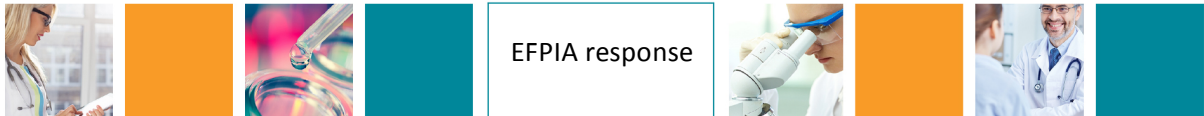


EFPIA response to Draft Opinion on Innovative payment models for high-cost innovative medicines

Author: EFPIA * Date: 07/12/2017



1. Executive summary

The mission of the Expert Panel on Effective Ways of Investing in Health (EXPH) is to elaborate evidence-based opinions on matters related to healthcare modernisation, responsiveness and sustainability at the request of the European Commission. In October 2017, the EXPH produced a draft Opinion on Innovative Payment models for high-cost innovative medicines.

The industry wishes to constructively engage with all stakeholders on the debate regarding innovative payment methods but has a number of serious concerns regarding the draft opinion and its contribution to a dialogue on this issue. This draft opinion is based on a partial and at times out of date review of evidence and contains numerous statements that are contradictory and unsubstantiated.

This is a missed opportunity in terms of providing an unbiased assessment of the facts as well as of the policy opportunities and challenges related to the elaboration of new payment models. Instead of taking a holistic and dynamic view, the draft opinion narrowly focuses on prices and pharmaceutical spending while ignoring the broader context that is critical to understanding sustainability. By mischaracterising data such as the trends in pricing and aggregate spending, the draft opinion is not of a sufficiently high standard. The Expert Panel has focused its analysis on issues beyond innovative payment models by looking into intellectual property and the licensing regime, rather than looking in detail at issues associated with an outcome-based approach and for example, considering the opportunity of real world evidence as set out in the Panel's terms of reference.

The draft opinion should not move forward as it stands without addressing these fundamental flaws in the framing and analysis of the policy problems, and consideration of possible alternative solutions.

1. Incomplete evidence base: The draft opinion has not reviewed the evidence on the cost of medicines and their impact on healthcare system.

The draft opinion argues that: "Expenditure with new molecules has outpaced the growth of GDP or the growth of other healthcare expenditure"[270ff]. However, recent data from the OECD shows that retail pharmaceutical spending per capita is less than the growth in other parts of the healthcare system (2009-2015)¹. OECD data shows that total retail spending on pharmaceuticals per capita in real terms across all nations declined at an average annual rate of 0.5% between 2009 and 2015². Between 2009 and 2015, expenditure on pharmaceuticals per capita declined by 0.9% in real terms on average in Europe-24³. In Europe, expenditure on pharmaceuticals represents on average 15% of total healthcare costs, with some countries spending as little as 8%⁴. The share of total health expenditure attributed to medicines has remained broadly consistent over the last fifteen years, though with year-to-year variability in some countries. This is consistent with a very recent analysis

¹ OECD, *Health at Glance*, 2017

² OECD, *Health at Glance*, 2017

³ OECD data from *Health at Glance 2017*, processed by EFPIA. Countries included are: Greece, Portugal, Ireland, Iceland, Netherlands, Denmark, Czech Republic, Hungary, France, Slovenia, Finland, Luxembourg, Slovak Republic, Belgium, Spain, Poland, Sweden, Germany, Italy, Austria, Estonia Switzerland, Norway, Latvia.

⁴ OECD database accessed in November 2017. European countries included are: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom. Cf footnote 17, for definition of pharmaceutical spending by the OECD.

based on IMS data which shows that after taking into account rebates and discounts, spending is growing substantially more slowly than commonly reported.⁵

The draft opinion argues that the financial sustainability of healthcare systems is under pressure due to the high prices of new medicines. However, the draft opinion does not recognise the value that innovative medicines deliver and fails to examine other components of health care spending. The draft opinion does not adopt a dynamic view of pharmaceutical spending which should not only take into account innovative medicines but also off-patent medicines where spending is falling. Finally, the draft opinion ignores some of the causes of the budgetary challenges that healthcare systems are facing (demographic changes) and fails to acknowledge the fact that medicines can create savings in other parts of the system. Expenditure on health should not only be seen as a cost (such as page 6 of the draft opinion) but also as an investment towards increased welfare, productivity and economic growth and assessed holistically over time.

2. Unsubstantiated opinions: The draft opinion contains unsubstantiated arguments on the value of innovation.

The draft opinion also contains unsubstantiated claims on the lack of true innovation. It frequently downgrades the importance of incremental innovation (cf 592 ff; 776 ff). From the industry perspective, both incremental and breakthrough innovation are important. Innovation often happens in small steps, yet, this contributes to significant advances for patients and transform patient outcomes over time. Intellectual property (IP) is a pre-requisite for innovation. In contrast, to the EXPH assertion, investment in both incremental and breakthrough is costly and risky. Providing IP protection for breakthrough or incremental innovations is therefore critical to future innovation and to expanding treatment options for patients. As it is the case in other industries, the process of innovation does not stop when a product is launched. The industry seeks to improve the product for the benefit of patients. Examples of the benefits of these improvements include:

- Making life easier for patients: Developing oral medications for type 2 diabetes patients to regulate their blood glucose levels, instead of injections or developing extended release formulations which require less doses per day and improve patients' compliance with a course of treatment.
- Expanding treatment applications: developing a medicine that is proven for the treatment of HIV in adults for preventing mother-to-child transmission of HIV.
- Developing new uses for a medicine: developing a rheumatoid arthritis medication for use in treating other autoimmune diseases, such as Crohn's disease.

3. Contradictory: The draft opinion contains many contradictory assertions on new payments models.

The draft opinion initially recognises that the principle of value-based pricing is sound in that it rewards innovation and creates positive incentives for R&D of medicines which will bring benefits to patients, healthcare systems and societies. The draft opinion also highlights the need to have "better rewards for higher therapeutic added value" [1669ff] and to "move towards acquisition of service rather than product" [1674ff.]. It then subsequently criticises value-based approaches as creating an incentive framework that encourages higher prices.

The draft opinion initially refutes the idea of "cost plus pricing" because this would create inefficiencies and would not create incentives for new innovation – a position that EFPIA agrees with. The draft opinion states that: "...new payment models should not be based on paying for R&D costs incurred" ([803 ff.]) It then suggests that cost information should be requested by payers and

⁵ Forecasting pharmaceutical expenditure in Europe: Adjusting for the impact of rebates and discounts, Espin J et al. Presented at ISPOR 20th European conference

provided by manufacturers during the pricing and reimbursement process. It calls for transparency of price and R&D costs related to the HTA submission [1563ff]. Indeed, the draft opinion argues that “creating greater transparency around the costs of pharmaceutical products and the price of medicines would provide better grounds for assessing affordability, equitable access, fairness in pricing and incentives to develop new medicines” [1126 ff.]

