European Union Review of Pharmaceutical Incentives: *Suggestions for Change*

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Medicines Law & Policy

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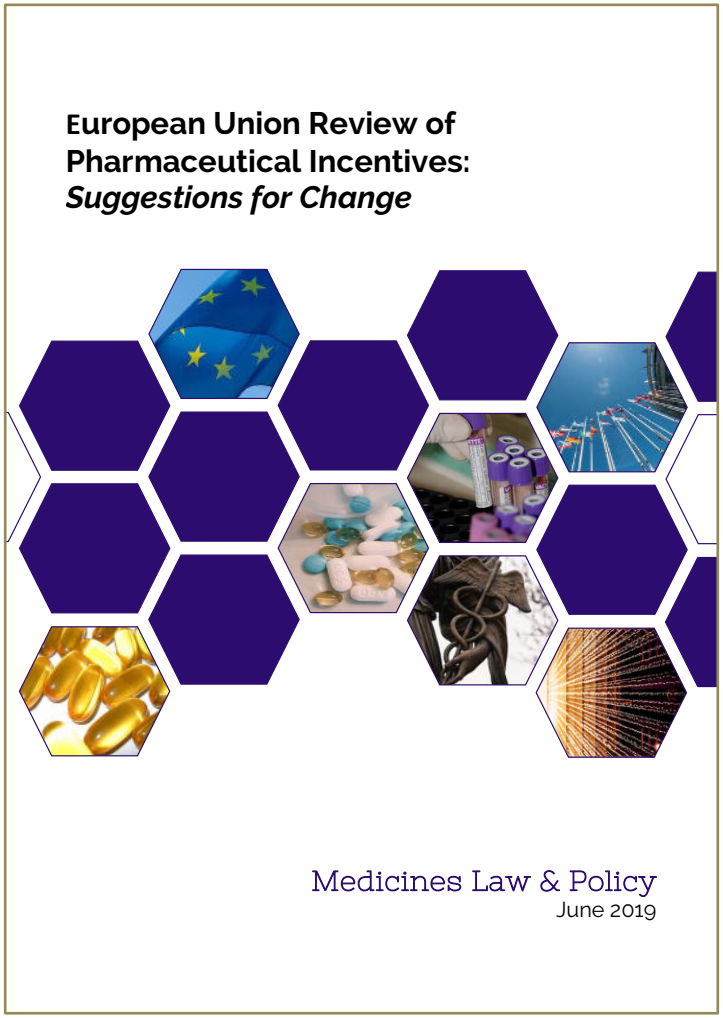
EU Review of Pharmaceutical Incentives

The Council of the European Union decided in June 2016 to find ways to "strengthen the balance in the pharmaceutical system in the EU and its Member States."

