Delinking biomedical R&D, including incentives, from monopolies and high prices

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The sustainability of access at the end of the day is going to come back to the issue how you finance R&D. . . . It is essential to de-link the prices of medicines [from] the development of new medicines in order to fulfil the promise of Doha and access to medicines for all.

Rachel Marusak Hermann, Doha+10: MSF Asks, What's Next For TRIPS And Health? *IP-Watch.Org*, November 22, 2011 (link)

It is complicated, but not as complicated as the current system of financing R&D.

The best proposals to eliminate monopolies as the incentive to invest in R&D set out systems have some complexity. However, the existing system of patent and regulatory exclusivities and policies on reimbursements are also complex, and I would argue, in practice, more complex, less transparent and far more arbitrary and less efficient in terms of the incentives provided.

What do people mean when they talk about delinkage?

Currently, the primary method of financing drug or vaccine development are the private investments induced by the prospect of a temporary monopoly.

The temporary monopoly can be enforced through exclusive rights on patented inventions, or monopolies enforced by regulatory agencies, or the legal protections of trade secrets on manufacturing of access to biologic resources.

The temporary monopoly is an inefficient and often arbitrary mechanism to reward biomedical innovations, and one that predictably leads to high prices. The restrictions on access are extensive and morally appalling. Inequality is associated with high prices.

The temporary monopoly, despite its many well known flaws, is defended as necessary for biomedical innovation. All efforts to weaken the monopoly or lower prices are opposed on the grounds that the weaker the monopoly and the lower the prices, the less innovation.

Delinkage is a proposal to eliminate the conflict between access and innovation, by delinking the methods of financing R&D from the temporary monopoly.

Why is delinkage important?

1. Today all debates over access end up pitting innovation and access against each other, and the constituency for innovation is pretty powerful.
2. When innovation is linked to high prices, it sets an unfavorable ceiling on equity and access.
3. Access to medicine may be a consensus goal, but it is not actually feasible unless incentives are delinked from the monopoly.
4. The current system is too expensive, too inefficient and too unfair.
5. High prices restrict access, making health outcome worse, in every country.
6. It is not possible to regulate the monopoly in the public interest.
7. The narrative that regulating the monopoly is more practical than a change in business models is wrong.

What are the alternatives to the temporary monopoly?

One alternative that everyone is familiar with is direct funding of research by governments, something that is common now, but normally offered as a complement rather than a replacement for the temporary monopoly. Some people favor increased direct funding by governments as sufficient and appropriate to eliminate the temporary monopoly.

Economists use the term innovation inducement prizes to describe rewards that are based upon an outcome or contest that acts as an incentive. The term prizes can be confusing to a more general audience, and sometimes it is better to use a different term. These innovation inducement prizes can be implemented in a many different ways. (Several examples are available here), and can be implemented as a complement or an alternative to the monopoly, and patents can still play a role.

Alternatives to the temporary monopoly

For purposes of the current discussions, the four most important prizes type are:

1. **Market entry rewards**: To provide rewards for products that receive marketing approval and are used and useful. Products that fail don't receive financial rewards.
2. **Milestone prizes:** Which can reward pre-marketing approval outcomes, such as the identification of a biomarker for a disease, the beginning or completion or a clinical trial, or some other milestone.
3. **Open Source Dividend:** Proposal to share a percentage of the market entry reward (or revenue or milestone prizes) with persons, communities or entities that openly share knowledge inventions, technology, know-how or access to cell lines or other biologic resources)
4. **Best of prizes:** Competitions which make awards for the "best" progress or other outcome, to reward ongoing research efforts.

Competitive Intermediaries. Rewards for upstream outcomes are more speculative and less objective than market entry rewards. One proposed solution for grants, milestone or other upstream prizes: mandate health plans to fund upstream open R&D, through intermediaries that compete for funding from the health plans. Health plans to choose the intermediaries they think will do the best job.

How would market entry rewards work? 1/3

Pre-2003 literature and proposals for innovation inducement prizes often focused on contest like prizes where a winning outcome was specific, difficult or or particularly impressive. These proposals were influenced by the examples such as the British Longitude Prize or various X-Prize competitions. Among the problems with such prizes were the **challenges of knowing in advance to appropriate winning achievement, how large a prize was necessary** to induce sufficient investments in R&D, **how good a product actually was** before it was tested in real world settings, or how to deal with **follow-on innovations**.

In 2002/2003, Tim Hubbard and I proposed a reward system for products that were successful in obtaining marketing approval, where the rewards would be paid out over time, with **ten annual paydays**, and the amount paid each year depending upon a competition between drug developers.