EFPIA agrees that a “cost plus approach” is not an appropriate payment model for pharmaceuticals. The ‘cost-plus’ method is inefficient since it inadequately rewards added therapeutic value and does not provide appropriate incentives. In addition, it is extremely difficult (or impossible) to disentangle costs of R&D for a specific product. The cost-plus pricing method represents a “static” approach, which focuses mainly on budgetary constraints and ignores both short-term and long-term benefits of innovative treatments. EFPIA also supports the need to move towards value-based pricing, which relies on a greater flexibility across markets and indications. A report from the OECD shows that greater flexibility that moves away from a “single price” can improve access and affordability [OECD (2008), *Pharmaceutical Pricing Policies in a Global Market*, p. 205]. This requires, however, that certain policies such as external reference pricing are revisited.

Transparency of prices and costs would lead to a “cost plus approach”, which would be detrimental to innovation and hinder patients’ access to new medicines. Confidentiality of net prices allows prices to be negotiated and adapted based on an individual country’s health and economic needs which is one of the key pillars of value-based pricing. Increased transparency and disclosing of net prices would lead to lower access to medicines in countries that today get rebates due to their lower income levels/ability to pay. Confidentiality of net prices creates incentives for innovation while facilitating access to medicines for countries with lower ability to pay⁶.

4. Confusing: The confusing assessment of Managed Entry Agreements underestimates their potential benefits

When discussing Managed Entry Agreements (MEAs), the draft opinion uses a range of terminology – sometimes it recognises the many different forms of MEAs (e.g. financial price/volume type agreements, coverage with evidence developments, performance-linked reimbursement etc.), but sometimes “MEA” seems to refer only to outcomes-based type schemes.

The draft opinion would also have benefited from a more detailed examination of all different types of innovative payments models and a discussion on the conditions under which the various models can deliver most value for stakeholders (e.g. depending on expected size of patient population, care setting (primary or secondary), disease area, healthcare system set-up etc.).

The draft opinion argues that: “they [MEAs] are designed to address the issue of uncertainty about the value of the effectiveness of the drug and not the (high) price tag or the rising pharmaceutical expenditure” [585ff.]. This assumption, which largely ignores the diversity of MEAs, is not correct. Indeed, governments and payers can use MEAs to address budget uncertainty through financial agreements (e.g. price-volume) and outcomes-based agreements (e.g. payment per results)⁷. Therefore, in contrast to the conclusions at the end of the chapter, MEAs – as a tool to find agreement on price (and margin) between payer and innovator – can help to manage pharmaceutical expenditure.

⁶ For instance, Dumoulin (2001) shows that price discrimination increases access by a factor of approximately 4– 7 times (cited by Danzon & Towse, 2003).

⁷ Klemp M et al. (2011), What principles should govern the use of managed entry agreements; *Int J Tech Ass in Health Care*.

5. Erroneous: The draft opinion provides unsubstantiated concerns regarding market power

Throughout the EXPH Draft Opinion, there is an extensive reference made to the exercise of market power by pharmaceutical companies, as well as to the high prices generated by the use of this market power (e.g. *“...high prices as a result of exercise of market power by pharmaceutical companies”* [410 ff.]). The document assumes that pharmaceutical companies have an excessive bargaining power. (e.g. *“That role of prices is much weaker in health care, as insurance protecting patients from the financial hardship associated with health care needs also withdraws the natural barrier to very high prices set by providers of care, including pharmaceutical companies”* [1662 ff.]).

Firstly, the panel has developed a theory on the impact of health insurance on price sensitivity and price levels. They argue that because patients are covered by national health insurance schemes, and hence are not responsible for paying the price of the medicines, this reduces the price sensitivity of the market, contributing to higher prices. On the contrary: first, patients as consumers would be in a weak position to negotiate the price in a context of a life-saving medicine (notwithstanding that this would be unethical). Second, delegating the negotiation to a payer (and agencies undertaking Health Technology Assessment (HTA)) de facto increases the negotiation power by having a single agent who negotiates on behalf of multiple consumers. Third, due to the fact that the payer is not affected by the respective disease/ health situation, he/she can make a neutral judgment about value. Finally, payers rely on sophisticated value assessment systems. In conclusion, patients may be less price-sensitive in terms of health resource use because of the insurance system; however, in today's environment the price is determined by the payer who is much more powerful than the individual patient. The EXPH has not included any analysis of the many mandatory price changes that have been applied to the industry over the last five years, which illustrate this point.

Secondly, the draft opinion does not take into account competition between on-patent medicines. This is perfectly illustrated by the case of Hepatitis C. As new, competing treatments entered the market, net prices of Hepatitis C drugs decreased significantly. Over time, the period of growth in expenditure is inevitably followed by patent expiries and generic competition that result in reduction in expenditure. For example, in Germany, 12% of drug spending in 1995 went towards the costs of antihypertensive or cholesterol lowering agents, yet today it is 4% of drug spending.⁸

Thirdly, from the industry perspective, it is important to recognise that a “legal monopoly” for a medicine that can be conferred by incentives does not necessarily translate into an economic monopoly: the vast majority of pharmaceutical products compete both with older products, other interventions, and with innovative products in their therapeutic class. Moreover, the European pharmaceutical industry works within the confines of an array of price regulations: price control, profit control, international price comparisons, external reference pricing and HTA. The price of a medicine is determined to reflect the clinical and economic value it brings to patients, healthcare systems and society. Competition between innovative companies within therapeutic classes and its impact on prices should not be underestimated. Between 2005-2011, half of second medicines in a class were approved within 2.3 years of the first medicine's approval – compared to 10.2 years in the 1930's.⁹

Finally, the pharmaceutical industry is subject to European competition law, as is every other sector. Indeed, the pharmaceutical industry has been subject to a detailed sector inquiry. On 8 July 2009, the European Commission published the conclusions of its 18-month pharmaceutical sector, which looked in detail at competition.¹⁰ This does not support the EXPH recommendations.

⁸ 2017 Quintiles IMS report on Understanding the Dynamics of Drug Expenditure.

⁹ Storz. 'Intellectual property issues of immune checkpoint inhibitors' (2016)

¹⁰ <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>

6. Policy options: The draft opinion promotes policy options, which would have a negative impact on the environment for R&D

The draft opinion should promote options, which could have a positive impact on the environment for research and development, ultimately benefiting patients, the healthcare system or society not pander to particular stakeholders.

The draft opinion makes a set of unsupported policy recommendations on the request for information on R&D costs, introducing a competition policy review of high prices asked by companies with cooperation of competition authorities. In Europe, given the regulated pricing and reimbursement environment for innovative medicines, these policies do not make sense and would have significant negative consequences.

In particular, the draft opinion does not adequately recognise the importance of intellectual property (IP) rights as a vital part of incentivising innovation and ensuring that new medicines are developed to address patient needs. The draft opinion gives the impression that IP protection stifles competition, however, this is not the case. IP protection creates the preconditions for competition. By filing for a patent, a patent holder actually makes publicly available their 'state of the art' which creates a spill-over learning effect that encourages other players to explore the science more fully. This enables further innovation, leading to more choice and more competition during the period where products have a degree of IP protection. Without the patent system, innovators would be encouraged to hide their innovation prior to launch. Thus, IP protection enables innovation beyond a specific company or product, allowing competitive conditions to drive prices down across countries and therapy areas. Today's innovative medicines are tomorrow's generics and biosimilars, already resulting in lower cost options for treating conditions like heart disease and depression today. This will extend to conditions like cancer, rheumatoid arthritis and other diseases in the near future. The draft opinion discusses radical measures like the use of prize models or even "compulsory licensing". This would have a chilling effect on future innovation. Increased use of aggressive price controls and other "last resort approaches" would hamper future innovation without improving access or sustainability.

