Additional notes on the submission on IPR-linked research mandates

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Note: These notes were prepared following the discussion at the hearing conducted by the United nations Secretary General's High Level Panel on Access to Medicines on Wednesday, March 16, 2016 in Johannesburg.

1. Changing the way in which the pharmaceutical industry operates by means of IPR-linked regulation

Regardless of the recommendations of the High Level Panel, pharmaceutical companies will continue to play a part in pharmaceutical R&D in the short to medium term and its business model is likely to remain tightly linked to patent rights. A key question before the panel should thus be whether there are potential legislative or regulatory measures that can be taken to ensure that the pharmaceutical industry operates in a way that is better aligned with the public interest.

Governments have the authority and the responsibility to regulate industries in the public interest. In the case of medical products this responsibility is even greater since the health of people and the right to health and the right to life is at stake.

One way in which governments could regulate the pharmaceutical industry is to make the granting and maintenance of pharmaceutical patent monopolies contingent upon compliance with certain regulations. The regulatory intervention we suggest is a research mandate – but we urge the panel to consider whether other regulatory interventions could also be implemented through such an IPR-linked mechanism.

We stress that the intention of a proposed IPR-linked research mandate is not only to increase investment in medical R&D, but also to bring about change to the ways in which the pharmaceutical industry operates. A company mandated to invest 30% of revenue will make substantially different business decisions than a company not subject to such a mandate. Such a company may, for example, be willing to take more risks in deciding how to allocate R&D funds – which could lead to the increased discovery of new molecular entities. We believe that it would be in the public interest to regulate the pharmaceutical industry in such a way as to increase investment in medical R&D and to decrease spending on marketing, litigation and excessive profits.

2. A research mandate versus taxes

Various taxation options aimed at raising funds for public interest medical R&D are worth considering. For example, profits on pharmaceutical products can be taxed with the revenue raised going to public interest research institutions such as the United States National Institutes of Health. We would suggest that the tax rate paid should increase rapidly as the level of profit increases. A mechanism of this nature could be considered as an alternative to the section of our proposal by which 20% of a company's R&D spending would have to go to independent public interest research institutions. One potential risk of a poorly implemented tax is that it could result in companies passing on the cost of the tax to consumers – thus leading to price increases.

However, in place of, or in parallel with taxes, research mandates may offer additional benefits. For example, a mandate to invest 30% of revenue on medical R&D is likely to have a greater impact on R&D investment at a company than a tax such as that described above. In addition, a mandate would force companies to spend money in certain ways, rather than just forcing companies to pay more tax. Thus, if the aim is not just to raise R&D funds, but also to change the way in which industry operates, a mandate is likely a more effective mechanism than a tax.

3. How can we ensure R&D funds are effectively invested in the public interest?

In our original proposal we suggest a dual allocation of funds with 30% of revenue mandated to be invested in medical R&D, and 20% of this to be paid to public research institutions. This amounts to 24% of revenue invested by the company on its internal medical R&D and 6% of revenue contributed by the company to public research institutions.

3.1. R&D internal to the company: Under the mandate a company's investment in its internal R&D processes may for example rise from 14% of revenue to 24% of revenue. In case of the largest pharmaceutical companies this will amount to billions of dollars in additional R&D investment. (1) In our proposal the only limit on how these funds is invested is that it must be on medical R&D. There is thus no obligation under our proposed mandate to direct this investment to areas of greatest medical need. It is likely though that the additional funds available to invest in R&D would increase investment in financially more risky areas such as the development of new molecular entities.

3.2. R&D external to the company: While the direction of internal R&D funds are left to the company's discretion in our proposal, the 6% of revenue that is paid to public interest research institutions must be invested in areas of greatest medical need. These funds could either be contributed directly to public interest research institutions in the country where the company is based or to an international R&D coordinating mechanism (along the lines of what is suggested in contributions on a potential R&D treaty or agreement). Whichever mechanism is used to distribute and allocate such funds, it must be (a) done in a way that is completely transparent and that (b) ensures that the products of R&D funded in this way have non-exclusive licenses in line with the principles of de-linkage.

4. Regulating of the marketing of medical products

As argued in point 1 above, governments have the power, and an obligation, to regulate pharmaceutical companies in the public interest. One such area in which the public interest requires increased regulation is the marketing of medical products. We argue that increased regulation of marketing would result in increased and better targeted investments in R&D. The key elements of the argument are as follows:

4.1.1. It is in the interest of patients that doctors prescribe medicines based on the best available scientific evidence since this will give patients the greatest chance of treatment success.