We proposed a **prize fund of a fixed size**, with a **zero sum competition** among suppliers of innovation. In other words, the better a company's drug was, the more money they would get from the fund, and the better their competitor's drugs were, the less they would get. The zero sum nature had three important advantages. First and most important, the funders of the prize fund would know, in advance, how to budget innovation incentives. Second, because the fund was fixed, the margin cost of providing access to a new innovation, in terms of the incentive, was zero, eliminating payer incentives to restrict access. Third, the suppliers of innovation would themselves be a lobby for transparency and good data to evaluate the benefits of products, because the more money their competitors received, the less they would receive.

How would market entry rewards work? 2/3

The criteria for evaluating product was designed to be flexible enough to evolve over time, responding to new thinking on how to best induce innovation, and to accommodate multiple objectives, such as ensuring sufficient investments in rare or neglected diseases, new antibiotic drugs or other health care challenges.

There were some fundamental features, however. The rewards were larger for products that improved health care outcomes, than products that merely matched outcomes. Rewards would be available for innovations that lowered manufacturing costs to provided other improvements to existing products.

For follow-on innovations, other rules were proposed. If a follow-on product was based on or benefitted from the development of an existing product, it would share its reward with the existing product. If products arrived on the market at roughly the same time, they would not be benchmarked against each other (a change made in response to comments from Dean Baker).

How would market entry rewards work? 3/3

The prize fund concept was first set out in a concrete plan in a bill that Bernie Sanders introduced in the House of Representatives. The bill was drafted in 2004 and introduced in 109th Congress, as HR 417. Sanders wanted to retain patents on inventions, but provide the patent holder with different rights. The patent holder could use the exclusive rights to block others from bringing a product to market, but once FDA approved, patent would be used to make claims on the prize fund rewards, and could not block entry by generic manufacturers.

The bill was reintroduced in several subsequent congresses, by Sanders in the Senate, and others in the House of Representatives.

The original Sanders bill focused on what now is often referred to as market entry rewards or final product prizes. Later versions would add the open source dividend and competitive intermediaries to deal with pre-approval incentives.

Is it possible to transition from the current system to one that eliminates monopolies?

The previous prize fund bills had an immediate transition, with different rules for new and legacy products. More recently the thinking is that a progressive implementation is better. One proposal is to begin by capping exclusivity at 14 years, and introducing small market entry rewards to compensate for the small negative impact on innovation. And later to cap exclusivity at 13 years, with larger market entry rewards, and so on until the monopolies are entirely replaced, over time.

The progressive implementation has many advantages, including by allowing policy makers to benefit from experience in managing the innovation inducement prices, and to create less of a conflict with investors in legacy product.

How large should a US prize fund be?

The size of a prize fund would depend upon the market or market segment where it is introduced, the extent to which society provides other R&D funding or subsidies, and the amount of innovation policy makers want.

In general, the greater the upstream R&D public sector funding and subsidies are, the less money that is needed for market entry rewards. For example, the current US Orphan Drug Tax Credit for clinical trials is 25 percent of trial costs and the NIH Budget is $51 billion. If the credit was increased to 50 or 75 percent or the NIH budget increased, the size of the market entry rewards would not need to be as large.

The Senate HELP Committee is asking the US National Academies to study delinkage and to say how large a prize fund or other measures would have to be to eliminate monopolies. Previous versions of the US prize fund bills have put the amount of the prize fund at between 50 or 60 basis points of GDP. In 2022, a 60 basis point fund would have been USD$153 billion, and amount equal to $4.25 billion per novel drug approved by FDA that year. The United States is only 25 percent of world GDP, and it is reasonable to expect that the rest of the world could match the US funding, making the incentive very large relative to current risk adjusted R&D costs.

How big a US prize fund, con't

For the US market, IQVIA estimated that spending at list prices was $858 billion in 2022, and payer spending net of discounts and rebates was $603 billion. The US Generics association estimates that branded medicines represented 82 percent of US spending on prescription drugs, but only 10 percent of all prescriptions. This suggests that generic products are available in the US market at (18/90)/(82/10) = 2.4 percent of the cost of branded products. If these figures are correct, the cost of the monopoly in the United States, holding consumption constant, was $603 * .82 * .976 = $483 billion in 2022, a number considerably larger than a $153 billion prize fund.

If innovation is a major objective, the prize fund could have been twice as big, 120 basis points of GDP, or $306 billion, and still be $177 billion cheaper than the current system. Or, the federal government could double the size of the NIH spending on biomedical R&D, or increase and expand the orphan drug tax credit, or any combination of measures that were less of a cost than the $483 billion cost of the monopoly.

In general, given the greater efficiency of a prize fund in making incentives cost effective, you could have the same impact on innovation for much less spending, or much more innovation for the same amount, or something in between. And, you would end price related rationing of access, not only the U.S., but undoubtedly worldwide.