In other areas, the EXPH sets out recommendations where initiatives already exist. For example, "select one neglected area and launch international prize initiative with patent being retained by the set of countries participating". There are already advanced market commitments (AMCs) for a series of products. The EXPH suggests that policymakers should "assess value of new products of uncertain benefit using sound and transparent health technology evaluation methods" without any discussion of current HTA methods. The panel advocates for the development of joint negotiation procedures when there are a series of initiatives currently being tested.

The draft opinion contains certain elements that could be the basis for further discussion and analysis such as the definition and measurement of value, new flexible payment models to better reward higher added value medicines and the recognition of the shift in the industry to provide a holistic healthcare services rather than only a product. However, given the inadequate quality of the analysis, the inconsistencies in the arguments, and the incoherence of the policy conclusions, EFPIA feels that the value of this draft opinion is questionable.

2. Specific comments on the study

Comments on summary

Page	Comments
Page 4 97-98ff	<p><i>“The growth of pharmaceutical expenditures due to new high-cost innovative medicines, under the current institutional framework, creates financial challenges to health systems.”</i></p> <p>For most OECD countries, pharmaceutical spending is not rising more quickly than other areas of health spending.¹¹ In fact, recent evidence shows that products and therapy areas responsible for a large slice of budget in 1995-2000 now account for a far smaller financial impact.¹² Moreover, recent data from the OECD shows that retail pharmaceutical spending per capita is more contained than the growth in other parts of the health care system (2009-2015).¹³ OECD data shows that the total spending on pharmaceuticals per capita in real terms across all nations declined at an average annual rate of 0.5% between 2009 and 2015.¹⁴ Between 2009 and 2015, expenditure on pharmaceuticals per capita declined by 0.9% in real terms on average in EU-24.¹⁵ In Europe, expenditure on pharmaceuticals represents on average 15% of total healthcare costs, with some countries spending as little as 8%¹⁶. The share of total health expenditure attributed to medicines has remained broadly consistent over the last fifteen years, though with year-to-year variability in some countries.</p> <p>QuintilesIMS (IQVIA) publishes European drug expenditure forecasts based on its audited volume data and, in most cases, publicly available list prices. However, it is well known that net prices, and therefore expenditure, can vary significantly from list prices. With increasing price pressures, list to net price divergence is believed to be growing.</p> <p>According to Espin J, et al. <i>“After adjusting for discounts and rebates, net expenditure growth in EU5 is predicted to be 1% - 2% over the next 5 years. This is below predicted healthcare expenditure growth in Europe and in line with long-term economic growth rates”</i>.¹⁷ However, the composition of healthcare spending is clearly changing and this means spending is increasing in some areas and decreasing in others – reinforcing the necessity to breakdown silos between budgets and the need to encourage an outcomes-</p>

¹¹ OECD (2015) Pharmaceutical Spending. *Health at Glance 2015fadop*

¹² Quintiles IMS (2017) Understanding the Dynamics of Drug Expenditure: Shares, Levels, Compositions and Drivers

¹³ OECD, *Health at Glance*, 2017. According to the OECD: *“Pharmaceutical spending covers expenditure on prescription medicines and self-medication, often referred to as over-the-counter products. In some countries, other medical non-durable goods are also included. Pharmaceuticals consumed in hospitals and other health care settings are excluded. Final expenditure on pharmaceuticals includes wholesale and retail margins and value-added tax. Total pharmaceutical spending refers in most countries to “net” spending, i.e. adjusted for possible rebates payable by manufacturers, wholesalers or pharmacies”*. Source: OECD website available: <https://data.oecd.org/healthres/pharmaceutical-spending.htm> (accessed December 2017).

¹⁴ OECD, *Health at Glance*, 2017.

¹⁵ OECD data from Health at Glance 2017, processed by EFPIA. Cf footnote n°3 for further details.

¹⁶ OECD database accessed in November 2017. European countries included are: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom

¹⁷ Forecasting pharmaceutical expenditure in Europe: Adjusting for the impact of rebates and discounts, Espin J et al. Presented at ISPOR 20th European conference

	<p>based approach.</p> <p>In any event, healthcare sustainability needs to look beyond pharmaceuticals. It should consider all of the demand- and supply-side factors impacting the sustainability of access to innovative therapies, such as resource levels, efficiency of the healthcare (HC) system, appropriateness of budget allocations across different types of HC services and products, cost/benefit of different types of inputs, etc.</p>
<p>Page 4 100ff</p>	<p><i>“to ensure that innovation “that matters” is produced”</i></p> <p>The EXPH has not defined what types of innovation matter and who decides this. Innovation should benefit patients, the healthcare system and society.</p> <p>There have been many attempts to define value for pharmaceuticals. Medicines should be considered innovative if they provide clear benefits for patients and/or if their dosing or administration makes the treatment more convenient for patients or their caregivers. The definition should include</p> <ul style="list-style-type: none"> • broader (non-health related) cost savings • benefits of increased productivity of patients and caregivers • reduction of the burden on carers • tolerability and ease of use <p>For instance, the WHO notes that <i>“from a public health perspective, however, the level of innovativeness of a medicine is primarily defined by the benefits the medicine generates for patients. These benefits can be in the therapeutic or clinical domain, the quality of life domain, but also in the socio-economic domain. Examples of benefits in the socio-economic domain include a medicine that would prevent (expensive) hospital admissions or that would enable patients to work”</i>.¹⁸ The EXPH does not consider any of this significant literature.</p>
<p>Page 4 107-108ff</p>	<p><i>“Greater price and cost transparency, including the acknowledgement that high prices (high costs to payers) may or may not have underlying high costs of R&D”.</i></p> <p>In the draft opinion, the EXPH rejects cost plus pricing. EFPIA agrees that a “cost plus approach” is not an adequate payment model for pharmaceuticals. The ‘cost-plus’ method is inefficient since it inadequately rewards added therapeutic value and does not provide appropriate incentives. In addition, it is extremely difficult (or impossible) to disentangle costs of R&D from the price of a specific product. The cost-plus pricing method represents a “static” approach, which focuses mainly on budgetary constraints and ignores both short-term and long-term benefits of innovative treatments. So, it is unclear why they reflect on the relation between price and cost of R&D in the summary. Many economists have shown that price transparency in the case of pharmaceuticals can have detrimental effects on access. For example, Glynn (2015) concludes that in the case of the pharmaceutical market, transparency particularly external reference pricing can harm patients.¹⁹</p>

¹⁸ Henry, D. et al. (2004) Background Paper 8.3 Pricing and Reimbursement Policies: impacts on innovation. [Last Accessed 23 June 2017] : http://www.who.int/medicines/areas/priority_medicines/BP8_3_pricing.pdf

