The Fund for R&D in Neglected Diseases (FRIND)

**History:** Novartis has a long-standing commitment to the fight against neglected diseases as exemplified by the large-scale Coartem malaria initiative, the leprosy donation program, the TB dots partnership and the Novartis Institute for Tropical Diseases in Singapore which focuses on research on dengue fever, tuberculosis and malaria.

Within the next two years several pharmaceutical companies including Novartis as well as other public and private players will have researched promising compounds for treating neglected diseases. The dilemma however is that funding has not yet been secured to ensure that these compounds are developed into quality medicines that can cure millions of patients worldwide.

To find a solution to this imminent shortfall in funding for the discovery and specifically the development of new treatments, Novartis has developed a project design for a Fund for R&D in Neglected Diseases (FRIND). This model is applicable to disease areas with large medical need but where no commercial returns can be expected.

**Description:** FRIND would raise and allocate resources to the discovery and development of the most promising compounds to address neglected diseases, whether placed with pharmaceutical industry/ biotech players, public research institutes or product development partnerships (PDPs). FRIND would have the following key characteristics:

- FRIND would initially focus on the TDR list of 10 neglected tropical diseases, although this scope is flexible and can be changed.
- FRIND would operate as an ex-ante financing mechanism, in which stepwise funding would be allocated to allow a compound to reach the next decision point in the development process. This is by the large majority of consulted stakeholders perceived to be the most feasible funding mechanism, in contrast to ex-post mechanisms as proposed elsewhere.
- FRIND would evaluate all compounds from any applicant with a therapeutic/diagnostic project fulfilling a medical need for a neglected disease, and would select and allocate funding to only the most promising compounds. A portfolio management team would prioritise projects based on purely scientific, medical, technical R&D, regulatory, and economics criteria. Hence FRIND would facilitate oversight and improved portfolio management in the fragmented field of neglected diseases R&D.
- FRIND would own the exclusive licenses for neglected disease indications of the funded compounds with an obligation that medicines developed will be made available at non-for-profit prices.

For more information:

Making drugs accessible to poor populations: a funding model

According to a recent publication by Mary Moran et al., public-private partnerships (PPPs) or product development partnerships (PDPs) involving non-governmental organizations (NGOs), academia and the pharmaceutical/biotech industry have generated a growing early pipeline of new drug therapies for neglected diseases such as malaria, tuberculosis, Dengue and parasitic diseases such as Leishmaniasis, human African trypanosomiasis and Chagas disease. This activity resulted in about 63 projects in 2005, several of which are in early clinical testing. A more recent survey is shown in Figure 1.

Despite the high attrition rate it is expected that several of these projects will approach full development towards registration with costs of several hundred million US dollars per project. A study by Dalberg, commissioned by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) and Novartis estimates that US$ 6–10 billion will be needed for that purpose in the next 10 years.

Historic funding has built a portfolio that is moving towards clinical trials

Historic funding... has created the pipeline of today

R&D Funding Received – PDPs (USD M)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gov</th>
<th>Private Entities</th>
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</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>76%</td>
<td>3%</td>
</tr>
<tr>
<td>Chagas</td>
<td>21%</td>
<td>24%</td>
</tr>
<tr>
<td>TB</td>
<td>447</td>
<td></td>
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</tbody>
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PDP Compounds by Disease – including industry **

<table>
<thead>
<tr>
<th>Disease</th>
<th>Early stage D0/1</th>
<th>Lead id D2</th>
<th>Lead op D3</th>
<th>Preclinical Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Reg</th>
<th>Phase 4</th>
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</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>2</td>
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<td>TB</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Chagas</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
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</tbody>
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*Chagas, HAT & VL are sourced from DNDi through 2006; Does not include IOWH **Some projects have not been included in graph due to uncertainty of stage in pipeline


Figure 1: An emerging pipeline for neglected diseases, from (2)
In comparison, in the same study the estimated cost of building this early pipeline was around US$ 0.5 billion, allocated by a variety of private and public donors to PDPs. There is no indication that the current donors could generate sufficient funds for full development of the neglected diseases pipeline. There is a danger that a very unfortunate situation will arise where innovative compounds for neglected diseases in the pipeline that show a promising proof of concept in early human studies will stall in further development for lack of funding.

The model proposed (see Figure 2) describes a possible way to address this situation that attempts to take into account the needs of all stakeholders. It has been discussed with several pharmaceutical companies and representatives of NGOs such as Médecins Sans Frontières, Oxfam and the World Health Organization, who have all indicated that they had no have fundamental objections and encouraged us to further develop it. The model is complementary to others such as Advanced Marketing Commitments and Prizes and the differences will be discussed.

