Orphan Drug Development Guidebook

Building Block U220

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	Right to Try Act (RtT)
References	https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try
Description	The Right to Try Act was signed into law on May 30, 2018. This law is another way for patients who have been diagnosed with life-threatening diseases or conditions who have tried all approved treatment options and who are unable to participate in a clinical trial to access certain unapproved treatments. The law defines eligibility criteria for the patient and for the investigational drug: (1) An **eligible patient** has: - Life-threatening disease or condition - Exhausted approved treatment options - Unable to participate in a clinical trial with the drug All the above is certified by a physician (2) **Investigational drug** can only be provided if it - Is not approved or licensed for any use - Has completed a phase 1 trial - Is either: o The subject of an NDA or BLA with FDA, or o Is under investigation in a clinical trial that "is intended to form the primary basis of a claim of effectiveness"

	- Is actively being developed and not on clinical hold FDA does not review or approve requests for Right to Try Act use. FDA's role is limited to receipt and posting of certain information submitted under the Right to Try Act. FDA will receive annual summaries from manufacturers or sponsors on use of an eligible investigational drug under the Right to Try Act. FDA will post a consolidated annual summary report of Right to Try Act use. Individual Right to Try Act requests do not require IRB review or approval; however, eligible investigational drugs under the Right to Try Act must meet certain criteria. The **physician** is responsible for getting written informed consent from the eligible patient or their legally authorized representative for Right to Try Act use. The Right to Try Act does not require a **sponsor** to provide an eligible investigational drug to an eligible patient. Right-to-try legislation also 1) spells out the **regulatory exemptions**, 2) which **regulations** must **still** be **followed**, 3) and **adds a requirement** for the investigational product sponsor. The **regulatory exemptions** include: some labeling requirements, interstate commerce regulations, record keeping to ensure GCP compliance, parts of the IND regulations, and parts of the IRB regulations. There are some **regulations** that **must still be followed**. These include: some labeling requirements, prohibition on any sort of preapproval promotion, and limitations on cost to the patient. The **limitations on cost to the patient** are actually determined by the FDA expanded access regulations, and limit the cost to recovery to the manufacturing costs. The **new requirement** is that the investigational product sponsor must provide an **annual report** to FDA that minimally includes the number of doses supplied, the number of patients treated, and any known serious adverse events (SAEs). It is not clear at this point what FDA is supposed to do with the reports.
Category	Regulatory Building Block
Geographical scope	United States of America
Availability	Patients who have been diagnosed with life-threatening diseases or conditions who have tried all approved treatment options and who are unable to participate in a clinical trial to access certain unapproved treatments.

Scope of use	• Alleviating the administrative burden for seriously ill patients to gain access to investigational products. • Reducing the risk for sponsor companies in providing patients with access. (Many sponsors are concerned both about their liability resulting from a negative clinical outcome and the impact of a negative clinical outcome on continued development of the product.)
Stakeholders	The **patient** suffering from a seriously life-threatening disease or condition, the **physician** who diagnose and validate the request for access to an unapproved investigational drug under the right-to-try act, the **sponsor/manufacturer** who provides information about whether the drug or biological product meets the criteria to be considered an eligible investigational drug for use under the Right to Try Act. (FDA does not review or approve requests for Right to Try Act use. FDA's role is limited to receipt and posting of certain information submitted under the Right to Try Act).
Enablers / Requirements	The Physician validating the patient's diagnosis consults with the sponsor of the investigational drug or biological product. The sponsor is in the best position to provide information about whether the drug or biological product meets the criteria to be considered an eligible investigational drug for use under the Right to Try Act (i.e., phase 1 data).
Output	This law is another way for patients who have been diagnosed with life-threatening diseases or conditions who have tried all approved treatment options and who are unable to participate in a clinical trial to access certain unapproved treatments.
Best time to apply and time window	After phase I clinical data are available and before the product is registered.
Expert tips	• A key difference between Early Access Program (EAP) and Right-to-Try is that with EAP there is still oversight by FDA. The EAP FDA regulations have been developed over the last 30 years to allow early access while reducing risk to the patient and ensuring systematic implementation. PROs: • Alleviating the administrative burden for seriously ill patients to gain access to investigational products

- Reducing the risk for sponsor companies in providing patient with access.

CONs:

- There are still some questions that remain about **patient eligibility**:
  - It is not clear how eligibility and informed consent will be documented
  - who is responsible for maintaining that documentation.
  - It is also unclear who would provide information about the risks and benefits of the investigational product to the patient which is needed in order for the patient to provide informed consent.
  - There are also questions about whether the product sponsor or the investigator/physician is responsible for administering these processes.

- There are no incentives for product sponsors to participate.
- No costs reimbursement is allowed beyond the manufacturing costs.
- Many of these products are manufactured by small biotech companies, and they simply do not have extra product to give to patients under Right-to-Try.
- The legislation offers some **limitations** in **liability for product sponsors**, however, these assurances do not appear to be enough to convince most investigational product sponsors to provide their product under Right-to-Try. (If this continues to develop, it may provide sponsors with more assurance. Clinical outcomes associated with the use of an investigational product will not be used to delay or adversely affect the review or approval of the product unless those outcomes are critical to determining the safety of the product, such as a serious adverse event).
- Granting very sick patients early access to investigational products with reduced regulatory oversight may be more likely to harm patients than help them.
- Providing access to investigational product outside of controlled clinical trials can delay the generation of data needed to make evidenced-based decisions about approval and use of new drugs.
- It is more important in most product sponsors' minds to get their therapeutics to the market quickly where they will be available to all patients that need it, rather than getting the product to a few patients now.
- Depending on the State of residence, patients may loose hospice coverage, may be denied home health care coverage, may lose health insurance, insurers may deny coverage for treatment of harm caused by investigational product.