6]. Unfortunately, very few PubMed-indexed articles try conveying basic information about the patent system and how academic investigators may find, read, and use relevant patent documents [7-9]. Moreover, even less have explained and exemplified the relevance of secondary patent protection which is a main issue when evaluating what type of patent protection is actually covering a candidate drug for repurposing [10-12], or have explained how identifying and interpreting the patent and regulatory data in official databases, such as the Orange Book [13-16]. Thus, it is important to provide investigators with a guidance about how to effectively identify main patent-related issues related to drug authorization with respect to rare diseases and repurposing. This BB provides investigators with an overview of basic concepts about: - General patent rights and enforcement proceedings (product claims Vs. use claims, patent Vs. market exclusivity, technical contents Vs. geographic scope of claims, legal challenge to patent rights, selection inventions, patent validity and expiry date, freedom to operate, etc.); - Specific issues related to drug repurposing for evaluating patent claims and access to drugs (second medical use, secondary patents, Supplementary Patent Certificates, Patent Term Extensions/Adjustment, patent evergreening, life cycle management, parallel import, patent "thickets", "pay-for-delay" settlements, etc.); - Evaluating the potential patent issues related to each type of drug repurposing, for instance, if the drug: ○ Is marketed under patent protection, ○ Is available as a generic drug and/or without patent protection, ○ Is no more (or never) marketed, or ○ requires some kind of improvements with respect to drug substance as initially developed or marketed in order to be used as therapy for a rare disease, and the repurposing process may involve developing specific solutions for dosage, route of administration, formulation, regimen, combination with other drug, chemical modifications, and relevant criteria and biomarkers for selecting patients or evaluating drug responses; and - Databases that index relevant drug information cross-referencing biomedical data with details about patent status, availability, and official indications in main jurisdictions, as recently reviewed in *Nucleic Acid Research* [17-20] or other journals [21].
Category	Contact with TTO and Patents
Type	Development resource

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Geographical scope	International
Availability	It covers information resources are freely available (unless indicated otherwise, in particular for copyright reasons or subscription-based access).
Scope of use	Support to investigators and developers involved in Drug Repurposing & Rare Diseases by identifying most relevant patent-related provisions that apply to access to drugs, in general or when repurposed for a rare disease by: - Making an informed decision on patent and legal feasibility for repurposing a drug; - Increasing awareness about the means to identify, use, and communicate relevant patent-related information for any legal and regulatory scope; and - Correcting some common opinions and practices about patent-related issues that apply to (pre)clinical research activities and access to drugs.
Stakeholders involved	Investigators involved in (pre)clinical research activities and data analysis; patients' organizations; technology transfer offices (TTOs) and business development professionals within academic institutions, agencies and companies that work in the fields of drug development, regulatory affairs, and health policy; patent attorneys, IP advisors, and IP managers.
Enablers/ Requirements	Previous experience in: - use of internet resources for scientific research and literature; - oppositions, litigations, due diligences, or other activities related to the evaluation of patent validity and enforcement of patent rights.
Output	Mitigation plan or alternative strategies to address any patent-related issues for a faster access to new therapeutic strategies in rare diseases by better understanding of main patent requirements that apply to the manufacturing, authorization, and use of drugs for a given indication and/or jurisdiction.
Best time to apply and time window	This BB is mainly applicable in the early phases of drug development, to gather all relevant information before/during the process for selection & (pre)clinical validation of drug candidates but it can support activities also in later steps, before taking any major commitment or decision when pursuing the regulatory proceedings and facilitating the access to the selected drug (acquisition, distribution, manufacturing, clinical use, safety, reimbursement).
Expert tips	PROs: - It helps empowering non-profit stakeholders with knowledge and skills of drug industry, building bridges and common understanding about major barriers to make repurposed drugs accessible to the patients;

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	- The information in this BB may be supported by/ support the activities described in other BBs, for instance when defining patent searches and monitoring the patent situation for specific compounds, indications, companies, and/or jurisdictions. CONs: - Non-English languages may be used, translation tools are needed; - Patent provisions may evolve and the guidance in the BB may become incomplete/incorrect; - The patent information that is identified using the guidance in the BB needs to be evaluated by specialists in legal proceedings and in drug life cycle management at national level (since many patent rules and other legal provisions applicable to drugs may differ at the country level), before taking any major commitment or decisions related to intellectual property and avoiding to be over-confident in such matters.