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Introduction to the world of patents (and a few other things)

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Function of patents

… to encourage inventors to make an investment in time and money in research and development by providing exclusive rights for a limited time in exchange for an early public disclosure of the invention.

Patent system is a social policy tool meant to create benefits for society.

But it comes at a cost.

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Cost of production and price New WHO Essential Medicines

Medicine	Originator price intro US	Cost of production[1]
bedaquiline	$ 30,000 (6 month)	$ 48 -101
sofosbuvir (SOF)	$ 84,000 (12 week)	$68 -136
SOF+ledipasvir	$ 95,000 (12 weeks)	$ 193
simeprevir	$ 66,360 (12 weeks)	$130 - 270
daclatasvir	$ 63,000 (12 weeks)	$10 - 30
imatinib	$ 30.000 - >$100,000 (1y)	$ 119-159
trastuzumab	$54,000 (1 y)	$ 242

1. http://cid.oxfordjournals.org/content/early/2014/02/13/cid.ciu012.full (cost of production of HCV medicines) | Hill A. etal.,Target prices for mass production of Tyrosine Kinase Inhibitors (TKIs) for global cancer treatment access - Presented at 18th ECCO - 40th ESMO European Cancer Congress, 27th September 2015, Vienna, Austria [abstract number: 1203] | Dzintars Gotham, Joseph Fortunak, Anton Pozniak, Saye Khoo, Graham Cooke, Frederick E. Nytko, III, Andrew Hill; Estimated generic prices for novel treatments for drug-resistant tuberculosis. J Antimicrob Chemother 2017 dkw522. doi: 10.1093/jac/dkw522

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Global rules on Intellectual Property

- 1995 World Trade Organization Agreement on Trade related aspects of intellectual property rights (TRIPS Agreement
- Mandates granting min. 20 year patents for WTO Members
- Contains important flexibilities.

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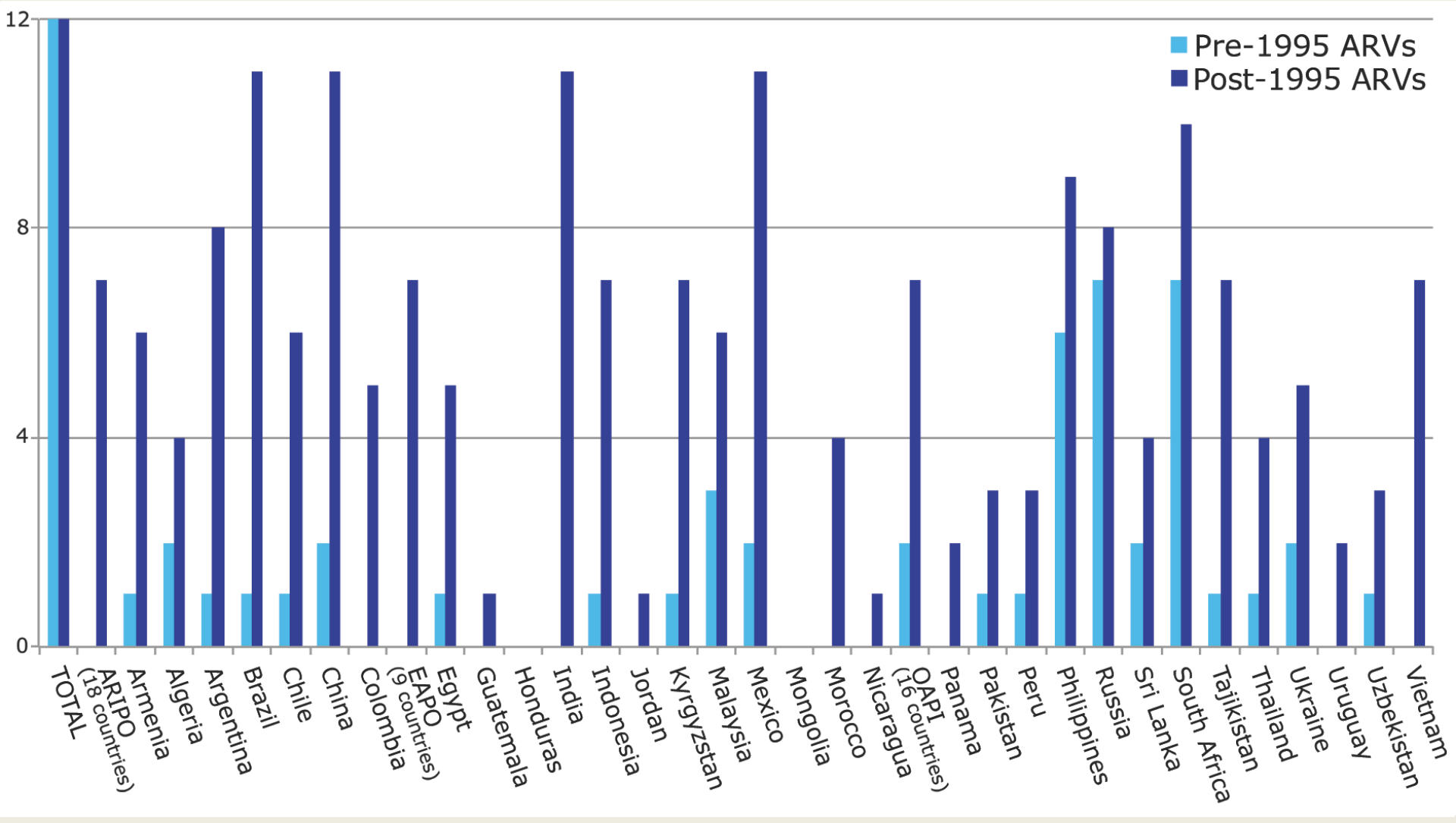
Patents on HIV Medicines



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2001 WTO Doha Declaration on TRIPS and Public Health

"the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health".

…

"we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all."