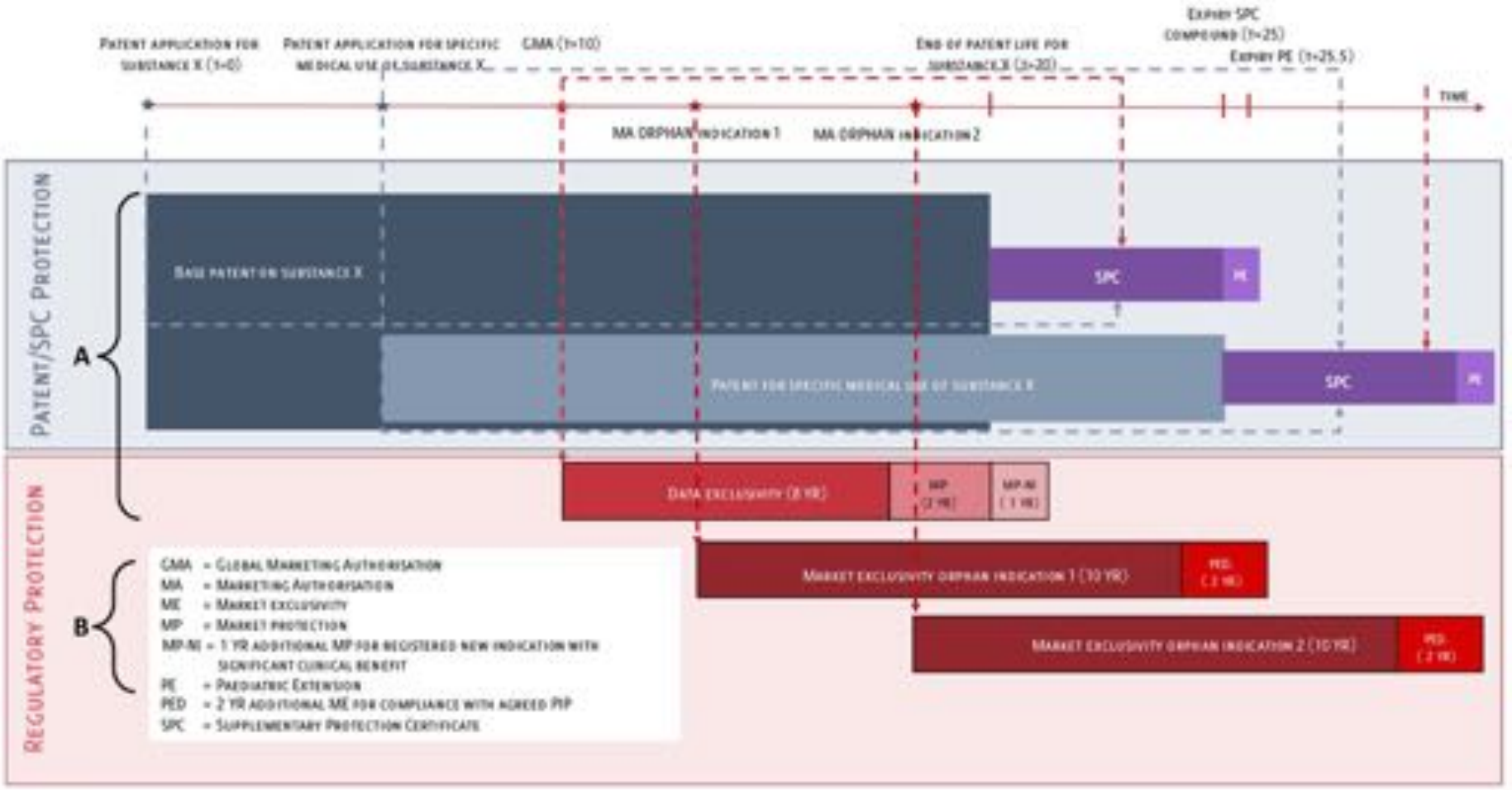
The ML&P Briefing Papers offer recommendations in the following areas under review:

- Supplementary Protection Certificate
- Data Exclusivity
- Orphan Medicinal Product



Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States [2016] C269/31. <https://www.consilium.europa.eu/en/press/press-releases/2016/06/17/epsco-conclusions-balancepharmaceutical-system/>.

Patent and regulatory market exclusivity



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

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Market exclusivity and medicines pricing

