

The Link between Biotechnology and Rare Disorders

Due to the high genetic component in many rare diseases – the vast majorities (some 70-80%) of rare diseases are genetic in origin – the role of biotechnology is significantly higher in the field of rare diseases.

Prior to the emergence of the biotechnology industry, drug development for these conditions was severely limited due to a lack of understanding of the underlying mechanisms of disease.

If scientists can identify specific variations in genes or cells linked to a condition, these so-called “biomarkers” can be used to identify people with a particular disease, or at risk of developing a disease, to help guide the development of treatments for that disease.

Biotechnology provides powerful and sophisticated tools to continually innovate and develop diagnostics, and treatments thereby increasing the number and types of diseases that will have products for their treatment in the future.

Importance of Having an Orphan Product Policy

Orphan product legislation around the world has significantly enhanced the availability of innovative therapies to treat rare disease patients who previously lacked effective treatment and were largely neglected and ignored by the medical community

Research is critical to understanding these conditions, and providing solutions. Many different types of orphan drug policy incentives have been developed including marketing exclusivity, fee waivers, protocol assistance and tax reductions for the clinical development costs to encourage research.

As of 2008, 25 years after the U.S. Orphan Drug Act was passed, an estimated 280 new therapies have entered the market in the USA, benefiting over 14 million patients, in comparison to the 10 Orphan Drug treatments for rare diseases in existence prior to the Act.

BIOTECanada recommends that Canada establish a national Orphan Product Policy with the necessary legislative and regulatory parameters to ensure Canadians who live with orphan diseases have the same access to life-saving treatments as people in other countries.

BIOTECanada Legislative Recommendations

(1) Establish a Definition

Looking to the European approach, the recommended definition of a rare disease should be: “An orphan disease or rare disorder is a life-threatening or chronically debilitating condition with a prevalence, not an incidence, of fewer than 1 in 2,000 people in Canada.”

(2) Regulatory-Making Authority

Grant Health Minister the regulatory-making authority to create specific class of provisions for orphan products.

(3) Regulatory Recommendations

(a) Support for Canadian R&D for designated orphan products

Research is critical to understanding rare disorders, and providing solutions. Many different types of orphan drug policy incentives have been developed over the years. BIOTECanada recommends consideration of:

- Clinical protocol assistance
- Tax incentives for qualified preclinical and clinical R&D
- Regulatory fee reductions/exemptions
- Expedited review of marketing application, that is aligned with the tenants of progressive licensing framework and be based on real world safety and effectiveness.
- Marketing exclusivity for the approved indication for a period of 12 years.
 - An additional year of market exclusivity should be granted in Canada if a paediatric indication is successfully pursued;
 - In order to break this “12 + 1” market exclusivity, a follow-on product should be required to conduct a comparative head-to-head trial showing superior efficacy or safety to the first orphan disease product.



(b) Provide grants for clinical studies of orphan products

Consider similar incentives to products for paediatric patients (“therapeutic orphans”) with a common disease and/or “neglected” diseases.

(c) Issue clear orphan product regulations

- Clearly define regulatory parameters to prevent abuse
- Ensure an emphasis on protocol assistance through all phases of clinical R&D and provide for “compassionate” use of promising investigational orphan products.

(d) Harmonize orphan designation process with other regulatory authorities

Greater cooperation/uniformity between regulatory bodies in processes and protocols would encourage companies to make simultaneous submissions, which in turn would reduce delays in filing in Canada and speed patients’ access to medicine.

- Filing of a “one-world” orphan designation dossier
- Final regulatory decisions, nevertheless, may be different
- Sharing confidential review information on designations

(a) Establish an Office or Bureau of Orphan Products

An office or bureau of orphan products would act to:

- Administer orphan products programs
- Conduct transparent and rigorous designation reviews
- Serve as advocate for sponsors of orphan products
- Operate independently of, but in concert with, Reviewing Directorates (RDs)
- Act as advisor to RDs on orphan-related issues
- Participate as observer in the regulatory review process
- Provide an informal, neutral forum for sponsors and RDs
- Advise, consult, and network with the orphan disease community to promote open and frank exchange of information on regulatory and scientific issues

Key Considerations for Moving Forward

The high costs (\$1.2 billion over an average of 8-10 years) of bringing a drug to market, concerns about the projected revenue based on market price for a drug, the financial responsibility to shareholders and the lack of patent protection are all weighty factors for pharmaceutical and biotech companies in considering the ethical obligation to provide drugs for rare disease patients.

Despite the progress in passage of orphan drug regulations in some countries, biotech companies still grapple with choices related to investment of time and money into research and development for orphan medicines due to limited resources.

Since rare diseases affect only a small patient population, without an enabling environment and measures to assist this process, many orphan drugs may never be produced.

Even once an orphan treatment has been successfully developed and received marketing authorization, there is no guarantee of access to the market. Canada has an alarmingly high rejection rate for orphan products - both at CEDAC during the recommendation process and at the provincial level. As of December 17, 2008 there were 34 Canadian companies with 54 FDA orphan designations for products they are developing (10 unique product designations in 2008). Meanwhile, of the 13 orphan products reviewed by CEDAC – 3 have been giving a conditional listing recommendation (77% rejection rate of Orphan products).

There are strong correlations between the presence of orphan drug regulations and drug innovation by pharmaceutical and biotech companies and this is mainly attributed to the incentives contained within those regulations to encourage sponsors of Orphan medicinal products to continue to engage in research and development that finds cures for rare diseases.

