5. Neglected diseases vs. rare diseases and orphan drugs

François Noël, December 2015

According to the Department of Science and Technology of the Brazilian Ministry of Health (DECIT/MS, 2010), **neglected diseases** are diseases that prevail under conditions of poverty and for which there is little interest from traditional pharmaceutical industries due to the lack of a significant market, given that they mainly affect low-income populations and are found predominantly in developing countries. Examples of neglected diseases include malaria, tuberculosis, dengue, chikungunya, schistosomiasis, onchocerciasis, leprosy, and lymphatic filariasis (elephantiasis), as well as human African trypanosomiasis (sleeping sickness), visceral leishmaniasis (kala-azar), and Chagas disease, the last three being considered **extremely neglected**. It should be noted that the World Health Organization more commonly uses the term *neglected tropical diseases* (http://www.who.int/neglected_diseases/diseases/en/), whose list does not include malaria and tuberculosis, for example, since these receive greater investment in research for the development of new drugs. Thus, neglected diseases affect millions of people in low- and middle-income countries where there is insufficient financial capacity to pay for new drugs financed by traditional and extremely costly research and development mechanisms. For neglected diseases, there is broad consensus that a viable pathway for new drug development lies in the creation of public-private partnerships (PPPs). Such partnerships can be fostered by initiatives like the Drugs for Neglected Diseases initiative (DNDi), initially conceived by the NGO Médecins Sans Frontières (Nwaka & Ridley, 2003), which currently focuses its efforts on extremely neglected diseases.

By contrast, so-called **orphan drugs** are medicines developed to treat **rare diseases**, sometimes also referred to as orphan diseases (Aronson, 2006; Richter et al., 2015). In this case, the lack of interest from the pharmaceutical industry is mainly due to the small size of the market, even when these diseases occur in high-income countries, were it not for incentive measures adopted by the Food and Drug Administration (the Orphan Drug Act, 1983), which triggered "traditional" market investments by the pharmaceutical industry. There is substantial divergence regarding the definition of a rare (or orphan) disease (Aronson, 2006; Richter et al., 2015); however, most jurisdictions (66%) adopt an average prevalence threshold between 40 and 50 cases per 100,000 people (Richter et al., 2015). In the United States, rare diseases are defined as those affecting fewer than 200,000 people or for which there is no reasonable expectation that the cost of developing a drug will be recovered through sales in the United States (Haffner, 2006).

Despite being "rare", these diseases, approximately 7,000 in total, affect 6-8% of the global population, corresponding to about 13 million people in Brazil (Arnold et al., 2015). Examples of **orphan drugs** (for rare diseases) include: Ceredase (Gaucher disease), dantrolene (malignant hyperthermia), imatinib (chronic myelogenous leukemia), tretinoin (acute promyelocytic leukemia), ifosfamide (testicular cancer), sotalol (ventricular tachycardia), and miltefosine (leishmaniasis).

References

Arnold, R.J.G. et al. Orphan drug legislation in the US/EU and Latin America. *F1000Research* 4:57, 2015.

Aronson, J.K. Rare diseases and orphan drugs. *Br. J. Clin. Pharmacol.* 61:243-245, 2006.

DECIT. Neglected diseases: strategies of the Ministry of Health. *Rev Saúde Pública* 44(1):200-202, 2010.

Haffner, M.E. Adopting orphan drugs - two dozen years of treating rare diseases. *N. Engl. J. Med.* 354(5):445-447, 2006.

Nwaka, S. & Ridley, R.G. Virtual drug discovery and development for neglected diseases through public–private partnerships. *Nat. Rev. Drug Discov.* 2(11):919-928, 2003.

Richter, T. et al. Rare Disease Terminology and Definitions - A Systematic Global Review. *Value Health* 18:906–914, 2015.