What about the rest of the world?

For a delinkage system to work you need to have entry and competition from generic manufacturers. The US is by itself a large enough market to make that happen for any product that now has sales in high income countries, but for most countries, the domestic markets are not large enough, making collaboration with other nations essential.

To work, a group of countries could collective make a large enough market to induce entry by generic suppliers, particularly if measures are taken to mandate technology transfer for manufacturing.

Country/Region	2022 GDP	Share
World	$100,562,011,134,034	100.0%
All high income	$61,535,768,880,817	61.2%
United States	$25,462,700,000,000	25.3%
China	$17,963,170,521,080	17.9%
European Union	$16,641,391,923,811	16.5%
Japan	$4,231,141,201,863	4.2%
Germany	$4,072,191,736,090	4.0%
India	$3,385,089,881,935	3.4%
United Kingdom	$3,070,667,732,359	3.1%
France	$2,782,905,325,625	2.8%
Canada	$2,139,840,023,674	2.1%
Sub Saharan Africa	$2,047,347,019,066	2.0%
Brazil	$1,920,095,560,995	1.9%
Australia	$1,675,418,665,067	1.7%
Mexico	$1,414,187,193,992	1.4%
Spain	$1,397,509,272,054	1.4%
Indonesia	$1,319,100,220,389	1.3%
Netherlands	$991,114,635,529	1.0%
Poland	$688,176,605,955	0.7%
Argentina	$632,770,284,409	0.6%
Thailand	$495,340,592,811	0.5%
Malaysia	$406,305,924,656	0.4%
Chile	$301,025,249,438	0.3%
Peru	$242,631,549,613	0.2%
Greece	$219,065,872,466	0.2%
Kenya	$113,420,008,179	0.1%
Uruguay	$71,177,146,197	0.1%

Voluntary or mandated

It is often appealing to consider approaches that are entirely voluntary, and sometimes a voluntary opt-in approach is necessary, for example, for a global push and pull fund that eliminates monopolies for a large number of countries and it is not practical to create legislative mandates or exceptions in every country. Or, if the entities providing coverage for products (reimbursements or purchases) have sufficient monopsony power to induce efficient opt-in decisions.

There are plenty of examples of voluntary proposals for prizes with full delinkage, such the Bolivia, Barbados, Suriname and Bangladesh proposals (slide 19), the Health impact fund, the MSF TB diagnostic prize proposal, some antibiotic prize funds considered in the US, and various opt-in patent and know-how buyout proposals associated with HIV, HCV or pandemic countermeasures, cell or gene therapies, etc.

To avoid are cases where the developers have the option of the monopoly or rewards from a prize fund, at the time of entering the market, when a product is medically necessary and where the prize fund only pays when products are less profitable as a monopoly.

The cost of a voluntary prize fund for cancer treatments in the U.S. or EU markets would depend upon how it is implemented. There are versions where the opt-in would act essentially as a poorly designed patent buyout fund, or where it is a compelling option for drugs that have competition within a therapeutic class. But in general, the longer term goal is to eliminate monopolies, and normalize full delinkage of R&D incentives from the monopoly.

Possible early implemations

- Only some diseases or technologies
  - Rare diseases (proposed by Andrew Witty while CEO of GSK)
  - Neglected diseases or technologies
  - Infectious diseases such as HIV, HCV,, etc
  - Gene and cell therapies classified as services and not drugs
  - Diabetes
  - Antibiotic drugs (Already has wide industry support, as least as a complementary incentive)
  - Tied to donor funding
- Pandemic countermeasures
- Members of a regional trade group or a sui generis coalition of the willing

International cooperation is hard

Hard to get consensus

- funding obligations,
- valuation of incentives,
- obligations for other funding mechanisms like research grants or contracts

