Ministry of Health & Family Welfare
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R&D as a public good and the delinking of product prices from the R&D costs, including cost of the incentives to inducement investments

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Introduction

Current efforts to promote access to affordable medicines rely excessively on voluntary negotiations over prices.

Monopolies are hard to regulate.

Norms on transparency and technology transfer are important.

Universal access to the best drugs is not realistic without full delinkage of R&D incentives from drug prices.

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Some context

Evidence from Orphan Drug Tax Credit

From 2010 to 2016, the average qualifying trial costs claimed for the U.S. Orphan Drug Tax Credit (ODTC) was $86 million to $102 million, per U.S. FDA approved orphan indication . Companies were able to take a credit of $43 to $51 million, on average, for each FDA approval.

The $86 to $102 million in pre-credit outlays is far lower than the average of $965 million on trial costs for a new drug approval, estimated by DiMasi and others in 2016. Some of the differences are explained by the smaller trials for orphan drugs and other differences in methodologies, although both figures include the costs of failed trials and exclude pre-clinical or cost of capital costs.

In 2013, the last year for which we have actual rather than projected data on the credit (from the IRS Statistics of Income), the total amount of the credit from all 132 corporate tax returns that claimed the credit was just over $1 billion, nearly the same amount as the DiMasi estimate of $965 million for a single drug. But in 2013, the FDA granted 265 orphan designations and approved 33 orphan indications, including 8 novel products which were approved for an orphan drug lead indication.

These data underline the need for greater transparency of R&D costs, and more sophistication and realism by policy makers regarding the costs of research and development for drugs qualifying as orphan products.

Source: http://blogs.harvard.edu/billofhealth/2017/11/15/what-does-the-orphan-drug-tax-credit-tell-us-about-drug-development-costs/

Facilitate competition for generic and biosimiliar products

Condition for registration of products. Make available the following to any generic drug manufacturer seeking marketing approval for any small molecule and biologic product

Materials:,

- Cellular clones and hybridoma stocks
- Plasmids, plasmid maps, and sequences of antibody complementarity determining regions (CDR)
- Physicochemical/ biophysical characterization

Methods:

- Growth conditions and protocols
- Attenuation or inactivation protocols
- Extraction and purification protocols
- Synthetic work-up and schemes

Testing. Sufficient quantities of the approved medication for a generic developer's testing

ETASU. Allow the developer to join, a single, shared system of elements to assure safe use (ETASU) of the medication.

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Aging

The percentage change in person 60 years or over will increase sharply by 2030, particularly in Latin America, Asia and Africa. Source: United Nations, Department of Economic and Social Affairs, Population Division (2015). World Population Ageing. 2015 (ST/ESA/SER.A/390).

	Persons aged 60 years or over (millions)				Percentage change		Distribution of older persons (percentage)			
	2000	2015	2030	2050	2000-2015	2015-2030	2000	2015	2030	2050
World	607.1	900.9	1402.4	2092.0	48.4	55.7	100.0	100.0	100.0	100.0
Development groups										
More developed regions	231.3	298.8	375.2	421.4	29.2	25.6	38.1	33.2	26.8	20.1
Less developed regions	375.7	602.1	1027.2	1670.5	60.3	70.6	61.9	66.8	73.2	79.9
Other less developed countries	341.9	550.1	938.7	1484.9	60.9	70.6	56.3	61.1	66.9	71.0
Least developed countries	33.9	52.1	88.5	185.6	53.8	70.0	5.6	5.8	6.3	8.9
Regions										
Africa	42.4	64.4	105.4	220.3	51.9	63.5	7.0	7.2	7.5	10.5
Asia	319.5	508.0	844.5	1293.7	59.0	66.3	52.6	56.4	60.2	61.8
Europe	147.3	176.5	217.2	242.0	19.8	23.1	24.3	19.6	15.5	11.6
Latin America and the Caribbean	42.7	70.9	121.0	200.0	66.1	70.6	7.0	7.9	8.6	9.6
Oceania	4.1	6.5	9.6	13.2	56.2	47.4	0.7	0.7	0.7	0.6
Northern America	51.0	74.6	104.8	122.7	46.4	40.5	8.4	8.3	7.5	5.9
Income groups										
High-income countries	230.8	309.7	408.9	483.1	34.2	32.0	38.0	34.4	29.2	23.1
Upper-middle-income countries	195.2	320.2	544.9	800.6	64.0	70.2	32.1	35.5	38.9	38.3
Lower-middle-income countries	159.7	237.5	393.9	692.5	48.8	65.9	26.3	26.4	28.1	33.1
Low-income countries	21.2	33.2	54.0	114.8	56.2	63.0	3.5	3.7	3.9	5.5