4.1.2. The primary aim of pharmaceutical advertising and marketing is to increase sales of a company's products by convincing doctors to prescribe the products or patients to request the products. This is not in the best interest of patients since it may lead to less effective, less safe, or more expensive medicines being prescribed. This wastes the money of patients and insurers and puts the health of patients at risk. (2)

4.1.3. Apart from the above public interest concerns, allowing pharmaceutical companies to aggressively advertise and market products creates certain perverse incentives. Had all pharmaceutical industry marketing and advertising been prohibited, companies would have been forced to compete simply on the quality, safety and efficacy of their products. This would increase the incentive to develop superior products. However, allowing pharmaceutical marketing and advertising enables a business model whereby inferior or so-called 'me too' drugs are made financially viable by the fact that they can flourish on the strength of advertising and marketing. There is no public benefit from this dynamic, since it contributes to both high prices and less useful investment in R&D.

There is thus a strong public interest case for legally prohibiting all forms of pharmaceutical advertising and marketing, including advertising in any forms of media, direct marketing by company representatives, sponsored training, educational or other events, free samples, gifting, and any other form of sponsorship or payment to medical professionals, medical researchers or medical academics or institutions.

There are two chief counter arguments to such a prohibition:

4.2.1. It is some times argued that it is in the public interest for companies to make patients and doctors aware of important new products. While it is true that doctors and patients should have access to up-to-date and evidence-based information on medical products, companies are not well placed to provide such information since they have a strong conflict of interest given that they sell some of the products in question. The public interest would be better served if national regulators or

other independent bodies were to publish regular updates and guidelines for doctors and patients on the best treatments for specific conditions. Such independent assessments could be funded through a small levy paid by pharmaceutical companies. Such a levy would cost a fraction of current marketing and advertising spend by industry – and thus both save the industry money and provide doctors and the public with a non-bias and up-to-date source of information on medical products and the evidence supporting their use. Comparative effectiveness research conducted in the United States provides a potential template for how such work could be approached. (3)

4.2.2. It is some times argued that limits on marketing of medical products introduces an unjustified limit on free speech. This question has been considered widely, and most jurisdictions (the United States and New Zealand are exceptions among OECD countries) accept that such limitations are warranted and in the public interest. It should be stressed though that such limits do not apply to the publication of the findings of clinical trials conducted on the medical products in question in medical journals or by national medicines regulators. It is important and in the public interest that all the published scientific evidence relating to a medical product should be in the public domain. In our view the publication in medical journals and in reports from medicines meets the public interest need for unbiased information regarding medical products. Such unbiased information should however be distinguished from the inherently bias and harmful information presented through advertising and marketing.

Apart from the direct public interest benefits of more rational prescribing, we encourage the panel to consider what impact the strict regulation of pharmaceutical advertising and marketing will have on the way in which the industry operates. We also urge the panel to take a strong position against all forms of pharmaceutical marketing and advertising and to recommend that countries undertake legislative reforms prohibiting all forms of pharmaceutical marketing and advertising.

Evidence and sources

1. Based on existing spending trends we can make rough estimates of the impact of a research mandate. These estimates are inherently uncertain since a mandate will fundamentally alter the business model of pharmaceutical companies. We nevertheless consider some estimates of the impact to be useful.

Our proposed mandate would, for example, increase Johnson & Johnson's annual investment in internal medical R&D from USD8.5bn to USD17.1bn. In addition, J&J will be forced to make a USD4.2bn contribution to external public interest medical R&D. J&J will also not be allowed to spend more than USD10.7bn on advertising and marketing. (Note that in line with section 4 of the notes above this number could be reduced to zero.)

By contrast, a company like Eli Lilly already spends 23.8% of revenue on R&D and would thus be less drastically impacted by a research mandate. The Eli Lilly example suggests that higher R&D investment is feasible and that the industry would survive regulatory interventions mandating greater R&D investment.

Company	Total Revenue ($bn)	R&D Spent ($bn)	% on R&D	Sales and Marketing ($bn)	% on Sales and Marketing
Johnson & Johnson	71.3	8.2	11.5%	17.5	24.5%
Novartis	58.8	9.9	16.8%	14.6	24.8%
Pfizer	51.6	6.6	12.8%	11.4	22.1%
Hoffmann-La Roche	50.3	9.3	18.5%	9.0	17.9%
Sanofi	44.4	6.3	14.2%	9.1	20.5%
Merck	44.0	7.5	17.0%	9.5	21.6%
GSK	41.4	5.3	12.8%	9.9	23.9%
AstraZeneca	25.7	4.3	16.7%	7.3	28.4%
Eli Lilly	23.1	5.5	23.8%	5.7	24.7%
AbbVie	18.8	2.9	15.4%	4.3	22.9%

Source: GlobalData

2. There is extensive information available on the impact of direct and indirect advertising and marketing on prescribing behaviour. Some of this evidence is in the public scientific literature. In addition, the Pulitzer-winning public interest journalism publication Pro Publica has done substantial work on this. Below we highlight some key evidence:

Ornstein, C., & Jones, R. G. (2015). Vying for Market Share, Companies Heavily Promote 'Me Too' Drugs. *ProPublica*. Retrieved March 22, 2016, from https://www.propublica.org.