¹⁹ Glynn, D. (2015) The case for transparency in pricing. *Competition Law*

<p>Page 4 112-113ff</p>	<p>“The patent system is the current best option for decentralized innovation efforts when consumers are price sensitive, but not necessarily otherwise.”</p> <p>The benefits of Intellectual Property (IP) rights have not been discussed in any detail in this draft opinion. IP allows companies to have exclusive rights to the innovation for a period of time. While acknowledging the heavy and complex regulatory system in which the industry operates, the EXPH views IP from a purely financial perspective, as a mechanism to maintain price above competitive equilibrium. They fail to sufficiently highlight 1) that IP is not pharma-specific, 2) the incentivizing role of IP which is particularly necessary to attract investment in this heavily regulated market, 3) the highly regulated nature of pharmaceutical development in fact decreases the duration of exclusivity as years of IP life are consumed long before first commercialization.</p> <p>The patent system has a proven history in developing lifesaving innovations. Other options are entirely hypothetical. The EXPH has developed a theory that that health insurance is the problem. Without health insurance, price sensitivity would be higher and this would constrain pharmaceutical prices. This theory is unsupported, indeed:</p> <ul style="list-style-type: none"> • National Health insurance results in a single purchaser, who negotiate price on behalf of consumers. Most analysis suggests this increases bargaining power (even resulting in a monopsonist purchaser).^{20,21} • There are many pricing and reimbursement rules that regulate the way prices are determined. Prices are not set by manufacturers.
<p>Page 4 119-120ff</p>	<p>“Have an assessment of exercise of market power in each price negotiation, as a result of insurance protection set by health systems, reducing the role of consumer’s price sensitivity in limiting price increases of new products under patent protection.”</p> <p>The pharmaceutical industry is subject to competition rules. In cases where there are concerns, these can be investigated by the competition authorities. However, the EXPH ignores the role of competition in the on-patent pharmaceutical market.</p> <p>In reality, companies compete with one another and this results in lower prices to the payer. This is illustrated by the case of Hepatitis C. As new, competing treatments entered the market, net prices of Hepatitis C drugs decreased significantly in the Europe, and the widely discussed high prices of these treatments is estimated to be 15-20% lower in 2016 after negotiated rebates.²²</p> <p>Evidence has shown that that competition is increasing. Indeed, we can observe that, over time, competitive products come to the market more and more quickly after the first medicine has been launched. In the 1970s, the average time between the first and the second medicine in a therapeutic category was 10.2 years. Between 2005 and 2011, the time had declined to an average of 2.3 years.²³</p> <p>Companies also face competition at patent expiry, which results in reductions in expenditure. For example, in Germany, 12% of drug spending in 1995 went towards the</p>

²⁰ Roberts, E.T., Chernew, M.E. and McWilliams, J.M. (2017) Market Share Matters: Evidence of Insurer and Provider Bargaining Over Prices. *Health Affairs*. 36(1). Available from: <https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2016.0479>

²¹ Kirkwood, J.B. (2016) Buyer Power and Healthcare Prices. *Washington Law Review*. 253(286)

²² Quintiles IMS (2017) Medicines Use and spending in the US: a review of 2016 and outlook to 2021

²³ Tufts Center for the Study of Drug Development (CSDD) (2015) Personalized medicine gains traction but still faces multiple challenges. *Tufts CSDD Impact Report*

	costs of antihypertensive or cholesterol lowering agents, today it is 4% of drug spending. This is a dramatic change together with an equally dramatic therapeutic success in reducing mortality of heart disease. ²⁴ Thus, it is grossly misleading to focus the analysis narrowly on areas of current growth.
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²⁴ Quintiles IMS Institute (2017) Understanding the Dynamic Composition of Drug Expenditure: Shares, Levels, Composition and Drivers

Comments on Section 1: Background

Page	Comments
Page 6 202ff	<p>“The emergence of high-price innovative medicines, implying high costs for health care payers, ...”</p> <p>Costs for healthcare payers are a composite of price and volume; therefore, high prices alone do not necessarily mean high budgetary impact for the system, especially because spending in some areas can create savings in other parts of the system. In light of the recent cancer care expenditure, the statement should be differentiated. Cancer medicines expenditure has more than doubled over the past 20 years; however, cancer care expenditure, including cancer medicines, has remained stable at 6% over the past 20 years.²⁵. This means that the use of medicines has offset other costs in cancer care.</p>
Page 6 209ff/213ff	<p>“Recent years have seen a growing number of new medicines with price increases that led health authorities and health care payers to question the implications for the financial sustainability of health systems”</p> <p>“Howard et al. (2015) document price increases in the anticancer drug market of about 10% a year in the past 20 years, after controlling for increased benefits (survival)”</p> <p>Price increases for individual innovative medicines are usually not possible in Europe. The statement is probably reflecting the fact that the cost of therapy per outcome has increased over time in some areas. The statement should be phrased differently. In addition, Howard et al. are referring to US list prices which – as the Opinion of EXPH states at various occasions – do not reflect the actual price paid and are less relevant for the European market.</p> <p>The EXPH opinion does not put the value of these medicines into context. Its narrow focus on budget impact does not take into account the outcomes that have been achieved thanks to investing in medical innovation. As Jönsson et al. show, medicines cost have offset direct and indirect cost (-11%) over time, which contributed to the stable spending on cancer as a share of total healthcare expenditure.²⁶</p> <p>Moreover, while the list price of anticancer drugs launched appear to be growing, the real cost of new anticancer drugs is not systematically increasing over time. This is because prices depend on a number of factors including pre-existing treatment options within a therapeutic class.</p> <p>As stated by Barron & Wilsdon <i>“Looking at individual therapeutic class (e.g., breast cancer, colorectal cancer, etc.), we observe that the cost of new anticancer drugs is not necessarily increasing over time when taking into account the benefits of these products. Two studies by Whalen et al. estimate the incremental cost per month of</i></p>

²⁵ Jönsson B et al. (2016), Comparator Report on Patient Access to Cancer Medicines in Europe Revisited
²⁶ Jönsson, B., Horfmacher, T., Lindgren, P. and Wilking, P. (2016) The cost and burden of cancer in the European Union 1995–2014. *European Journal of Cancer*

	<p><i>median OS (overall survival: the length of time from either the date of diagnosis or the start of treatment for a disease that patients diagnosed with the disease are still alive)²⁷ (mOS) gained with the use of approved targeted therapies for colorectal cancer for first, second, and third-line treatment of mCRC in Spain and in France respectively, and shown that the incremental cost per mOS gained did not appear to increase with FDA approval date”.</i>²⁸</p> <p>This analysis does not take into the wider cost of cancer to the healthcare system and the cost of other forms of treatment. Evidence on cost per month of value gained should be examined, evidence for recent drugs indicate that some new oncology drugs are delivering additional value and at a lower cost compared to pre-existing products.</p>
<p>Page 6 211-212ff</p>	<p><i>“Detailed information on prices of new pharmaceuticals in different countries is often not available as they result from secret price negotiations”</i></p> <p>The negotiations are not secret. The financial terms are commercial confidential but the existence of agreements is commonly disclosed.</p>
<p>Page 6 215-219ff</p>	<p><i>“The main explanation offered by Howard et al. (2015) for the high prices is based on the roles of health insurance in making patients insensitive to drug prices (allowing companies to increase prices without losing demand) and of anchor effects of previous prices (by which a price increase over a previous high price is tacitly deemed as natural, even if the reference point comes from other, non-competing, pharmaceutical products).”</i></p> <p>The argument that price sensitivity is lower due to the existence of health insurance is unsubstantiated as demonstrated in our response to line 1659. In addition, the Howard et al. (2015) article analyses the US market, which has a considerably different structure from European markets. The sample for the analysis is the launch price of 58 anticancer drugs approved in the US between 1995 and 2013. This has several limitations. First, the time span is very broad, medicines and pricing mechanisms in 1995 are very different from those in 2017. Second, the sample is small and limited to one therapeutic area. Third, the focus is on US list prices: net prices are not considered, nor the role and the margins to distributors. Importantly, the same authors also note that “as pressure has mounted on governments to reign in health spending, European health systems have adopted a more aggressive bargaining stance, backed by a credible threat of non-coverage”.</p>