Delinkage

The current incentive for inducing investment in R&D is a temporary legal monopoly, during which companies charge high prices. To replace the incentive based upon high prices, there has to be a replacement. Something concrete and realistic. The basic features of delinkage models include:

- Direct funding (including research grants and contracts)
- Subsidies (including but not limited to tax credits)
- Incentives (including mechanisms sometimes referred to as market entry rewards or innovation inducement prizes)
- International cooperation

Delinkage 2

One of the major challenges in delinkage concerns the transition from the current system, where company invest in the expectation it is possible to secure and monetize and monopoly, to a system where the R&D is essentially a public good.

Progressive delinkage is one approach for the transition. Governments commit to a long run goal of total delinkage, and a dismantling of the system of legal monopolies, and systematically build up and alternative financing mechanisms, while progressively lowering drug prices and/or shortening the term of effective monopolies.

Delinkage 3

Major challenges for delinkage

1. Culturally and politically, policy makers are conservative, risk adverse
2. It is necessarily to create a sufficiently large market for generic products to induce entry and competition
3. The transition legal/finance issues differ among countries,
4. Setting and managing cross-country obligations for funding R&D in delinkage requires resolving different preferences for innovation
5. Incentives for countries to provide sufficient funding for delinkage mechanisms to be a credible and sustainable alternative are important.

Recommendations for National Governments

1. **Transparency and technology transfer**

   a. Require sufficiently detailed disclosure (including separately the outlays on each trial) of R&D costs and R&D subsidies for every regulated medical technology.
   b. Require drug manufacturers to provide sufficient disclosures of technical information and access to materials in order to facilitate entry by competitors offering generic/biosimiliar products.

Recommendations for National Governments

2. Regulating monopolies

a. Use compulsory licensing (or limits on remedies to infringement) to end monopolies when prices are excessive, so that **the monopoly rather than the patient is at risk** when negotiations on prices reach an impasse.

b. Reduce the term of exclusivity and/or prices when the cumulative **global revenue** from sales for specific products **exceeds benchmarks**.

Recommendations for National Governments

3. Delinkage

a. Step one: identify specific proposals to implement delinkage that would have important benefits and plausible feasibility. Easy cases involve HIV, HCV, AMR or CAR-T. More challenging cases involve cancer and rare diseases, or all drugs and vaccines.
b. Step two: work with other like minded countries, and agree on terms of reference for feasibility studies.
c. Step three: fund and then evaluate the feasibility studies.
d. Goals:
    i. By 2018: Agree upon TOR for one more feasibility studies
    ii. By 2019: Complete feasibility studies;
    iii. By 2023: eliminate exclusive rights to manufacture and sell drugs for at least some disease/technology areas.

Recommendations for National Governments

4. CAR T

a. Ensure there are appropriate exceptions in national patent laws to permit physicians and other health care personnel to perform CAR T and other cell based therapies without being subject to sanctions for the infringement of patents.

b. Replace the incentive now provided by the temporary monopoly with innovation rewards, funded by health care providers or reimbursement entities.

Recommendations for WHO/International Organizations 1/2

1. Publish data on the gaps of access to new drugs for cancer.
2. Hold a seminar of the appropriate IP and incentive regimes for CAR T and other cell based therapies.
3. Create norms for transparency of R&D spending on specific products and the flow of investments in R&D.
4. Collect and publish data on the costs of conducting clinical trials, and government and charity subsidies for R&D.
5. Collaborate with other governments in considering feasibility studies of full and progressive delinkage
6. Set target dates for full delinking, in specific geographic and/or disease/technology areas. Goals include:
    i. By 2018: Agree upon TOR for one more feasibility studies
    ii. By 2019: Complete feasibility studies;
    iii. By 2020: Convene meeting to work with group of countries willing to jointly implement one or more delinkage scenarios.

Recommendations for WHO/International Organizations 2/2

7. Rethink the R&D treaty proposals

   a. Change to the form to an agreement, avoiding the complexities and challenges of treaty ratification and modification.
   b. Do not limit the benefits of the global cooperation to developing countries.
   c. Focus on the incentives to collaborate on funding priority R&D.
   d. Allow countries to meet some of the obligations by research performed by domestic institutions, programs and researchers businesses.

Thank you

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http://keionline.org

http://delinkage.org

http://cancerunion.org