TRIPS Flexibilities

(non exhaustive)

- Compulsory licensing/Government Use
- Parallel import
- LDCs transition – delays obligation to grant/enforce medicines product patents and data protection
- Special CL for export (2017 TRIPS amended: 31bis)

http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm

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THE USE OF TRIPS FLEXIBILITIES

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TRIPS Flexibilities 2001-2016

Zoom Out

Policy & practice

Medicine procurement and the use of flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights, 2001–2016

Ellen FM 't Hoen,[a] Jacquelyn Veraldi,[b] Brigit Toebes[c] & Hans V Hogerzeil[a]

Abstract Millions of people, particularly in low- and middle-income countries, lack access to effective pharmaceuticals, often because they are unaffordable. The 2001 Ministerial Conference of the World Trade Organization (WTO) adopted the Doha Declaration on the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement and Public Health. The declaration recognized the implications of intellectual property rights for both new medicine development and the price of medicines. The declaration outlined measures, known as TRIPS flexibilities, that WTO Members can take to ensure access to medicines for all. These measures include compulsory licensing of medicines patents and the least-developed countries pharmaceutical transition measure. The aim of this study was to document the use of TRIPS flexibilities to access lower-priced generic medicines between 2001 and 2016. Overall, 176 instances of the possible use of TRIPS flexibilities by 89 countries were identified: 100 (56.8%) involved compulsory licences or public noncommercial use licences and 40 (22.7%) involved the least-developed countries pharmaceutical transition measure. The remainder were: 1 case of parallel importation; 3 research exceptions; and 32 non-patent-related measures. Of the 176 instances, 152 (86.4%) were implemented. They covered products for treating 14 different diseases. However, 137 (77.8%) concerned medicines for human immunodeficiency virus infection and acquired immune deficiency syndrome or related diseases. The use of TRIPS flexibilities was found to be more frequent than is commonly assumed. Given the problems faced by countries today in procuring high-priced, patented medicines, the practical, legal pathway provided by TRIPS flexibilities for accessing lower-cost generic equivalents is increasingly important.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

The challenges posed by the high price of antiretroviral medicines in the late 1990s, coupled with widespread patenting of these medicines, led to efforts to ensure that the World Trade Organization's (WTO's) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) could be implemented more flexibly to allow for the procurement of low-priced medicines.[1] In 2001, a Ministerial Conference of the WTO adopted the Doha Declaration on the TRIPS Agreement and Public Health (that is, the Doha Declaration).[2] The declaration recognized both the importance of intellectual property for the development of new medicines and concerns that intellectual property rights affected medicine pricing. It lists several measures that countries can take to ensure access to medicines for all, such as the use of compulsory licensing to produce or purchase lower-priced generic medicines. Paragraph 7 of the declaration removed the obligation to grant and enforce medicine patents and data protection for WTO Members designated by the United Nations as least-developed countries, initially until 1 January 2016, this is referred to as the least-developed countries pharmaceutical transition measure. In 2002, the WTO's Council for TRIPS formally adopted a decision implementing Paragraph 7 and later extended the transition period until at least 2033.[3,4] Of the 48 countries designated least-developed countries, 36 are currently WTO Members.[5]

Compulsory licensing is the right granted by a government authority to make use of a patent during the patent term without the consent of the patent holder, for example, for the production or supply of generic medicines. According to Article 31 of TRIPS, a government can also authorize use of a patent for its own purposes: this is called public noncommercial use and is also referred to as government use. A public noncommercial use licence can be assigned either to a state agency or department or to a private entity. When a compulsory licence or public noncommercial use licence is issued, the patent holder is generally entitled to adequate remuneration for use of the patent.[6]

The extent to which countries have deployed TRIPS flexibilities, such as compulsory licences or public noncommercial use licences, for procuring medicines remains underreported. Previous studies have documented well-known and widely publicized cases of compulsory licensing, but have not examined the use of TRIPS flexibilities in procurement.[7,8] Moreover, several reports in the literature perpetuate the belief that, since 2001, the use of TRIPS flexibilities has been sporadic and limited.[9–11]

The aim of our study was to document the use of TRIPS flexibilities to gain access to lower-priced generic medicines. Although we recognized that the TRIPS Agreement offers a range of flexibilities relevant to national pharmaceutical and patenting policies, including the right of countries to define and apply patentability criteria and to refuse to grant patents for certain subject matter (e.g. plants and animals), we focused on measures that can be directly applied to the procurement and supply of medicines. The most relevant measures for increasing access to medicines were: (i) compulsory licensing (including public noncommercial use licensing); (ii) the least-developed countries pharmaceutical transition measure;

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(Submitted: 20 July 2017 – Revised version received: 21 November 2017 – Accepted: 8 December 2017 – Published online: 5 February 2018)

- 176 instances (89 countries) 2001-2016
- 100 (56.8%) CL/GU
- 40 (22.7) LDC non-enforcement of patents
- 1 PI
- 3 research exception
- 32 non-patent related
- 137 (78%) HIV

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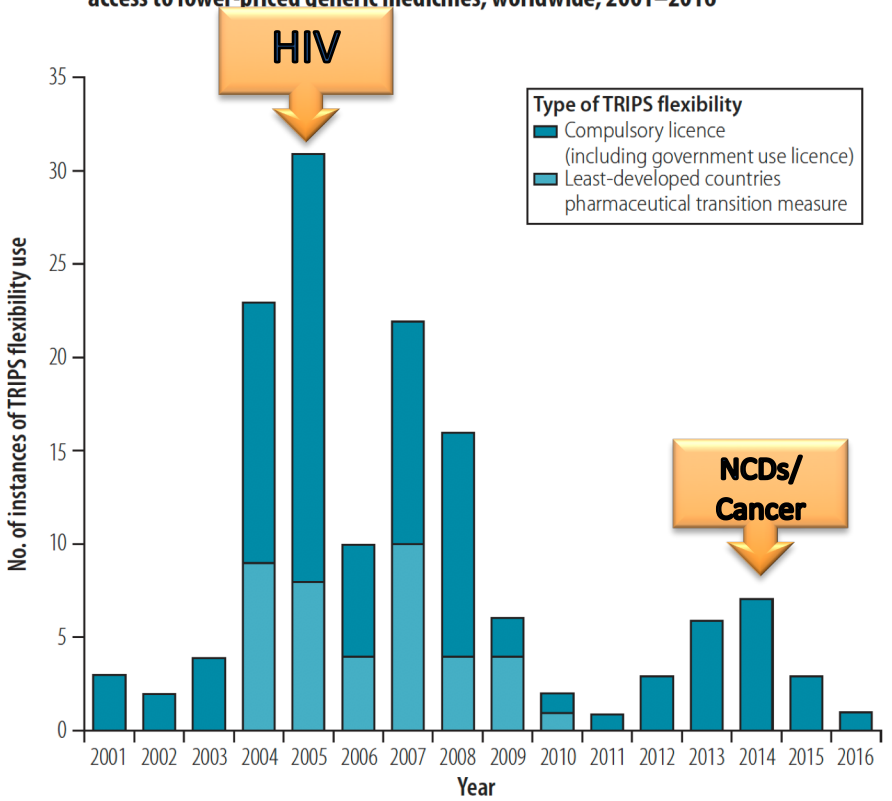
TRIPS flexibilities and medicines