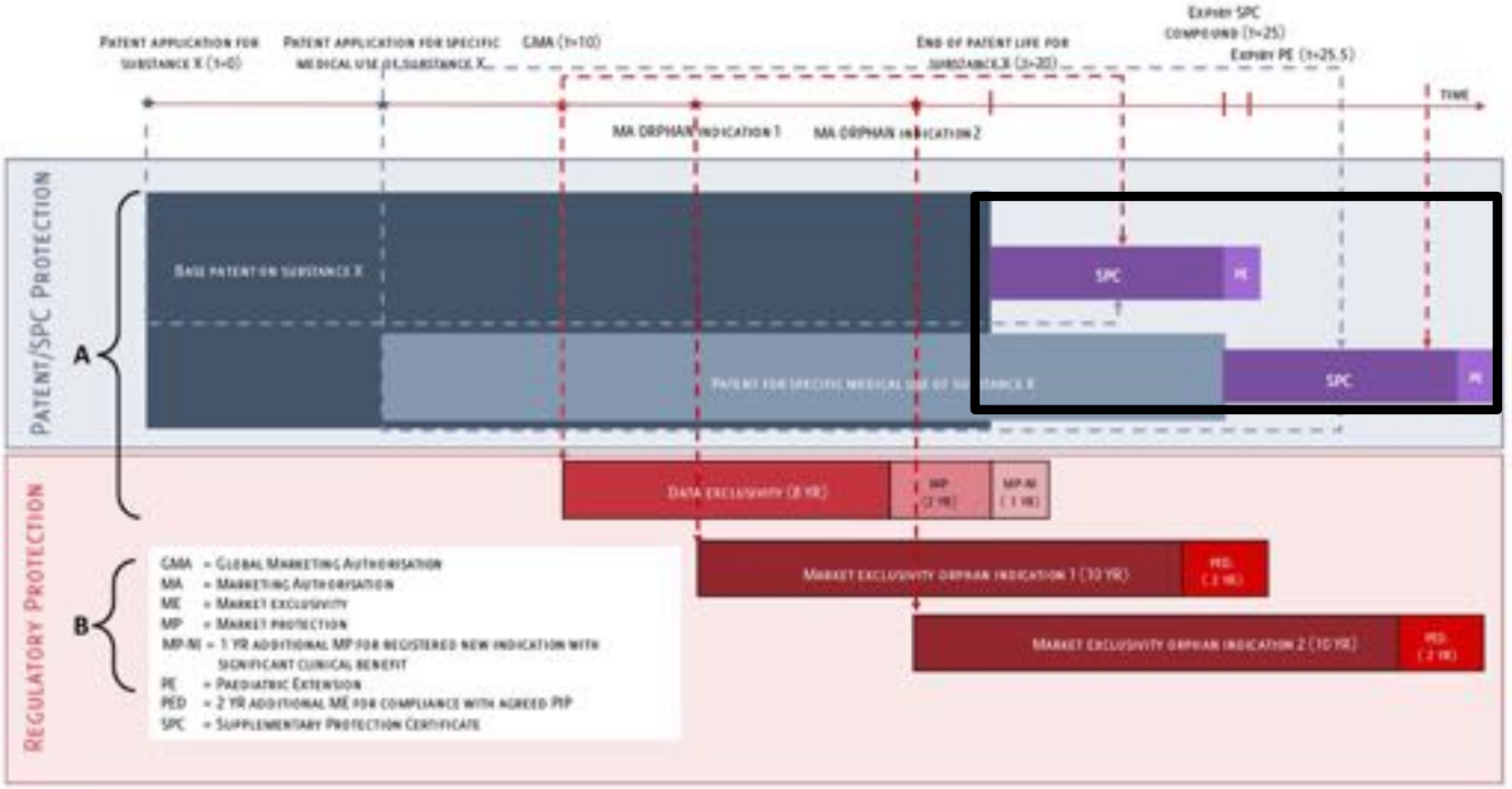
Cancer medicines

Medicine	Lowest-highest list prices in EU	Target price
Bortezomib (Multiple myeloma)	$982 (Spain) - $1,123 (UK) per month	$255 per month
Dasatinib (Chronic myeloid leukaemia)	$2,146 (UK) - $3,624 (Latvia) per month	$12 per month
Everolimus (Breast cancer)	$3,155 (UK) - $3,958 (Latvia) per month	$1,086 per month
Gefitinib (Lung cancer)	$1,786 (France) - $2,568 (Latvia) per month	$13 per month
Imatinib (Chronic myeloid leukaemia)	$2,261 (Latvia) - $32,906 (Spain) per year	$172 per year
Erlotinib (Lung, pancreatic and others)	$26,416 (France) - $36,678 (Latvia) per year	$240 per year
Lapatinib (Breast cancer)	$33,549 (Spain) - $49,887 (Latvia) per year	$4,020 per year
Sorafenib (Kidney and liver cancer)	$45,162 (France) - $67,877 (Latvia) per year	$1,450 per year

Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) medicines

Medicine (Indication)	List price/ pill in UK	Target price/ pill	Current price/ treatment in UK	Target price/ treatment
Daclatasvir (HCV)	$379.44	$0.08	$31,872.96	$6.72
Darunavir (HIV)	$12.90	$1.45	$387 a month	$43.50 a month
Efavirenz+emtricitabine+tenofovir (HIV)	$23.09	$0.15	$692.70 a month	$4.50 a month
Ledipasvir+sofosbuvir (HCV)	$603.26	$1.02	$50,673.84	$85.68
Sofosbuvir (HCV)	$541.40	$0.57	$45,477.60	$47.88
Tenofovir disoproxil fumarate (HIV)	$8.85	$0.07	$265.50 a month	$2.10 a month

Supplementary Protection Certificates



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Supplementary Protection Certificates

- Introduced by Regulation (EEC) No 1768/92, now Regulation (EC) No 469/2009
  - Up to **5 years of additional patent-like protection** to a registered medicine

- To compensate for lack of commercial exploitation before the medicine's regulatory approval & increase pharma R&D in EU
  - Ensure **15 years of effective patent protection**
  - Deemed necessary "to cover the investment put into the research"

Sui generis rights

- Applied within 6 months of:
  - Market authorisation of medicinal product (first registration) or
  - Grant of *basic* patent (product, process or application)

- SPC term = patent filing date – market authorisation filing date – 5 years

- Only one SPC/product (active ingredient or combination)

Higher prices of medicines with SPCs

Example of the HIV medicine TDF/FTC (Truvada)

Country	SPC status	Price (30 tablets) in €
The Netherlands	Never granted	30,65
France	Revoked	170
Switzerland	In force	800

25 years of SPC regulation

- Over **20,000 SPCs** granted since adoption of Regulation (**45% of products**)
- **Diverse interpretation** of Regulation by patent offices:
  - SPCs granted in some countries/rejected in others
- Plethora of judicial decisions and CJEU cases
  - Product, *basic* patent, SPC beneficiary, second medical use indication
- **No reduction in price of medicines** under SPC protection
- **No evidence of increase of R&D** in EU
- **No evidence that patent protection is insufficient** "to cover the investment put into the research"