²⁷ National Cancer Institute (N.D) NCI Dictionary of Cancer Terms. Available from: <https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=655245>

²⁸ Barron, A. and Wilsdon, T. (2016) Challenging perceptions about oncology product pricing in breast and colorectal cancer. *Pharmaceutical Medicine*. 30(6): 321-326. Available at: <https://link.springer.com/article/10.1007/s40290-016-0167-1>

Comments on Section 3.1: The challenges to health systems

Page	Comments																																																																																								
Page 8, page 9 270ff	<p><i>“It is now well documented that expenditure with new molecules has outpaced the growth of GDP or the growth of other health care expenditures.” “Expenditure with new molecules has outpaced the growth of GDP or the growth of other healthcare expenditure”.</i></p> <p>The EXPH Opinion says that it is well documented that medicines have outpaced growth in GDP. However, they have not provided any evidence to support this assertion. As noted above, in response to lines 97-98, for most OECD countries, pharmaceutical spending is not rising more quickly than other areas of health spending.²⁹</p>																																																																																								
Page 8 278	<p>“The growth in new pharmaceuticals is a composite of growth in new molecules being available and the price increases compared to previous therapeutic alternatives”</p> <p>As noted above (lines 97-98) retail pharmaceutical expenditure has not increased in recent years. Moreover, pharmaceutical spending concerns both new medicines and generics once molecules lose market exclusivity. However, the EXPH Opinion does not include any consideration of the cost savings from generics and biosimilars.</p> <p>Overall, spending on pharmaceuticals has not increased unsustainably. Even if we look at areas like orphan medicines, the expected revenue growth is moderate. Over time with generics and biosimilars expected to enter the market, OMP spending is expected to plateau.</p> <p>OMP spending as a share of healthcare in Europe.³⁰</p> <p>Budget impact of orphan drugs as percentage of total pharmaceutical spend (2002 – 2020)</p> <p>Payer expectations of orphan drug expenditure are higher than predicted levels of total pharmaceutical spend</p> <table border="1"> <caption>Estimated data from the graph: Orphan drug expenditure as % of total drug spend</caption> <thead> <tr> <th>Year</th> <th>Estimate from current study (%)</th> <th>Retrospective estimates (%)</th> <th>Predictive estimates (%)</th> </tr> </thead> <tbody> <tr><td>2000</td><td>0.0</td><td></td><td></td></tr> <tr><td>2001</td><td>0.0</td><td></td><td></td></tr> <tr><td>2002</td><td>0.0</td><td></td><td></td></tr> <tr><td>2003</td><td>0.0</td><td></td><td></td></tr> <tr><td>2004</td><td>0.5</td><td>[9]</td><td></td></tr> <tr><td>2005</td><td>0.8</td><td></td><td></td></tr> <tr><td>2006</td><td>1.2</td><td>[10]</td><td></td></tr> <tr><td>2007</td><td>1.8</td><td>[11]</td><td></td></tr> <tr><td>2008</td><td>2.5</td><td>[12]</td><td></td></tr> <tr><td>2009</td><td>3.2</td><td>[13]</td><td></td></tr> <tr><td>2010</td><td>4.0</td><td></td><td></td></tr> <tr><td>2011</td><td>4.5</td><td></td><td></td></tr> <tr><td>2012</td><td>4.8</td><td></td><td></td></tr> <tr><td>2013</td><td>5.0</td><td></td><td>[12]</td></tr> <tr><td>2014</td><td>5.2</td><td></td><td></td></tr> <tr><td>2015</td><td>5.3</td><td></td><td></td></tr> <tr><td>2016</td><td>5.4</td><td></td><td></td></tr> <tr><td>2017</td><td>5.5</td><td></td><td></td></tr> <tr><td>2018</td><td>5.5</td><td></td><td></td></tr> <tr><td>2019</td><td>5.5</td><td></td><td></td></tr> <tr><td>2020</td><td>5.5</td><td></td><td></td></tr> </tbody> </table> <p>Legend: — Estimate from current study X Retrospective estimates from published studies [number denotes study reference] O Predictive estimates from published studies</p>	Year	Estimate from current study (%)	Retrospective estimates (%)	Predictive estimates (%)	2000	0.0			2001	0.0			2002	0.0			2003	0.0			2004	0.5	[9]		2005	0.8			2006	1.2	[10]		2007	1.8	[11]		2008	2.5	[12]		2009	3.2	[13]		2010	4.0			2011	4.5			2012	4.8			2013	5.0		[12]	2014	5.2			2015	5.3			2016	5.4			2017	5.5			2018	5.5			2019	5.5			2020	5.5		
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²⁹ OECD (2015) Pharmaceutical Spending. *Health at Glance 2015*

³⁰ Schey C. (2011) Estimating the budget impact of orphan medicines in Europe: 2010 - 2020. *Orphanet Journal of Rare Diseases*

Comments on Section 3.2: The challenges to innovative payment models

Page	Comments
Page 8 286ff	<p><i>“There is little systematic knowledge on pharmaceutical markets, optimal R&D levels and pricing and marketing strategies by companies”</i></p> <p>There is a vast literature on pharmaceutical markets. Many of these reports have been commissioned by the European Commission and the OECD.^{31,32} The EXPH should review this literature and take into account the analysis undertaken before coming to conclusions.</p>
Page 9 288ff	<p><i>Pharmaceutical companies have been found to be high performers for their investors.</i></p> <p>The profitability of the pharmaceutical industry should be compared with other research-intensive industries to make meaningful comparisons and this should take into account the performance of smaller companies (particularly given the importance the OECD places on them investing in earlier stages of development). For example, data illustrates that the Return On Equity (ROE) of the aerospace sector (a highly research intensive industry) is far greater than that of the pharmaceutical industry.³³</p> <p>Profits in the pharmaceutical industry reflect the level of risks and the complexity of the R&D process, which characterises this industry (it also takes approximately 15 years from R&D to market launch of one product), but also other factors such as the increasing pressure on pricing. Finally, contrary to many other products from other industries, the lifecycle for innovative pharmaceutical products is limited in time due to the fact that medicines go off- patent and then have to compete with generics, in effect providing a built-in cost reduction mechanism, in contrast to other parts of healthcare. The return on R&D has fallen during the last few years, from 10.1% in 2010 to 3.7% in 2016.³⁴ In their study, Deloitte et al also examine Bloomberg data to find that the average industry cost of capital stands at approximately 8.4% - almost 5 percentage points above the 2016 figure for the original cohort (of pharmaceutical companies that Deloitte have been tracking since 2010).</p>

³¹ European Commission (2016) Links between Pharmaceutical R&D Models and Access to Affordable Medicines. Directorate General for Internal Policies. Available from: [http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587321/IPOL_STU\(2016\)587321_EN.pdf](http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587321/IPOL_STU(2016)587321_EN.pdf)