Fig. 1. **Use of Trade-Related Aspects of Intellectual Property Rights flexibilities to gain access to lower-priced generic medicines, worldwide, 2001–2016**



TRIPS: Trade-Related Aspects of Intellectual Property Rights (Agreement on).
Note: The least-developed countries pharmaceutical transition measure applies to World Trade Organization (WTO) Member States designated by the United Nations as least-developed countries and removes them from the obligation to grant and enforce medicine patents in accordance with Paragraph 7 of the Doha Declaration.

't Hoen EFM, Veraldi J, Toebes B, Hogerzeil HV. Medicine procurement and the use of flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights, 2001–2016. Bulletin of the World Health Organization. 2018 Mar 1;96(3):185. http://www.who.int/bulletin/volumes/96/3/17-199364.pdf

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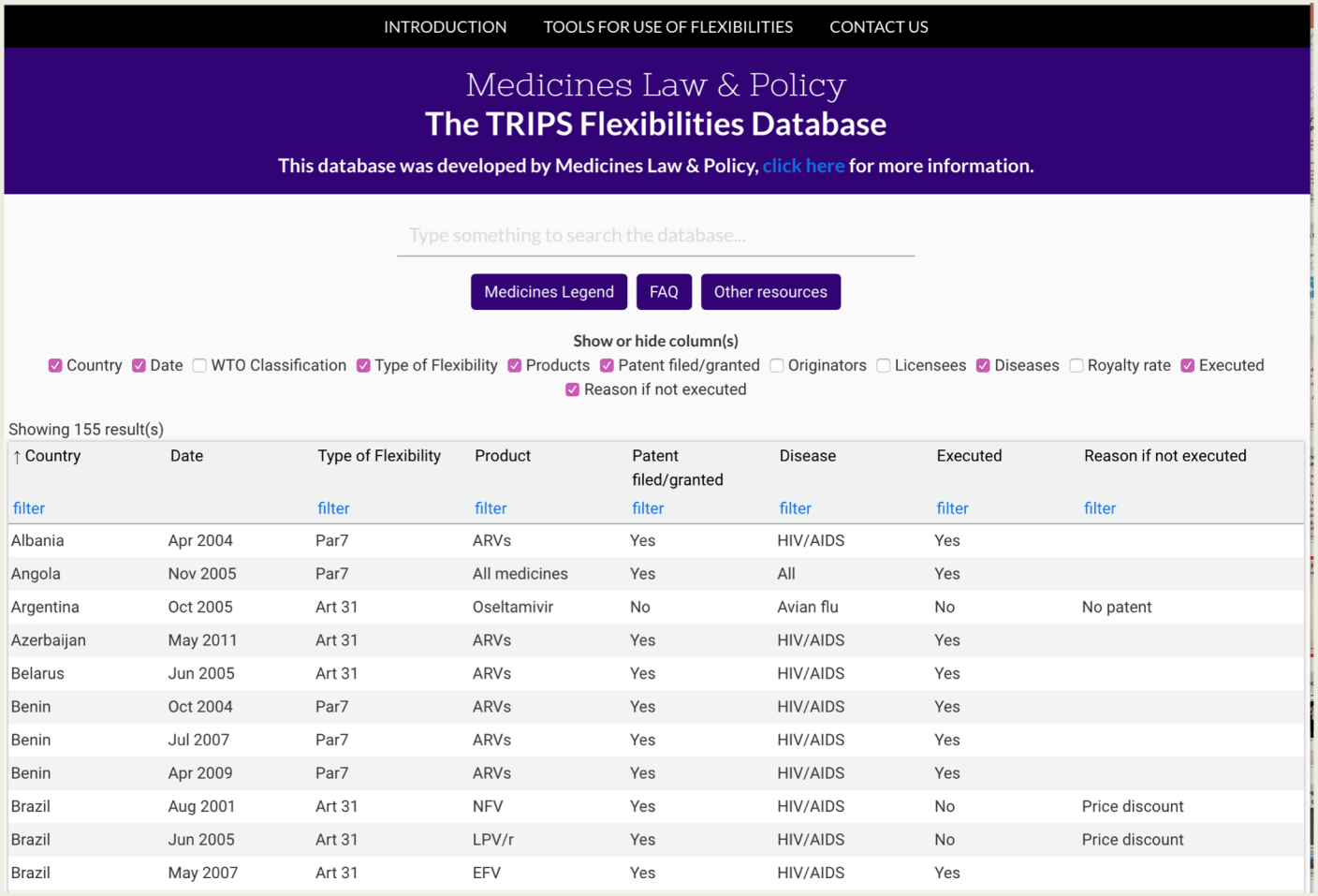
TRIPS Flexibilities Database

http://tripsflexibilities.medicineslawandpolicy.org/



INTRODUCTION TOOLS FOR USE OF FLEXIBILITIES CONTACT US

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The TRIPS Flexibilities Database

This database was developed by Medicines Law & Policy, click here for more information.

Type something to search the database...