Recommendations

1. Make granting of SPCs **conditional on evidence** of insufficient effective patent protection/ R&D costs

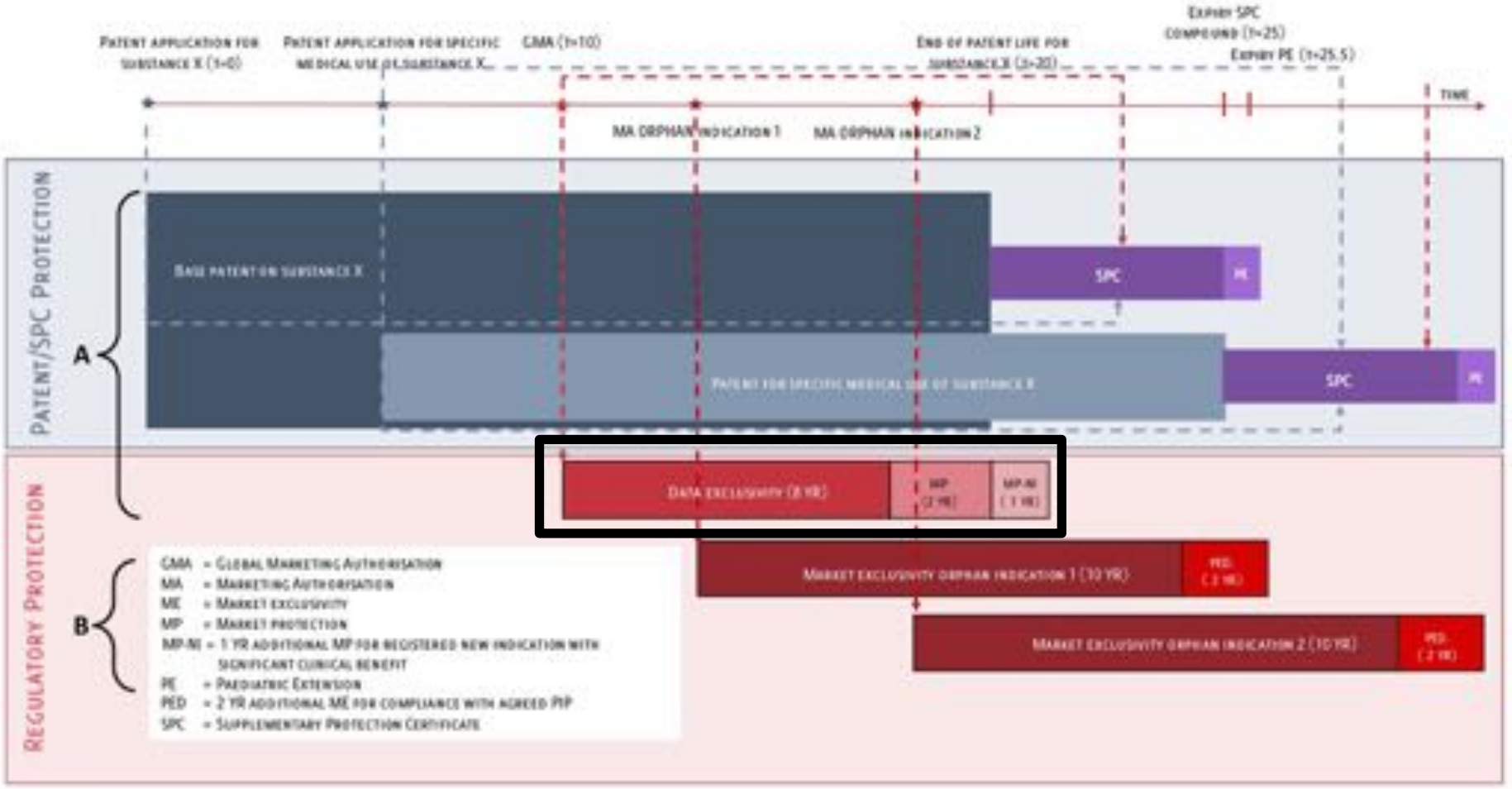
2. **Review of medicine's reported profits** before entry into force of SPC

3. Give third parties an opportunity to submit **"observations" to pre-empt SPC entry** into force

4. Extend **SPC revocation procedures** to to all EU countries, modelled on patent opposition procedures

5. Tie SPC entry into force to **affordable pricing** of medicinal product

Data Exclusivity



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Data Exclusivity 1/3

- Data exclusivity was first introduced in the EU in 1987 (Directive 87/21/EEC)
  - 6 years / 10 years biologics
  - 2004 EU exclusivity regime expanded: '8+2+1 rule' (Directive 2004/27/EC)

- Data exclusivity first introduced in the US in "Hatch-Waxman Amendments" in 1984

- To protect the investment in the production of test data needed to obtain marketing authorisation by **preventing use by generic companies** for a certain period of time

- During the period of data exclusivity, a generic **competitor product cannot be considered for registration**

Data Exclusivity 2/3

- **No international obligation** to provide data exclusivity
  - WTO TRIPS 39.3: protect certain kind of data related to new chemical entities (NCEs) against unfair commercial use
  - A majority of WTO members do not provide data exclusivity