- “The information, from a database known as Open Payments… shows that the drugs most aggressively promoted to doctors typically aren’t cures or even big medical breakthroughs... In almost all cases, older, cheaper products are available to treat the same conditions.”

Ornstein, C., Jones, R. G., & Tigas, M. (2016). Now There's Proof: Docs Who Get Company Cash Tend to Prescribe More Brand-Name Meds. *ProPublica*. Retrieved March 22, 2016, from https://www.propublica.org.

“Doctors who received industry payments were 2 to 3 times as likely to prescribe brand-name drugs at exceptionally high rates as others in their specialty.”

Orlowski, J. P., & Wateska, L. (1992). The effects of pharmaceutical firm enticements on physician prescribing patterns. There's no such thing as a free lunch. PubMed, 102(1), 270-273. Retrieved March 22, 2016, from http://www.ncbi.nlm.nih.gov

- “We examined the impact on physician prescribing patterns of pharmaceutical firms offering all-expenses-paid trips to popular sunbelt vacation sites to attend symposia sponsored by a pharmaceutical company. The impact was assessed by tracking the pharmacy inventory usage reports for two drugs before and after the symposia. Both drugs were available only as intravenous preparations and could be used only on hospitalized patients. The usage patterns were tracked for 22 months preceding each symposium and for 17 months after

each symposium. Ten physicians invited to each symposium were interviewed about the likelihood that such an enticement would affect their prescribing patterns. A significant increase in the prescribing pattern of both drugs occurred following the symposia. The usage of drug A increased from a mean of 81 +/- 44 units before the symposium to a mean of 272 +/- 117 after the symposium (p less than 0.001). The usage of drug B changed from 34 +/- 30 units before the symposium to 87 +/- 24 units (p less than 0.001) after the symposium. These changed prescribing patterns were also significantly different from the national usage patterns of the two drugs by hospitals with more than 500 beds and major medical centers over the same period of time. These alterations in prescribing patterns occurred even though the majority of physicians who attended the symposia believed that such enticements would not alter their prescribing patterns."

Mackey, T. K., MAS, Ph.D, & Liang, B. A., PhD, MD, JD. (2015). It's Time to Shine the Light on Direct-to-Consumer Advertising. *Annals of Family Medicine,* 13(1), 82-85. Retrieved March 22, 2016, from http://www.ncbi.nlm.nih.gov

- "Over the past few decades, US pharmaceutical marketing has evolved in new and unexpected ways, as the business of health care has become part of a growing "eHealth" landscape. Increasingly, patients and other cosumers, clinicians, and the industry have started to embrace emerging forms of digital technology that can influence health care information sourcing, consumption, and delivery."
- "Consumers, public health and health care professionals, and policy makers should collectively advocate for greater transparency of DTCA to better understand its influence on pharmaceutical and health care unilization and consumer behaviour."
- "Proponents emphasize DTCA's potential to educate consumers, while critics argue that DTCA leads to overemphasis on benefits vs risks, inappropriate prescribing, and increased national drug expenditures."

Hansen, R. A., Schommer, J. C., Cline, R. R., Hadsall, R. S., Schondelmeyer, S. W., & Nyman, J. A. (2005). The association of consumer cost-sharing and direct-to-consumer advertising with prescription drug use. *Research in Social and Administrative Pharmacy*, 1(2), 139-157. Retrieved March 22, 2016, from http://www.ncbi.nlm.nih.gov

- "Compared with low-advertising markets, individuals residing in markets with high levels of advertising and paying provider co-payments of $10.00 or more were more likely to use the advertised product. In the same markets, higher prescription drug co-payments were associated with a decreased likelihood of using the advertised product. A similar relationship was not observed for the non-advertised competitor."

Payments, Promotion, and the Purple Pill

Ridley, D. B. (2015). Payments, Promotion, and the Purple Pill. *Health Economics*, 24(1), 86-103. Retrieved March 22, 2016, from http://www.ncbi.nlm.nih.gov

- "Detailing has an economically and statistically significant ($p < 0.001$) impact on demand in the antiulcer market. Detailing might be used by manufacturers to offset sales lost from higher copayments."

3. Sox HC. Comparative Effectiveness Research: A Progress Report. Ann Intern Med. 2010;153(7):469-472. doi:10.7326/0003-4819-153-7-201010050-00269 http://annals.org/article.aspx?articleid=746204