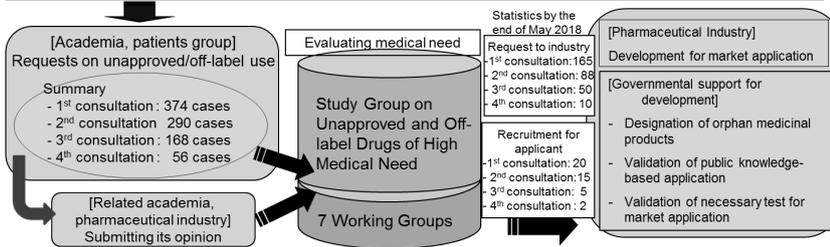


Orphan Drug Development Guidebook

Building Block J310

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	Study Group on Unapproved and Off-label Drugs of High Medical Need
References	<ul style="list-style-type: none"> • MHLW’s website: Study Group on Unapproved and Off-label Drugs of High Medical Need (Japanese) <ul style="list-style-type: none"> ◦ https://www.mhlw.go.jp/stf/shingi/other-ivaku_128701.html
Description	<p>The objective of the Study Group is to evaluate medical need, investigate necessary studies for market approval, and request company to develop medicinal products to solve the problem of unapproved drug and off-label use with medical need. Public consultations are conducted to gather requests from public.</p> <div style="border: 1px solid black; padding: 10px; margin-top: 10px;"> <p>Criteria in Study Group</p> <p><input type="checkbox"/> Unapproved drugs in Japan Approved in either of 6 western countries: US, UK, Germany, France, Canada, and Australia.</p> <p><input type="checkbox"/> Off-label use drugs in Japan Approved in either of these 6 western countries, including with a specific dosage that is widely used based on a certain evidence.</p> <p><input type="checkbox"/> Accelerating scheme for practical use Unapproved in all the 6 western countries but satisfies a certain criteria</p> <p>The drug has to satisfy both of (1) and (2), with high medical need</p> <p>(1) Severity of the target disease is either below:</p> <p>(a) life threatening (lethal) (b) irreversible progression and significantly-affected daily life (c) other type of significantly-affected daily life</p> <p>(2) Medical usefulness is either below:</p> <p><Unapproved drugs, off-label use></p> <p>(a) no existing therapy in Japan (b) efficacy/safety in clinical trials in these countries is clearly superior to the existing therapy (c) its treatment is regarded as a standard therapy in these countries, and its efficacy is highly expected in Japan despite of differences of medical environment</p> <p><Accelerating scheme for practical use></p> <p>(a) no existing therapy in Japan (b) efficacy/safety in domestic or international clinical trials is clearly superior to the existing therapy</p> </div> <div style="margin-top: 10px;"> <p style="text-align: center;">Process Flow</p>  <p>The process flow diagram illustrates the following steps:</p> <ul style="list-style-type: none"> [Academia, patients group] Requests on unapproved/off-label use: Summary of consultations: 1st (374 cases), 2nd (290 cases), 3rd (168 cases), 4th (56 cases). [Related academia, pharmaceutical industry] Submitting its opinion: Input to the evaluation stage. Evaluating medical need: Central stage involving the Study Group on Unapproved and Off-label Drugs of High Medical Need and 7 Working Groups. Statistics by the end of May 2018: <ul style="list-style-type: none"> Request to industry: 1st (165), 2nd (88), 3rd (50), 4th (10) consultations. Recruitment for applicant: 1st (20), 2nd (15), 3rd (5), 4th (2) consultations. [Pharmaceutical Industry] Development for market application: Includes [Governmental support for development] such as: <ul style="list-style-type: none"> - Designation of orphan medicinal products - Validation of public knowledge-based application - Validation of necessary test for market application </div>

ITEM	DESCRIPTION
	<p>Submit requests/gather information on applicability → Evaluate medical need → Develop the product</p>
Category	Regulatory Building Block
Geographical scope	Japan
Availability	Applicants developing medicines for rare and non-rare diseases
Scope of use	The scope of this initiative is to evaluate medical need, investigate necessary studies, and promote drug developments for market approval to solve the problem of unapproved drug and off-label use with medical need.
Stakeholders	<ul style="list-style-type: none"> • Patient Group • Academia (Academic Societies) • Individuals • Drugs developers • Study Group (Physicians, Pharmacists, and other medical professions)
Enablers/ Requirements	<p>Applicable criteria</p> <ul style="list-style-type: none"> • Unapproved drugs in Japan <ul style="list-style-type: none"> ○ Approved in either of 6 countries (US, UK, Germany, France, Canada, and Australia (but not Japan)) • Off-label use drugs in Japan (Approved for other indication in Japan) <ul style="list-style-type: none"> ○ Approved in either of above 6 countries, or

ITEM	DESCRIPTION
	<ul style="list-style-type: none"> ○ widely used in either of above 6 countries with a specific dosage, based on a certain evidence ● Accelerating scheme for practical use <ul style="list-style-type: none"> ○ Unapproved in all 6 countries but satisfies a certain criterion such as the existence of ongoing/completed investigator-initiated phase III trial in Japan or adequate evidence from clinical study.
Output	Request of drug development and various support to company
Best time to apply and time window	At the time of public consultation conducted
Expert tips	<p>For more information, please refer to information in Japanese.</p> <p>PROs:</p> <p>Possible Incentives currently applicable to development on Unapproved Drugs or Off-label Drugs</p> <ul style="list-style-type: none"> ● Priority Review ● Orphan Drug Designation ● Conditional Early Approval System for Drugs