- EU generally requires data exclusivity **commitments in Free Trade Agreements** (FTAs)

- Data exclusivity is automatic:
  - **does not require an application** nor evidence of its need
  - data exclusivity is granted **regardless of the level of investment** in generating the test data
  - **quietly enforced through medicines regulation**

Data Exclusivity 3/3

- EU Data Exclusivity regime **most generous globally**
- Generally **co-exists with other forms of exclusivity** (20 year patents + 5 year SPCs)
- **May bolster weak medicines patents** by discouraging patent challenges
- **No evidence that it encourages innovation**

Data Exclusivity and Compulsory Licensing

- Compulsory licence (CL) / government use (GU) of a patent **important public health safeguard**
- Today, CL / GU requested / considered in 10 European countries
- **No explicit exception / waiver in data exclusivity regulation** in case of public health measure (even in case of emergency)
- Data exclusivity **may obstruct effective use of CL / GU** by prohibiting registration of generic products
- **Recognised in voluntary licences** (via the Medicines Patent Pool), US New Trade Policy, in *EU Regulation on compulsory licensing of patents for the manufacture of pharmaceutical products for export to countries with public health problems outside the EU* (article 18)

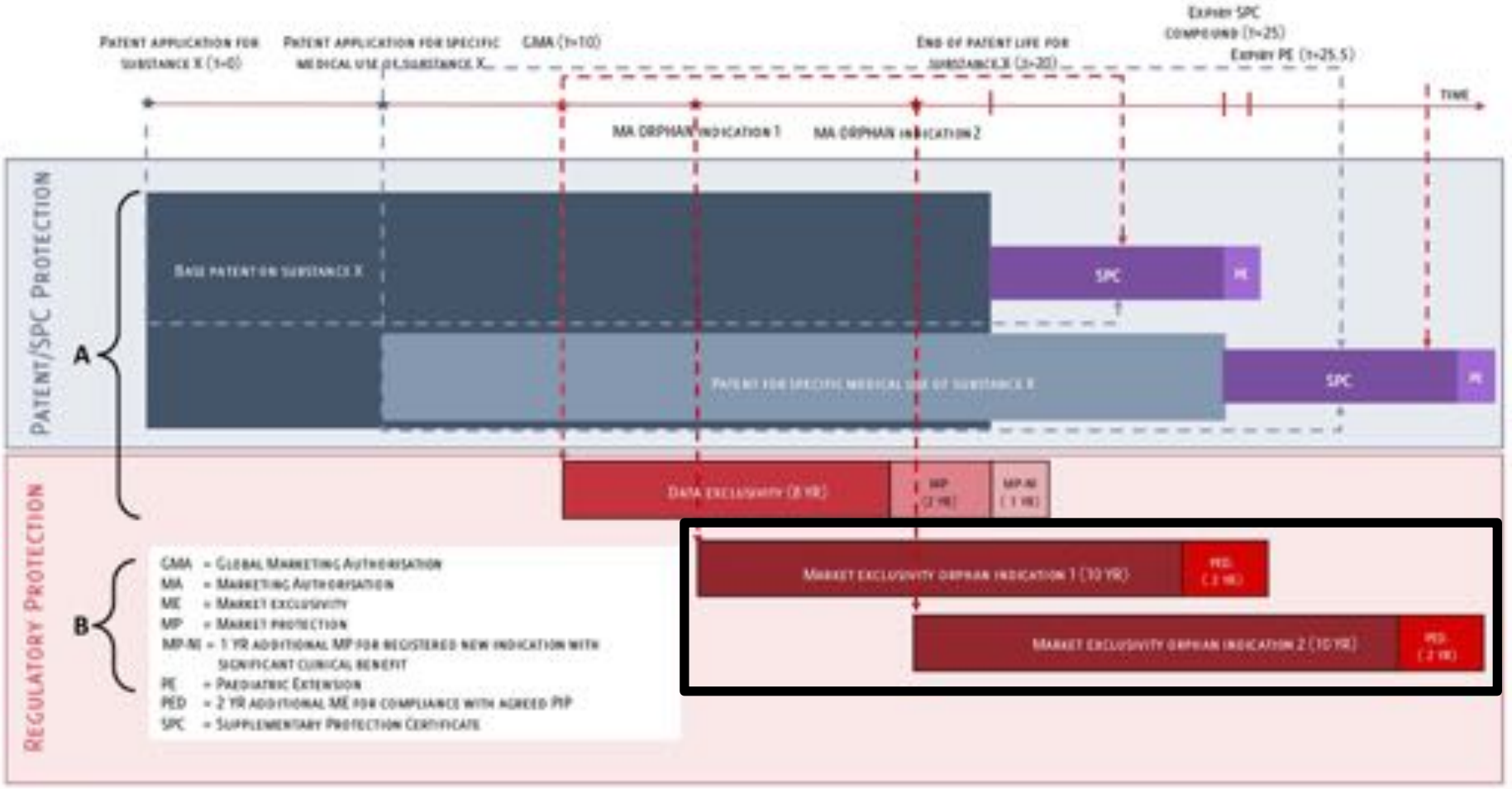
Recommendations

1. Replace the data exclusivity regime with a **data compensation** regime

2. **Remove the requirement from trade negotiations** with other nations to implement data exclusivity

3. **Introduce waivers** to data and market exclusivity to facilitate effective compulsory licensing / government use / crown use or other measures needed for public health

Orphan Medicinal Products



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Orphan Medicinal Products

- Regulation EC 141/2000
- Targets rare diseases **≤ 5 patients/10,000 of population**
- Estimated to be at least **8,000 such rare diseases** and c. 30 million EU citizens affected
- A mix of **push and pull incentives**