Medicines Legend | FAQ | Other resources

Show or hide column(s)

Country | Date | WTO Classification | Type of Flexibility | Products | Patent filed/granted | Originators | Licensees | Diseases | Royalty rate | Executed | Reason if not executed

Showing 155 result(s)

↑ Country	Date	Type of Flexibility	Product	Patent filed/granted	Disease	Executed	Reason if not executed
filter		filter	filter	filter	filter	filter	filter
Albania	Apr 2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Angola	Nov 2005	Par7	All medicines	Yes	All	Yes	
Argentina	Oct 2005	Art 31	Oseltamivir	No	Avian flu	No	No patent
Azerbaijan	May 2011	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Belarus	Jun 2005	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Benin	Oct 2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Benin	Jul 2007	Par7	ARVs	Yes	HIV/AIDS	Yes	
Benin	Apr 2009	Par7	ARVs	Yes	HIV/AIDS	Yes	
Brazil	Aug 2001	Art 31	NFV	Yes	HIV/AIDS	No	Price discount
Brazil	Jun 2005	Art 31	LPV/r	Yes	HIV/AIDS	No	Price discount
Brazil	May 2007	Art 31	EFV	Yes	HIV/AIDS	Yes	

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Show or hide column(s) Country | Date | WTO Classification | Type of Flexibility | Products | Patent filed/granted | Originators | Licensees | Diseases | Royalty rate | Executed | Reason if not executed

Showing 22 result(s)

↑ Country filter	Date	Type of Flexibility filter	Product filter	Patent filed/granted filter	Disease filter	Executed filter (1)	Reason if not executed filter
Argentina	Oct 2005	Art 31	Oseltamivir	No	Avian flu	No	No patent
Brazil	Aug 2001	Art 31	NFV	Yes	HIV/AIDS	No	Price discount
Brazil	Jun 2005	Art 31	LPV/r	Yes	HIV/AIDS	No	Price discount
Cameroon	Jan 2005	Art 31	NVP, 3TC, 3TC/AZT	Yes	HIV/AIDS	No	No response
Canada	Oct 2001	Art 31	Ciprofloxacine	Yes	Anthrax	No	Price discount
Ecuador	Jan 2003	Art 31	3TC/AZT	Yes	HIV/AIDS	No	Price discount
India	Jan 2008	Art 31	Sunitinib, Erlotinib	Yes	Cancer	No	Withdrawn
India	Mar 2013	Art 31	Dasatinib	Yes	Cancer	No	Rejected
India	Jun 2015	Art 31	Saxagliptin	Yes	Type II Diabetes	No	Rejected
Italy	Feb 2006	Art 31	Sumatriptan	Yes	Migraine	No	Voluntary licence
Kenya	Sep 2004	Art 31	3TC	Yes	HIV/AIDS	No	Voluntary licence
Kenya	Sep 2004	Art 31	3TC/AZT	Yes	HIV/AIDS	No	Voluntary licence
Kenya	Sep 2004	Art 31	AZT	Yes	HIV/AIDS	No	Voluntary licence
Kenya	Oct 2004	Art 31	NVP	Yes	HIV/AIDS	No	Voluntary licence
Korea	Jan 2002	Art 31	Imatinib	Yes	Cancer	No	Rejected
Korea	Dec 2008	Art 31	T-20	Yes	HIV/AIDS	No	Rejected
Korea	Oct 2009	Art 31	Oseltamivir	Yes	H1N1 Influenza	No	Rejected
Norway	May 2018	Art 31	nusinersen	Yes	Spinal muscular atrophy	No	Rejected
South Africa	Oct 2003	Art 31	AZT, 3TC, AZT/3TC, NVP	Yes	HIV/AIDS	No	Voluntary licence
Thailand	Jan 2008	Art 31	Imatinib	Yes	Cancer	No	Donation
United States of America	Oct 2001	Art 31	Ciprofloxacine	Yes	Anthrax	No	Price discount
United States of America (Loui...	May 2018	Art 31	HCV medicines	Yes	HCV	No	Subscription model for lowering price be

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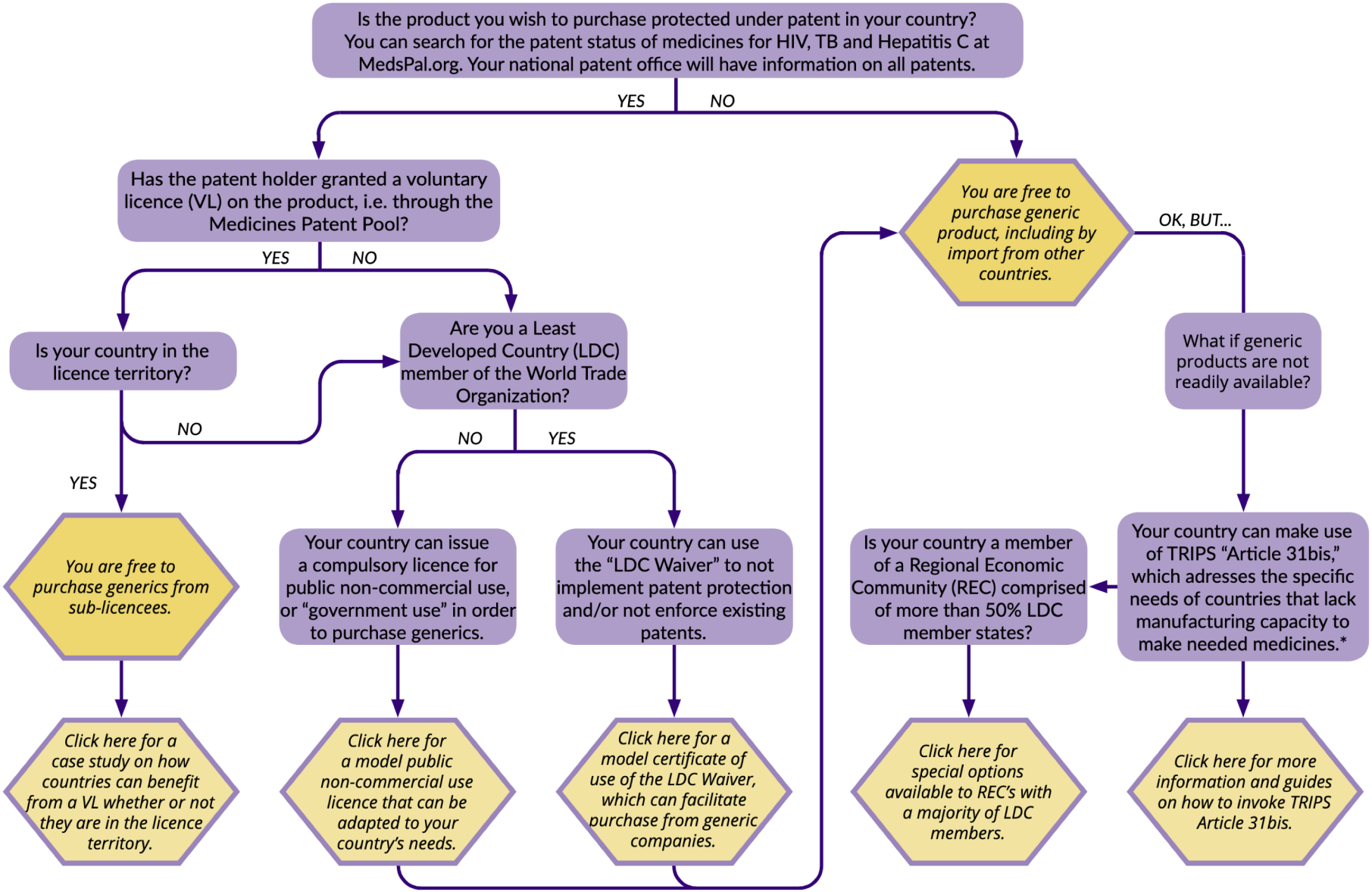
Tools