³² OECD (2017) New Health Technologies. Available from: <http://www.oecd.org/publications/managing-new-technologies-in-health-care-9789264266438-en.htm>

³³ Damodaran, A. (2017) Return on Equity by U.S. Sector. [Data Last Accessed 21 July 2017]: http://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/roe.html

³⁴ Deloitte Center for Health Solution & Global data, Balancing the R&D equation, measuring the returns from pharmaceutical innovation (2016)

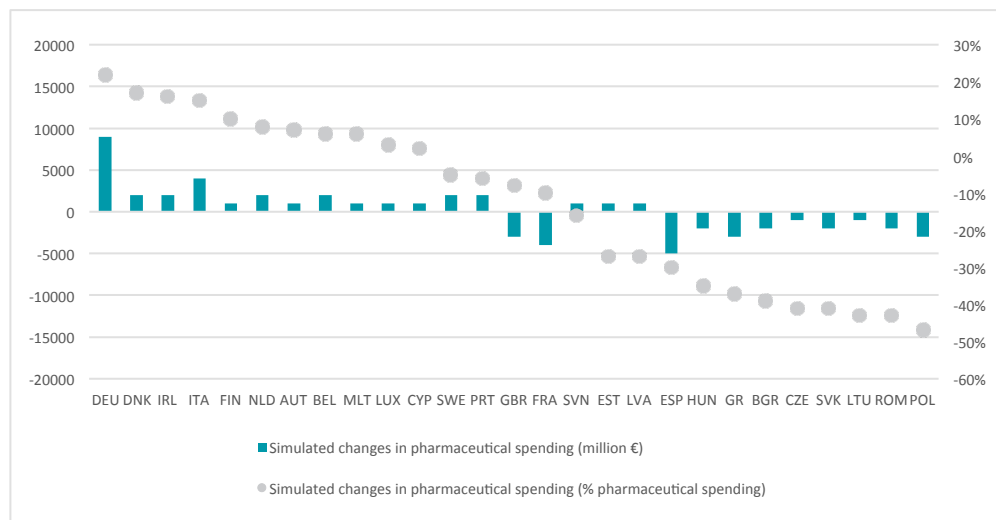
	<p style="text-align: center;">Return on late-stage portfolio, 2010-16 - original cohort examined</p> <table border="1"> <thead> <tr> <th>Year</th> <th>Absolute IRR (%)</th> <th>Number of assess in late-stage development</th> </tr> </thead> <tbody> <tr> <td>2010</td> <td>10.1</td> <td>206</td> </tr> <tr> <td>2011</td> <td>7.6</td> <td>184</td> </tr> <tr> <td>2012</td> <td>7.3</td> <td>195</td> </tr> <tr> <td>2013</td> <td>4.8</td> <td>194</td> </tr> <tr> <td>2014</td> <td>5.5</td> <td>181</td> </tr> <tr> <td>2015</td> <td>4.2</td> <td>189</td> </tr> <tr> <td>2016</td> <td>3.7</td> <td>189</td> </tr> </tbody> </table>	Year	Absolute IRR (%)	Number of assess in late-stage development	2010	10.1	206	2011	7.6	184	2012	7.3	195	2013	4.8	194	2014	5.5	181	2015	4.2	189	2016	3.7	189
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<p>Page 9 291ff</p>	<p><i>“Companies’ expenditure breakdown by category often reveals that R&D costs represent a smaller share than promotion and marketing costs (Mossialos, 2017)”</i></p> <p>The draft opinion fails to capture the benefits of marketing and the importance of providing comprehensive information on safety and efficacy to customers so they can be used in the right patients. As medicines become increasingly specialised and serve smaller populations, more targeted activities such as patient empowerment (awareness and knowledge) and adherence to therapy, are necessary to commercialise the medicine. In addition, there are a vast number of prescribers and other relevant health care professionals, which justifies the fact that medical representatives provide information to health care professionals. National legislation and or voluntary codes of conducts by industry strictly govern the interaction between industry and doctors.</p> <p>Moreover, the comparison between R&D and marketing expenditure is meaningless and outdated. The data related to marketing often refers to SG&A spends, which is found in the companies’ financial statements. These costs stand for Selling and General and Administrative Expenses that include regulatory and compliance costs. These are high for pharmaceutical companies, next to sales and marketing-related practices, as well as salaries and the overall cost to run a pharmaceutical company.</p> <p>Finally, it is important to highlight that the pharmaceutical and biotechnology sector is the highest research-intensive industry worldwide. According to the European Commission’s R&D Investment Scoreboard (2016),³⁵ pharmaceuticals and biotechnology rank highest in terms of R&D investment worldwide (Fig. 3.1, p. 55). The European Commission’s report also notes “the top 50 large companies listed by R&D intensity (R&D to sales ratio) are dominated by the high tech sectors of biotechnology & pharmaceuticals, software and technology hardware” (p. 8). R&D intensity for pharmaceuticals is 15% globally, followed by software and computer services (10.6%) and technology hardware & equipment (8.4%).</p>																								
<p>Page 9 295</p>	<p><i>“A common, general, denomination for these arrangements is outcomes-based managed entry agreements (also known as market entry agreements or market access agreements).”</i></p> <p>The EXPH draft opinion uses a range of different definitions for MEAs, sometimes referring to outcomes-based agreements and sometimes including financial agreements. This creates confusions throughout the draft opinion.</p>																								

³⁵ European Commission webpage [last access 27 November 2017]: <http://iri.jrc.ec.europa.eu/scoreboard16.html>

“The several forms and variants of these agreements deal with different aspects, such as hidden price discounts (of value to companies as such discounts bypass international referencing practices used in many health systems), /.../”

Confidential net prices can be also of value for the payers, for instance by allowing lower prices in lower-income markets. Increased transparency and disclosing of net prices would lead to lower access to medicines in countries that today get rebates due to their lower income levels/ability to pay. The negative impact of price convergence has been evidenced by a range of studies.³⁶ The intuition is straightforward, a system where countries reward innovation on the basis of their ability to pay allows lower income countries to afford innovative medicines. If high-income countries require the same price as low-income countries, low-income countries will pay the average price and this will make medicines less affordable.