  - Protocol assistance
  - Fee waiver
  - Framework for EU and Member State R&D funding
  - 10 year market exclusivity

Orphan designation – Art.3(1)

- **Prevalence route** (>99%)
  - Prevalence of not more than 5 / 10,000 persons

Or

- **Return on investment (ROI) route** (<1%)
  - Prevalence can be more than 5 / 10,000 but likely insufficient return
  - Past and expected future development, production and marketing costs, including grants and tax incentives received and an estimate and justification for expected future revenues

And

- No satisfactory method of diagnosis, prevention or treatment is authorised, or if there is, significant benefit

Orphan Medicinal Product Exclusivity – Art.8(1)

- From the date of approval of an orphan medicine, **no *similar* product can be applied/approved for marketing for 10 years** *for the same therapeutic indication*

- *Unless:*
  - **Authorisation** of orphan medicine holder
  - **Insufficient supply** of orphan medicine
  - Similar medicine "**safer, more effective or otherwise clinically superior**"

Withdrawal Clause … withdrawn

- Draft Art.8(2) Commission proposal:
  - 10 year exclusivity reduced to 6 years if Art.3 criteria no longer met,

  or
  - Unreasonable profit from price charged

- Final Art.8(2):
  - 10 year exclusivity reduced to 6 years if Art.3 criteria no longer met, **inter alia** the product is sufficiently profitable
  - So this only applies in case of ROI route, < 1%

Recommendations 1/2

1. Fully operationalise Article 8 (2) of Regulation 141 / 2000 by **defining the line between 'sufficient' and 'excessive' profitability** and therefore between 'sufficient' and 'insufficient' Return on Investment

2. The **prevalence threshold** of not more than five per ten thousand people in Article 3 (1)(a), equivalent to a maximum current EU patient population of circa 250,000, **should be re-examined** in the light of experience gained since 2000

3. **A mechanism similar to the 'withdrawal clause'** from the early drafts of the Regulation should be re-introduced to the present Art. 8 (2)