- For use in procurement of medicines
- Model licenses
- Non enforcement declaration for LDCs
- Helpful decision making charts to select most appropriate tool

Tools

There are several model uses of TRIPS flexibilities available from Medicines Law & Policy, depending on your particular circumstances and needs. To find the right tool for your purposes, follow the flow chart below. The yellow hexagons link to model uses of the appropriate tool on the Medicines Law & Policy site.



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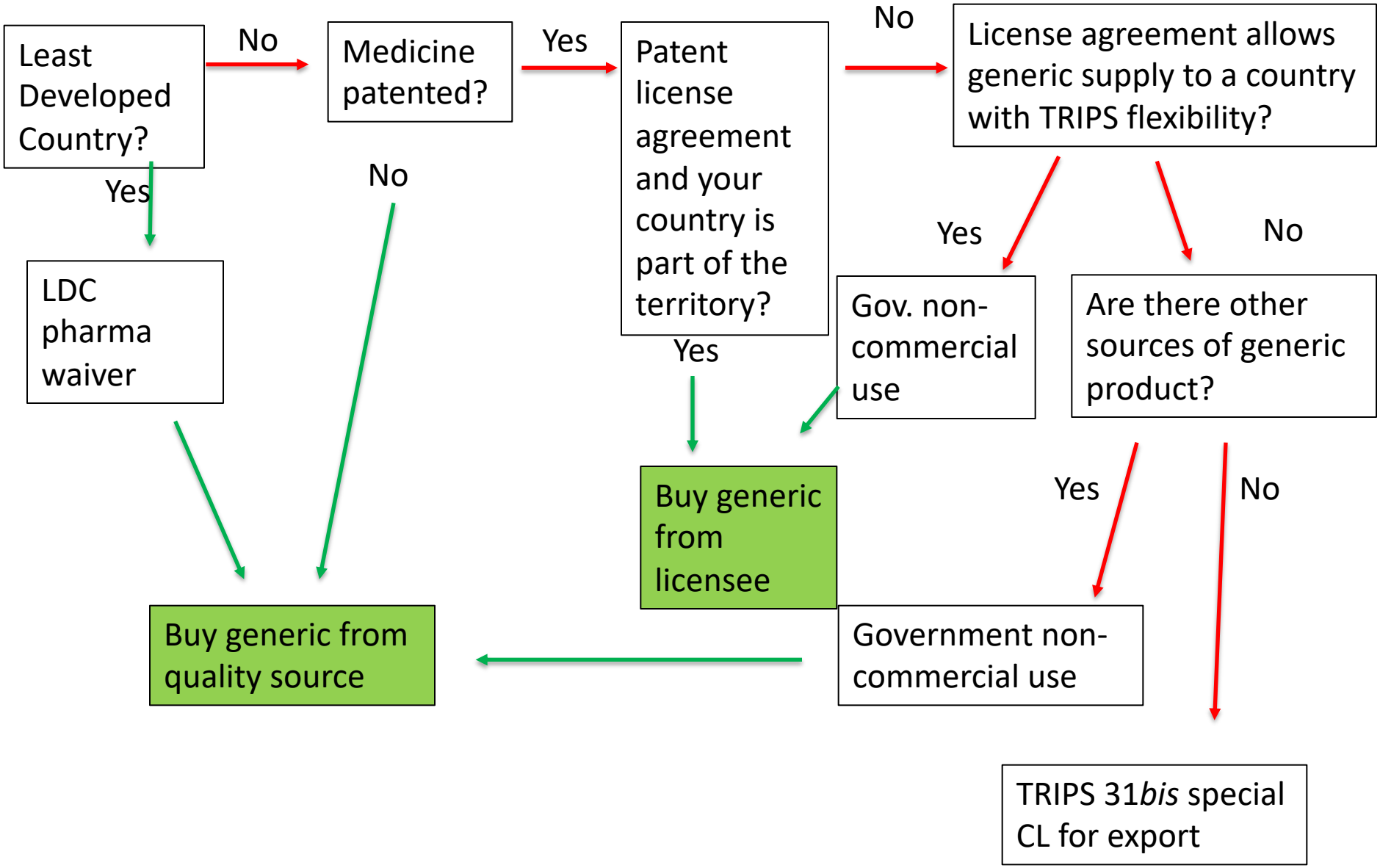
* Some high income countries have opted out of the use of this provision.



Info on patent status: MEDSPAL.ORG

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Compulsory Licensing Developments in Europe

- France 2018 -> Cancer researchers request GU for cancer drugs
- Germany 2016 -> Court ordered in patent dispute re HIV med
- Greece 2016 -> High cost of new meds/withdrawal of cancer med
- Ireland 2017 -> Resolution by the Irish Medical Association
- Italy '05, '07 -> Competition authority issued CLs
- Romania 2015 -> Hepatitis C –request by civil society
- Russia 2018 -> Lenalidomide
- Scotland 2018 -> Request by cancer patients (Perjeta –pertuzumab)
- Spain 2015 -> Hepatitis C patients demand
- The Netherlands 2019 -> MoH/EZ established commission on CL
- UK 2019 -> requests by cancer patients/CF patients (Orkambi)
- Switzerland 2019 -> request by cancer patients (Perjeta -pertuzumab)

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TODAY, ARE PATENTS THE LEAST OF OUR WORRIES?