Simulated savings vs. simulated cost in EU member countries due to a price convergence towards the EU average³⁷



“Unfortunately, neither the arrangements (price-based versus clinical outcome-based) nor the outcomes (improvement in certainties of clinical benefit, improvement in cost benefit ratio) in many of the new payment models being used are made public. This undermines the international price reference system in Europe, used by most countries in some form”

This paragraph illustrates one of the contradictions of this draft opinion. Indeed, this acknowledges that value-based pricing is a better payment model than cost-plus pricing in order to create incentives for the development of medicines in area of greater needs for patients. However, at the same time, it supports transparency and therefore the convergence of prices through International reference pricing. By doing so, it seems to ignore that international reference pricing and convergence of prices can be detrimental to patients’ access due to the fact that prices will not reflect the economic situation of every European countries notably those with a lower ability to pay. Therefore, it does not make sense to say that MEAs will undermine the international price reference, which is not an objective per se. The objective should not

³⁶ De Cock, J. (2013) Access to medicines: can differential pricing be an answer? *Presentation to the European Parliament*

³⁷ De Cock, J. (2013) Access to medicines: can differential pricing be an answer? *Presentation to the European Parliament*

	<p>be to ensure a better access to medicines for patients and international price reference in Europe should be revised to better fit that purpose.</p>
<p>Page 11 359-361ff</p>	<p><i>“The R&D cost of developing a new pharmaceutical product is independent of how many countries decide to use it and for how many indications the product is adopted”.</i></p> <p>Expanding a medicine to new indications requires additional clinical studies for these indications, meaning additional costs. Wide variations in the evidence supporting the approval of supplemental indications are documented. The importance of efficacy trials for new indications has been discussed in a recent report reviewing new FDA approvals.³⁸</p>
<p>Page 12 367ff</p>	<p><i>“Without some reference level for the average price across indications and/ or countries, allowing differential pricing does not have necessarily the same social welfare implications”.</i></p> <p>Here again the draft opinion advocates for the transparency of the average price across indications and / or countries. However, confidentiality of net prices is necessary to make the system of differential pricing work. Transparency of net prices would lead to a convergence of prices, which could be detrimental to innovation and hinder access to medicines in countries with lower ability to pay.</p>
<p>Page 12 378-379</p>	<p><i>“Only some countries will have the ability to manage these agreements, and oversee the results. Replication in every country will be challenging for small countries due to costs of setting and using monitoring mechanisms.”</i></p> <p>Many countries make use of MEAs. Indeed, the EXPH reports data from Eminent developed for the European Commission which shows that a wide range of countries use MEAs from Lithuania to Malta.³⁹ This would seem to contradict the EXPH conclusions.</p>
<p>Page 12 380</p>	<p><i>“There are clear economies of scale in the management of entry agreements for new pharmaceutical products”</i></p> <p>This is an unsubstantiated assertion. Many countries use MEAs. Indeed, in many countries these are agreed at the regional and even hospital level. MEAs are often tailored to the needs of individual countries. This means that the co-ordination cost of agreeing these MEAs across countries and regions is high. It is not at all clear that there are economies of scale in the management of MEAs.</p>
<p>Page 13 392-394</p>	<p><i>“Implicitly, the discussion takes as granted that health technology assessment together with a threshold approach for incremental cost-effectiveness ratio (or a variant of it) is the adequate institutional setting, allowing firms to set prices with considerable freedom as long as these prices allow the threshold to be met.”</i></p>

³⁸ Wang Bo, Kesselheim Aaron S. (2015) Characteristics of efficacy evidence supporting approval of supplemental indications for prescription drugs in United States, 2005-14

³⁹ The European experience”. EMINet Available at: http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/mea_report_en.pdf and Espin J et al (2011) “Experiences and Impact of European Risk-Sharing Schemes focusing on oncology medicines”. EMINet Available at: http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/risksharing_oncology_012011_en.pdf

The EXPH asserts that there is a consensus that thresholds based HTA systems are the “adequate institutional setting”. There is no such consensus. There are many studies showing that cost-effectiveness methods are not appropriate to appraise the value delivered by particular categories of medicines (e.g. orphan drugs^{40,41,42}). In addition, the use of ICER thresholds is also controversial. As noted in the same reference cited by the OECD, “setting thresholds too high or too low costs lives”.⁴³ The shortcomings of strict cost-effectiveness thresholds have even been recognised by NICE, who are taking part in a project, which aims to explore beyond the simplistic health-related quality of life measure. In addition, the project aims to examine metrics that capture the additional benefits of treatment that are excluded from the ICER-based approach, such as independence, social and emotional wellbeing.⁴⁴ Studies have also found that strict ICER thresholds are inflexible and do not account for innovation in technology, inflation, and increased costs of capital.⁴⁵ Many healthcare systems also use cost-effectiveness methods to appraise innovative medicines but do not have defined thresholds (e.g. France,⁴⁶ Sweden⁴⁷). However, there is no evidence showing that prices are not constrained in these systems.

A pure ICER-based approach is not applicable for orphan medicines. For orphan drug assessment, requirements for evidence quantity and quality must reflect challenges associated with rarity. The main challenge of rare diseases is the evidential uncertainty resulting from the limited information on the natural history of the disease and small patient numbers in clinical trials. In the absence of robust data, rare disease experts should inform value assessments, including healthcare professionals and patients.

Finally, the EXPH draft opinion claims that the current pricing approach results in value being captured by the innovative industry. This conflicts with available evidence. In breast cancer patients, specialty pharmaceuticals improve quality of life. In one study, estimates comparing the cost of cancer care and the social value of survival gains from that care suggest that from 1990-2000 there was a net social surplus of \$1.9 trillion in the U.S. alone.⁴⁸ For breast cancer specifically, 87 percent of those survival gains were due to advances in treatment. In separate study on the USA, Lichtenberg (2014) finds

⁴⁰ Orphan medicinal products. *European Commission website*. [Last Accessed 23 June]: https://ec.europa.eu/health/human-use/orphan-medicines_en

⁴¹ Orphan Drug Act- relevant excerpts (2013) *FDA website* [Last Accessed 23 June 2017]: <https://www.fda.gov/forindustry/developingproductsforrareconditions/howtoapplyfororphanproductdesignation/ucm364750.htm>

⁴² Goldberg, R. (2016) Not at any price: How ICER robs Myeloma patients of life and hope. *Center for Medicine in the Public Interest*

⁴³ Culyer, A.J. (2015) Cost-effectiveness thresholds in health care: a bookshelf guide to their meaning and use. *Centre for Health Economics*

⁴⁴ NICE (2017) NICE to work with partners on developing new ways to measure quality of life across health and social care. Press Release: 13 June 2017

⁴⁵ Khan, Z.M. (2015) Are current ICER thresholds outdated? Does MCDA offer a more holistic approach to assessing the value of innovative technologies? *Market Access Solutions LLC*

⁴⁶ Rochaix, L. (2015) Incorporating Cost-Effectiveness Analysis into Comparative-Effectiveness Research: *The French Experience*. *Health Affairs blog*. [Last Accessed 23 June 2017]: <http://healthaffairs.org/blog/2015/04/03/incorporating-cost-effectiveness-analysis-into-comparative-effectiveness-research-the-french-experience-2/>

⁴⁷ Bending, M.W. (2014) The application of the cost-effectiveness threshold in give countries. *Mapi*

⁴⁸ Lakdawalla, D.N., Sun, E.C, Jena, A.B., Reyes, C.M., Goldman, D.P., and Philipson, T.J. (2010) An economic evaluation of the war on cancer. *J Health Economics*