Recommendations 2/2

4 Where marketing authorisation (and orphan exclusivity) is granted for an orphan medicinal product which **essentially 'formalises' the use of a product which has previously been used 'off label'** or has been compounded by pharmacists, ensure that:

- the **prior users can continue to make the same use** of the product that they have before
- commercial **reward is matched** to the relatively small development risk and cost

Conclusions 1/2

1. Adequate incentives for R&D are important but there **must be a clearer link between risk and reward**

2. Historical reasons underpinning the EU's generous data and market exclusivity system are **no longer valid**

3. The **idea of 'sufficient' profit should guide policy makers**, with 'sufficiency' estimates driven by transparency of cost and pricing

4. **Flexibilities inherent in patent law should not be rendered ineffective** by exclusive rights granted through the medicines regulatory system

Conclusions 2/2

5 **Free trade agreements should not be used to demand** third countries implement more stringent intellectual property (IP) protection than they are required under WTO rules

6 Greater diversity in incentives **away from the 'one size fits all approach'** based on market monopolies → requires broader discussion than proposals made here today

7 **Implementing the proposals for change will help rebalance current system towards serving the public interest**

Thank you!

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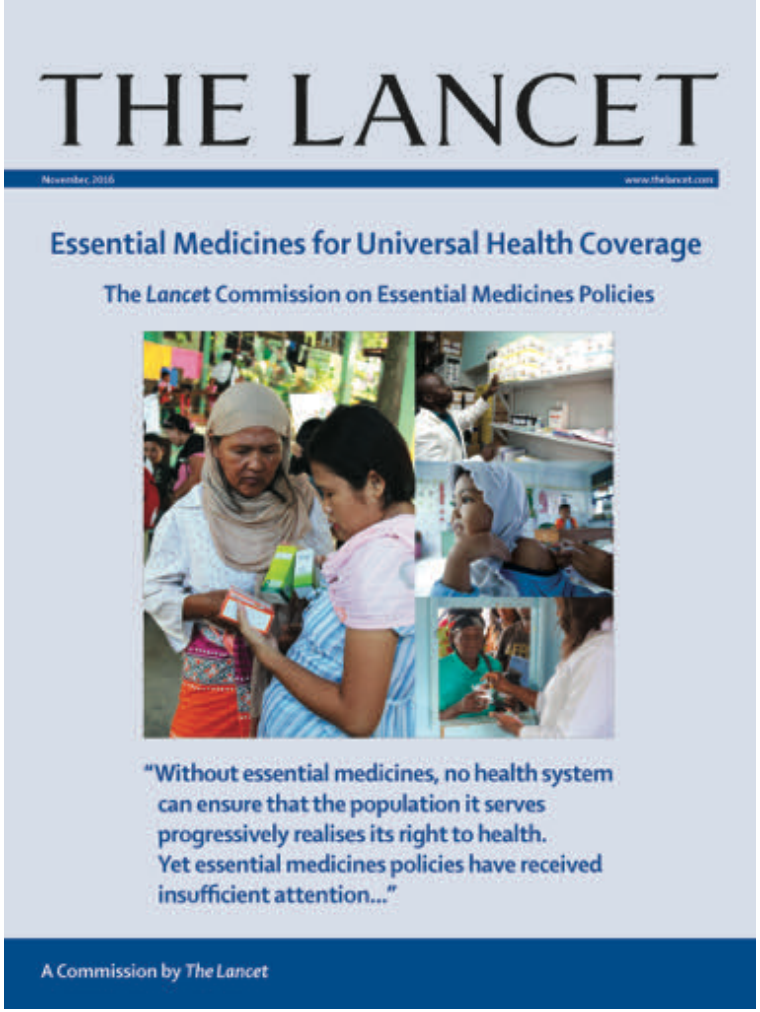
Additional Slides

Dutch Ministers on access to medicines:

"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), speaking in the Lancet.
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31905-5/fulltext



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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."*