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Patent and non-patent exclusive marketing rights

- Patents (minimum 20 years)
- Patent extensions e.g. Supplementary Protection Certificate (EU)
- Orphan medicine market exclusivity (USA 7/EU10-12 yr)
- Pediatric medicine market exclusivity
- Regulatory test data and market exclusivity (EU 8+2+1)

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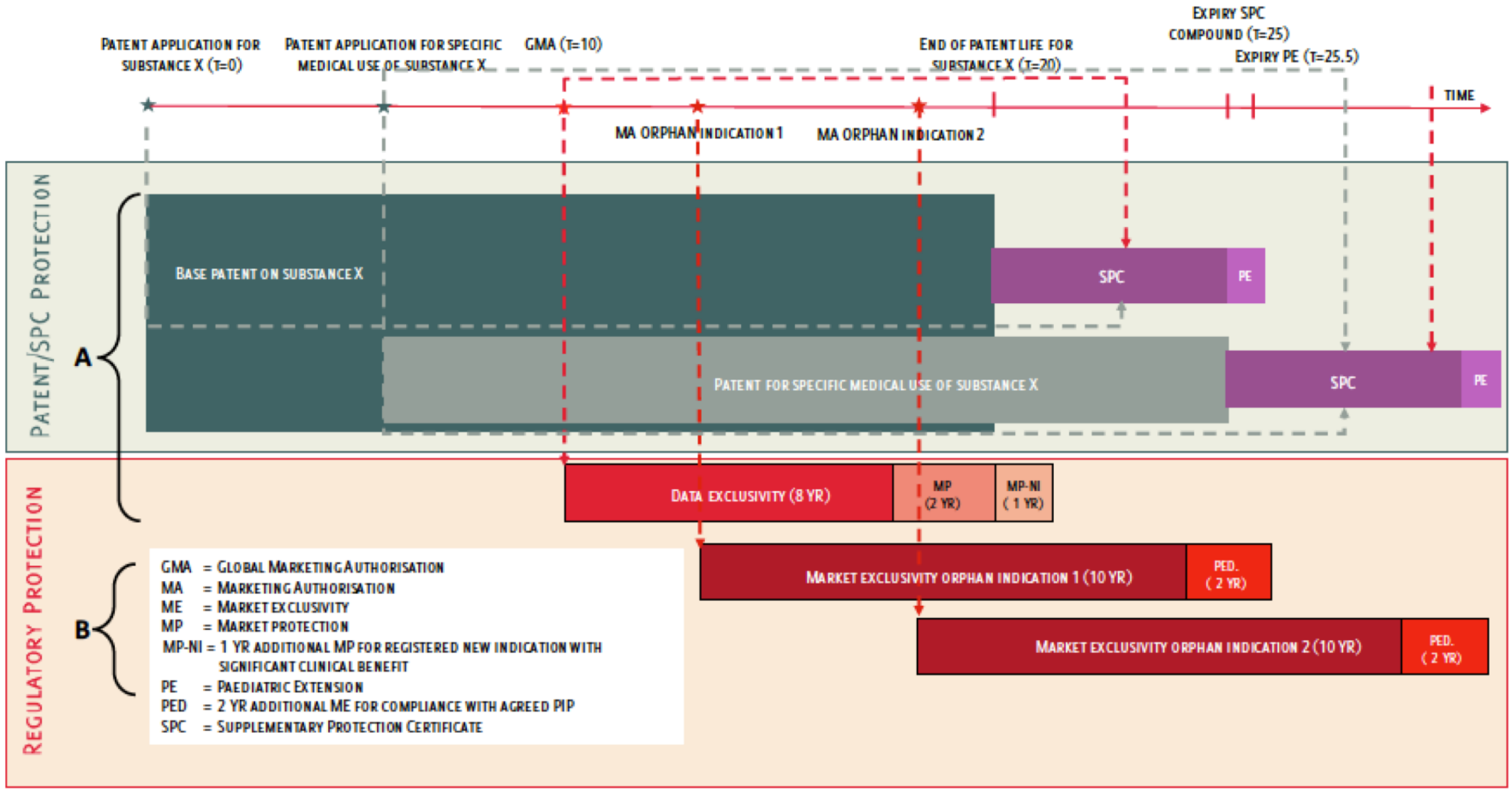
Patent and Regulatory Market Exclusivity

Figure 52 Relation between the different patent/SPC and regulatory protections for pharmaceutical products



Source: http://www.technopolis-group.com/report/effects-of-supplementary-protection-mechanisms-for-pharmaceutical-products/

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DEVELOPING NEW MEDICINES IS COSTLY

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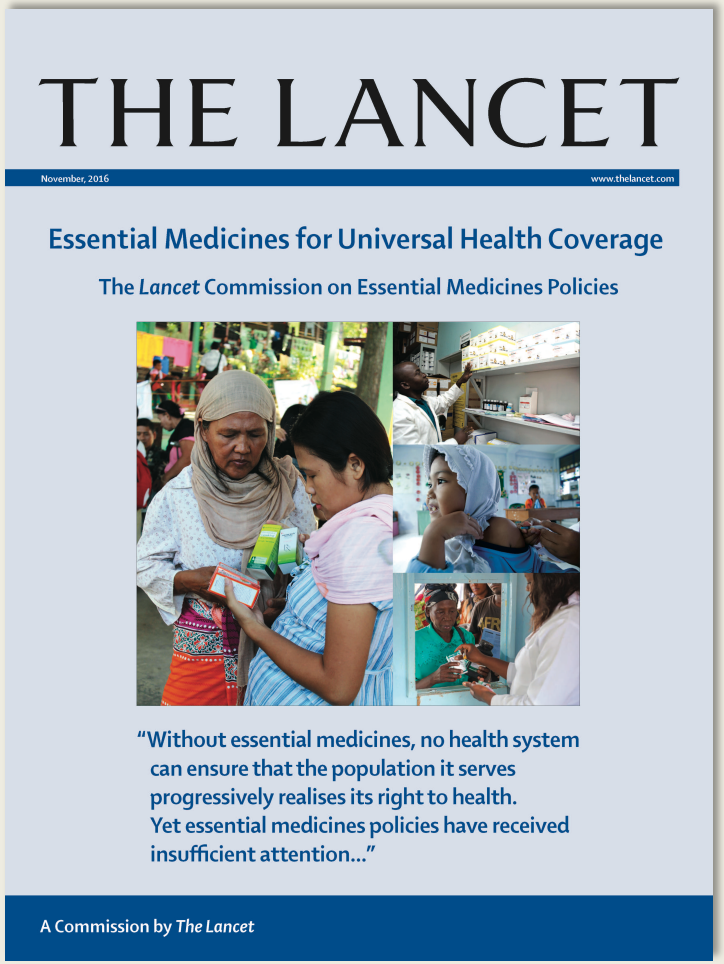
Dutch Ministers on Access to medicines in 2017 - The Lancet

