Orphan Drug Development Guidebook

Building Block I418

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	Natural History Studies
References	PAVIN P. Exp. Opin. Orph. Drugs vol. 3 2015
Description	Natural histories studies are a major issue in Rare Diseases research. RDs are characterized by a variety of phenotypes and severity inside the same genetic condition. A Natural History is the understanding of a disease progression throughout the lifespan of a patient. The collection of data from a significant number of patients affected by diverse phenotypes inside the same condition contribute to describe the history of a disease. Natural histories studies may help to address the special needs of the Orphan Drug Development Process and the approval of Orphan Drugs. The understanding of the development and progression of diseases will help in understanding how therapies may impact the progression of the disease delaying it or stopping it. The knowledge of the natural histories of disease help the policy makers and the payers to better evaluate how to sustain orphan drugs. At present, natural histories are most of the time build with scarce data due to the reduced number of patients diagnosed at different ages, delay in the diagnosis which is preventing to generate data from birth to the diagnosis, different management protocols and availability of therapies. In fact, the availability of therapies in EU countries is changing the natural progression of the disease, for this reason natural histories studies

	cannot be performed in countries where Orphan Drugs are reimbursed. However, the lack of proper natural histories is the cause of controversy for the reimbursement of orphan drugs.
Category	Development Practices Building Block
Geographical scope	International
Availability	Applicants developing medicines for rare diseases.
Scope of use	– To follow the progression of the disease from birth for the entire lifespan of the patient – To describe the different phenotypes of a disease – To understand the real impact of therapies at different moments of the diseases – To generate better guidelines regarding the management of patients – To perform better genetic and clinical counselling regarding the prognosis of a rare disease – To help the policy maker and payers to better decide the reimbursement and sustainability of Orphan Drugs – To help policy makers and payers to better understand the impact of reimbursed drugs
Stakeholders	• Healthcare professionals • Pharmaceutical industries • Patient organizations • Policy makers and payers
Enablers / Requirements	Enablers: ERNs representatives, Patients Organization and Pharmaceutical Industries, Policy Makers and Payers. Requirements: • Inform (e.g. how to perform a clinical history study); • Consult (written – e.g. surveys); • Consult and involve (direct interactions – e.g. stakeholder meetings, workshops, stakeholder conferences);

	• Cooperate / participate (direct interactions - e.g. technical expert groups)
Output	Report on the situation of natural history studies with case reports. Generation of recommendation regarding the methods to generate natural history studies, generation of collaborative agreement for the generation of natural history.
Best time to apply and time window	The tool has its best use as early as possible at the beginning of the development.
Expert tips	PROs: – Early diagnosis, generation of data relevant to the understanding of the evolution and different phenotypes of rare diseases, generation of useful data to better understand the real safety efficacy and efficiency of therapies, generation of data usefeul for the suteinability and reimbursement of RDs therapies.