A model to fund R&D for neglected diseases (Fund for R&D in Neglected Diseases, FRIND). The model (Figure 3) is designed to apply only to disease areas with large medical need but where no commercial returns can be expected and where normal market mechanisms therefore do not apply and where pharmaceutical and biotech companies can only invest very limited R&D funds. Examples are the 10 diseases on the TDR list.

Funding and governance. The fund can be financed by the current donors to PDPs but in view of the magnitude envisaged governments of both developed and developing nations will have to contribute. Representatives of the donors would constitute the Board of the fund in which the disease scope, product scope (e.g. medicines/vaccines only, or to include diagnostic methods etc.) and the strategy would be defined. The Board would not be involved directly in the portfolio management within the strategy. The mission of the fund must include the obligation to make available the therapies it funds to poor patients in the developing world for free or at an affordable price, or at least at no profit (if a profit can be made, then the normal market mechanisms will be applicable). FRIND would only finance the R&D component and would need partners/other donors for manufacturing and distribution.

Potential applicants. Any entity, academic, biotech/pharmaceutical company or PDP with a therapeutic/diagnostic project fulfilling a medical need for a neglected disease within the scope of FRIND can apply to the fund.

Portfolio management team/scientific advisory board. The members of the portfolio management team should have the same profile and skills found in large pharmaceutical companies’ portfolio decision teams, i.e. scientific-, medical, technical-R&D, regulatory-, economics- experts familiar both with the therapeutic area and the environment in which the new drugs should be applied (field experts).

Prioritization and allocation principles. The portfolio decisions should be made exclusively on scientific, medical, technical and economic criteria excluding political factors as much as possible. To reduce potential waste of resources it is essential to apply a fund allocation rule where having estimated the totality of funds required for the entire development of the product, the portfolio team would then only allocate the funds
needed to reach the next decision point. At this stage the new results would be evaluated and a new decision to continue funding to the next stage or stop would be made.

Overcoming the fragmentation of the neglected disease portfolio. An analysis of the current neglected disease portfolio indicates that even within single diseases there are several actors working in parallel and with limited communication between them (Figure 3).

It is expected that the fund under discussion would become the major source of funds for R&D for neglected diseases and one consequence would be that the portfolio management team would eventually see most projects within a disease area which would allow them to compare them, invest in the best ones or combine them.

Intellectual property protection. Intellectual property protection is essential for fostering investments in research for new medicines worldwide and should not be an impediment to access to medicines in the developing world. In the context of FRIND, intellectual property could be handled as follows:

The inventors of the new product to be funded by FRIND (academic institutions, biotech companies, PDPs or pharmaceutical companies) would usually patent their inventions and retain ownership. If any of the entities above apply to FRIND for funding of their project in R or D they in return would allocate an exclusive licence to the fund for the particular neglected disease within the mission of FRIND. The inventors would retain the rights for all other applications. This is important because nature does not distinguish between diseases of the rich and poor. For instance, a compound developed for Dengue fever, a neglected disease of increasing impact, might very well show useful activity in hepatitis C, an indication with commercial blockbuster potential, because both the Dengue virus and the hepatitis C virus (HCV) are genetically close because both belong to the genus Flaviridae. The inventor might very well want to develop the commercial application (HCV) using their own funds to later sell it with profit where a commercial market exists. If, however, the entity marketing such a therapy uses data that has been elaborated in a FRIND funded activity, royalties and/or milestones should be due to the fund to reimburse their expenses for the data generation.

Discussion
There are several alternative models in discussion to stimulate R&D in neglected diseases, e.g. Advance Market Commitments (AMC) or Prize mechanisms as proposed by James Love. The current FRIND proposal overcomes a major drawback of the two models discussed above. Any entity that wants to access either AMC or Prize money needs to invest at
risk in the full development of its product for neglected
disease and as about 7 out of 10 projects in clinical phase
one fail before registration all that investment would be lost.
This is a major disincentive not only for pharmaceutical
companies but is outright unaffordable for many PDPs,
academic institutions or small biotech firms. In addition
since many advances in the treatment of disease are
incremental, the concept of a “prize” for the first successful
product is inappropriate and might be a disincentive to
parallel activities. In contrast the current FRIND model would
fund the individual R&D phases upfront and would bear the
risk. An additional benefit is that through FRIND a portfolio
management approach across different players might be
established that allows more optimal allocation of (scarce)
donor resources to the most promising R&D projects.

The model proposed here and AMC or Prizes are not
mutually exclusive but rather complementary to increase the
probability of the creation of urgently needed new therapies
for neglected diseases. The brief description of the model in
this paper is intended to stimulate discussion and to evaluate
its acceptance from the main stakeholders and potential
donors. It has already received constructive contributions
from NGOs such as MSF, representatives from WHO, Oxfam
and other pharmaceutical companies and is currently being
presented to national governments. If sufficient support for
this concept can be generated a more detailed model will be
elaborated in a second phase.

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