"We cannot achieve any real progress without acknowledging that the current patent-based business model and the way we apply international patent rules need to change. ***The system is broken…. Patent and intellectual property exclusivities are the only cornerstone of the current model. Companies can ask the price they like. This will no longer do. We need to develop alternative business models.*** *And if public money is used for the development of new medicines, agreement upfront is needed about what this public investment will mean for the final price. We believe that companies must provide full transparency regarding the costs of research and development (R&D). "*

NL Ministers E. Schippers (Health) and L. Ploumen (Foreign Trade and Development Cooperation)
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31905-5/fulltext



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Conclusion

- High medicines pricing have their roots in the financing model of pharmaceutical R&D.
- Based on granting of market exclusivities without a “sufficiency check”.
- This is not a situation we can “compulsory license” out of.
- Time to review of current pharmaceutical incentives.
- New models of R&D financing are needed that delink price from cost.
- Greater transparency on cost and pricing.

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Thank you!

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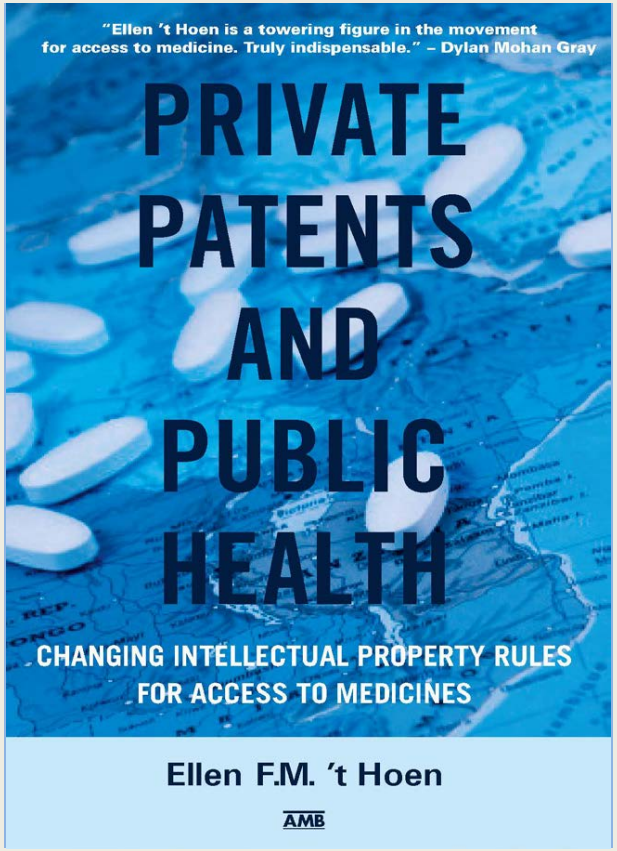
For background sources please visit:

www.medicineslawandpolicy.org

http://tripsflexibilities.medicineslawandpolicy.org/



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REST SLIDES

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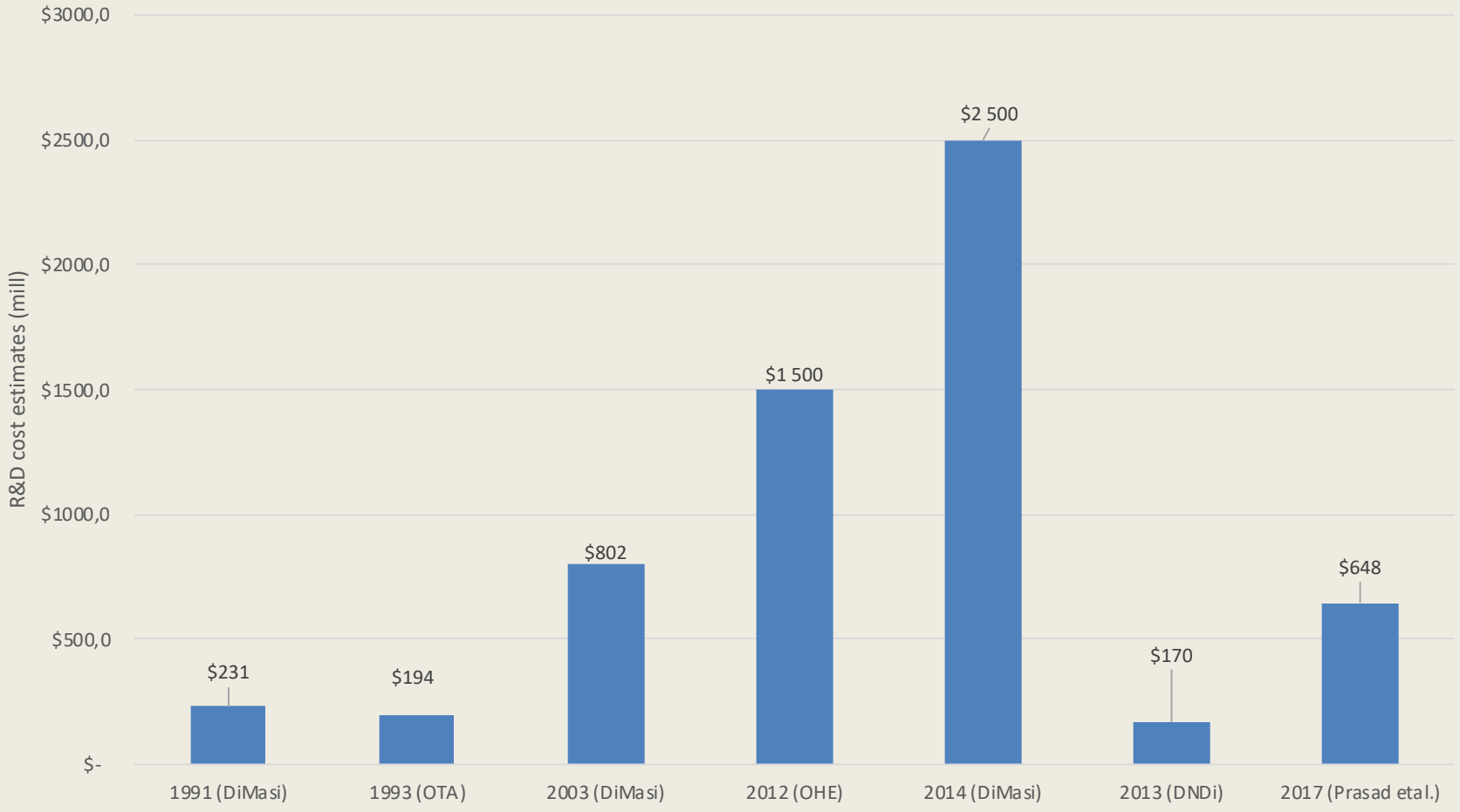
Transparency in Cost of R&D