Some global negotiations

https://www.keionline.org/global-norms-rnd-funding

- 2003, May 28. WHA/56.27 Intellectual property rights, innovation, and public health.
  - Collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries
- 2005, February 7: Civil Society Proposal for Medical Research and Development Treaty (MRDT)
- 2006: Report of the Commission on Intellectual Property Rights, Innovation and Public Health
- 2006: WHA59.24 May 27. Public health, innovation, essential health research and intellectual property rights: towards a global strategy and plan of action
  - Establishes an intergovernmental working group (IGWG) to draw up a global strategy and plan of action aimed at securing an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries, proposing clear objectives and priorities for research and development, and estimating funding needs in this area;
- 2007, May 24. WHA60.30 on Public Health, Innovation and Intellectual Property.
  - to encourage the development of proposals for health-needs driven research and development for discussion at the Intergovernmental Working Group that includes a range of incentive mechanisms including also addressing the linkage between the cost of research and development and the price of medicines, vaccines, diagnostic kits and other health-care products and a method for tailoring the optimal mix of incentives to a particular condition or product, with the objective of addressing diseases that disproportionately affect developing countries
- 2008, April. Working Document by Barbados and Bolivia proposes five different proposals to delink R&D costs from drug prices.
- 2008, May 24. WHA61.21. Global strategy and plan of action on public health, innovation and intellectual property.
  - Explore and, where appropriate, promote a range of incentive schemes for research and development including addressing, where appropriate, the de-linkage of the costs of research and development and the price of health products, for example through the award of prizes, with the objective of addressing diseases which disproportionately affect developing countries.
- 2009, April. Bangladesh/ Barbados/ Bolivia and Suriname proposals to the WHO on delinkage.
- 2010, January 15. WHO published final report Expert Working Group (EWG) on Research and Development Financing.
- 2012, April 5. WHO publishes the Report of the Consultative Expert Working Group (CEWG) on Research and Development: Financing and Coordination. (See USTR foia)
- 2016. September 14. Final Report of the United Nations Secretary-General's High-Level Panel on Access to Medicine.

April 2008. Bolivia and Barbados proposals to the WHO

Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis

Prize for the Development of New Treatments for Chagas Disease

Priority Medicines and Vaccines Prize Fund (PMV/pf)

Cancer Medicines and Vaccines in Developing Countries. Prizes as a Reward Mechanism for New Cancer Treatments

Licensed Products Prize Fund (LP/pf) for Donors A Solution for Donor-Supported Markets: Rewards Linked to Competitive Supply of Products for HIV-AIDS, TB, Malaria and Other Humanitarian Uses

April 15, 2009. Bangladesh/ Barbados/ Bolivia and Suriname proposals to the WHO

Prize Fund for Development of Low-Cost Rapid Diagnostic Test for Tuberculosis

Chagas Disease Prize Fund for the Development of New Treatments, Diagnostics and Vaccines

Prizes as a Reward Mechanism for New Cancer Treatments and Vaccines in Developing Countries

Prize Fund to Support Innovation and Access for Donor Supported Markets: Linking Rewards for Innovation to the Competitive Supply of Products for HIV-AIDS, TB, Malaria and Other Diseases for Humanitarian Uses

Proposal for WHO Discussions on a Biomedical R&D Treaty

Where do we go from here?

Feasibility studies of delinkage

- National Academies Study (See: 112th Congress, S.2516, Section 906; and more recently. 118th Congress, S.2333, Section 308).
- WHO
- EU
- Other fora

Other studies

- Quantifying the costs of the monopoly in terms of spending and restrictions on access.
- Modeling optimal designs of market entry rewards, based upon stylized data on R&D costs (transparency helps here)
- Proposing/evaluating practical measures to ensure sufficient transfer of manufacturing know-how is realistic. (such as in the 117th Congress, HR 4811, Section 6. Manufacturer Provision of Information; or the “measures complementing the compulsory license” in COM(2023)224 - Proposal for a regulation of the European Parliament and of the Council on compulsory licensing for crisis management and amending Regulation (EC) 816/2006).

In the short term:

- Push and pull funds
  - Antibiotic drugs (including as alternatives to EU proposals for patent extension vouchers)
  - Pandemic countermeasures
  - Cell and gene therapies
- Open source dividend as stand alone proposal, at 1 to 4 percent of turnover.
- R&D mandates to fund open science.
- etc

S.2333, Section 308, National Academies Study on Prizes

(1) alternative models for directly funding, or stimulating investment in, biomedical research and development that delink research and development costs from the prices of drugs, including the progressive replacement of patents and regulatory exclusivities on new drugs with a combination of expanded support for research and innovation prizes to reward the successful development of drugs or achievement of related milestones;

(2) the dollar amount of innovation prizes for different stages of research and development of different classes or types of drugs, and total annual funding, that would be necessary to stimulate investment sufficient to achieve such successful drug development and related milestones;

(3) the relative effectiveness and efficiency of such alternative models in stimulating innovation, compared to the status quo that includes patents and regulatory exclusivities;

(4) strategies to implement such alternative models described in paragraph (1), including a phased transition over time;

5) the anticipated economic and societal impacts of such alternative models, including an assessment of impact on—

(A) the number and variety of new drugs that would be developed, approved, and marketed in the United States, including such new drugs intended to prevent, diagnose, or treat a rare disease or condition;

(B) the rate at which new drugs would be developed, approved, and marketed in the United States;

(C) access to medication and health outcomes;

(D) average lifespan and disease burden in the United States;

(E) the number of manufacturers that would be seeking approval for a drug or bringing a drug to market for the first time;

(F) Federal discretionary and mandatory spending; and

(G) public and private insurance markets.

That’s it for now

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