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Lancet Commission, UNHLP (and others) recommend "Delinkage"

The concept of delinking costs from prices is based on the premise **that costs and risks associated with R&D should be rewarded, and incentives for R&D provided by means other than through the price of the product.** If the R&D cost of new medicines did not have to be recouped through high prices, those medicines would be free of market exclusivity and could be made more widely available and more affordably priced through better competition.

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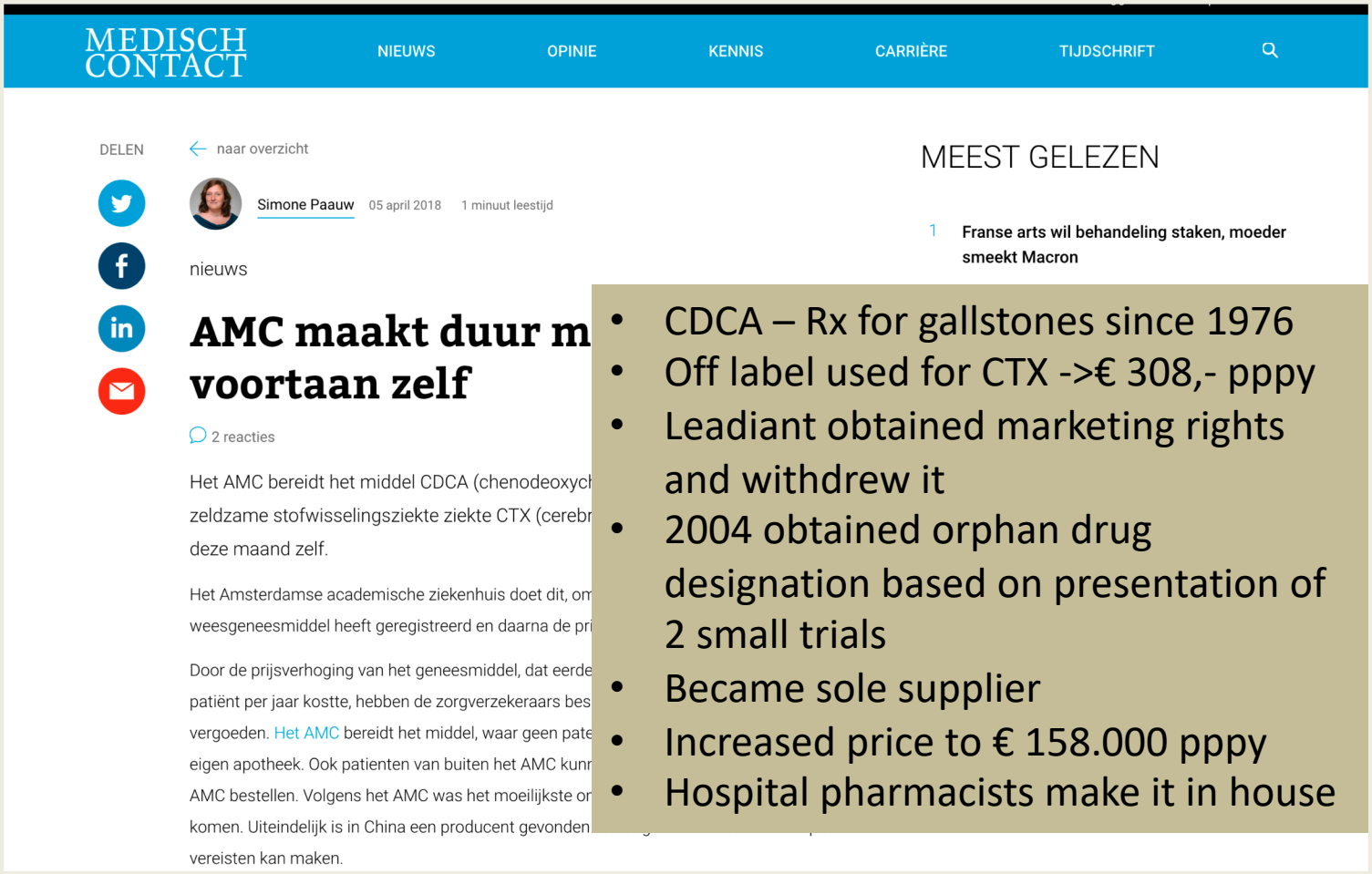
Gaming the Orphan Drug Act: CDCA in the Netherlands



- CDCA – Rx for gallstones since 1976
- Off label used for CTX ->€ 308,- pppy
- Leadiant obtained marketing rights and withdrew it
- 2004 obtained orphan drug designation based on presentation of 2 small trials
- Became sole supplier
- Increased price to € 158.000 pppy
- Hospital pharmacists make it in house