	<p>that pharmaceutical innovation can also bring savings and be cost effective: the value of reductions in work loss days and hospital admissions attributable to pharmaceutical innovation was estimated to be three times as large as the cost of new drugs consumed between 1997 -2010.⁴⁹</p> <p>Confidential discounts as a result of negotiations are common and significant.⁵⁰ Discounts can range up to 20% of list prices. Quintiles IMS data illustrates lower pharmaceutical spending growth, as measured by invoice prices which account for discounts and rebates.⁵¹ This evidence suggests that ICER thresholds do not determine the invoice price of treatments.</p>
<p>Page 13 401-402ff (and Page 38 1076ff)</p>	<p><i>“Patent protection implies that there are no close competing products”.</i></p> <p><i>“As we do not have a competitive market for new pharmaceuticals due to the existence of patents (...)”</i></p> <p>There is a perception that IP protection stifles competition, but this is not the case. IP protection creates the preconditions for competition. By filing for a patent, a patent holder actually makes publicly available their ‘state of the art’ which creates a spill-over learning effect that encourages other players to explore the science more fully. This enables further innovation, leading to more choice and more competition during the period where products have a degree of IP protection. Without the patent system, innovators would hide their innovation prior to launch. Thus, IP protection enables innovation beyond a specific company or product, allowing competitive conditions to drive prices across countries and therapy areas:</p> <ul style="list-style-type: none"> • In the treatment of Hepatitis C, since the launch of the transformative therapy Sovaldi in 2014, five other innovative products have been introduced.⁵² In France, although first to enter, Sovaldi now holds less than 24% market share, and average list prices have declined by 30%.⁵³ • For novel oral anticoagulants in cardiovascular disease, three new medicines followed the launch of dabigatran in 2008, leading to a price decrease of almost 60% in Spain.⁵⁴ • Even with rare diseases, more choices have followed from IP incentives: in conditions like cystic fibrosis, chronic lymphocytic leukemia and pulmonary arterial hypertension, the orphan drug provisions have ensured that there are at least three alternative therapies available where none previously existed.⁵⁵ <p>Today’s innovative medicines are tomorrow’s generics and biosimilars, already resulting in lower cost options for treating conditions like heart disease and depression today. This will extend to conditions like cancer, rheumatoid arthritis and other diseases in the near future.</p>

⁴⁹ Lichtenberg F.R. (2014) The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010. *J Human Capital*
Morgan, S.G., Vogler, S. and Wagner, A.K. Payers’ experiences with confidential pharmaceutical price discounts: A survey of public and statutory health systems in North America, Europe, and Australasia. *Health Policy*

⁵¹ Quintiles IMS (2016) Outlook for Global Medicines through 2021

⁵² Maas, Hepatitis C Drug Competition Results in Cost Discounts, Broader Member Access, Health Business Daily (2015)

⁵³ Data from QuintilesIMS MIDAS, analysis by EFPIA (2017)

⁵⁴ Data from QuintilesIMS MIDAS, analysis by EFPIA (2017)

⁵⁵ EMA, European public assessment reports.

<p>Page 17 509ff</p>	<p><i>“The pharmaceutical Benefits Board is the entity in charge”</i></p> <p>The draft opinion needs to be up-to-date. The Swedish authority is now called TLV (Pharmaceutical and Dental Benefits Agency) and has the website www.tlv.se. The description in Box 2 also seems to be somewhat out-dated, and disregards the difference between retail pharmaceuticals and pharmaceuticals for hospital use. Negotiation is a key element of the introduction of innovative medicines for hospital use today (indeed, there are three party negotiations between TLV, the company and the county council).</p>
<p>Page 19 559ff</p>	<p><i>“The confidentiality of prices bring countries to a situation that is usually termed prisoners’ dilemma. Individually it is optimal to sign agreements of prices that are confidential while globally countries could be better off by keeping a coordinated action on price determination for pharmaceuticals”</i></p> <p>Contrary to what is stated in the paragraph above, many economists have shown that the system of differential pricing is the best fitted for the pharmaceutical sector given the high costs and risks associated with R&D. Indeed, it would not be efficient in the long run to charge price at marginal cost as this would deter innovation. Given these circumstances, it is preferable to have a system where companies are able to fix prices above marginal costs (this is allowed by the patents) and according to the ability of countries’ to pay for the products (differential pricing). This system of differential pricing allows countries with lower ability to pay to buy products at lower costs compared to a system of unified pricing. One of the conditions to make the system of differential pricing work is the confidentiality of net prices. Transparency of net prices would lead to the convergence of prices, which would deter access to innovation for the poorest countries. Therefore, while confidentiality of net prices may not always be optimal for all individual countries (as some countries with higher ability to pay may buy medicines at a higher price), it is optimal on a global level as it creates incentives for innovation while facilitating access to medicines for countries with lower ability to pay. For instance, Dumoulin (2001)⁵⁶ shows that price discrimination increases access by a factor of approximately 4– 7 times (cited by Danzon & Towse, 2003).</p> <p>The sentence “globally countries could be better off by keeping a coordinated action on price determination for pharmaceuticals” is not backed by any evidence. On the contrary, economic theory shows that differential pricing is a more efficient system and has higher welfare effects globally because it enables both static and dynamic efficiencies. Static efficiency looks at the most efficient outcome from current medicines on the market while dynamic efficiency also considers the impact of policies on long-term investment in R&D and innovation. Differential pricing requires several conditions to work: confidentiality of net prices, a revision of external reference pricing and the regulation of parallel trade.</p> <p>Transparency of net prices will lead to a situation of free riding on behalf of countries with a higher ability to pay and a lower elasticity of demand. However, this would be detrimental to the countries with a lower ability to pay. The following paragraph explains this in details:</p> <p><i>“If price differences are unsustainable, due to parallel trade and external referencing, then manufacturers will tend to charge a single price that is between the differentiated</i></p>

⁵⁶ Dumoulin, J. (2001). “Global Pricing Strategies for Innovative Essential Drugs.” Int J Biotechnology 3(3/4), 338–349.

	<p>prices that would have been offered. Under such uniform pricing, consumers with relatively inelastic demand may have somewhat lower prices due to associating with consumers with elastic demand. Although the high income, inelastic users may try to justify this “as eliminating cost-shifting” it could more appropriately be called free riding by the high-income, price inelastic consumers, on the low-income, price elastic consumers” (Danzon & Towse, p. 190).⁵⁷</p>
Page 19 565-567ff	<p>“(…) prevent the complete exclusion from the reimbursement of expensive medicines with (still) uncertain clinical benefit and thus grant access to medicines, so that the patient's hopes do not have to be disappointed “</p> <p>Granting fast access to new medicines is not just about not disappointing patients – there are often good, clinical reasons to introduce medicines based on preliminary data even though there may not be evidence on long-term benefits yet.</p>
Page 19 570-572ff	<p>“MEAs (a) provide access to medicines with uncertain clinical benefit and - at a later stage - it is difficult to argue against patients why they are not reimbursed anymore (dynamic consistency problem)”</p> <p>This is a more general issue than just relating to MEAs – healthcare systems should as a matter of good practice monitor the effect of different therapies on patients and reassess in situations when the patient is not responding to treatment. So, this argument cannot be hold against MEAs in general.</p>
Page 20 569ff	<p>“These agreements may also bring disadvantages, with the following ones being listed in the existing literature: MEAs (a) provide access to medicines with uncertain clinical benefits (…)”</p> <p>The draft opinion cites different drawbacks for MEAs. However, in this list, some affirmations do not correspond to drawbacks but rather to conditions for a successful implementation of outcomes-based MEAs. For instance, the draft opinion says that MEAs are associated with additional costs for implementation, especially when they are based on the clinical outcomes data, and that this requires a well-functioning IT support.</p> <p>The draft opinion uses the term MEAs as a generic term to describe all MEAs and also as a term to refer to “outcomes-based MEAs”. Moreover, the topic related to the IT infrastructure needed to support outcomes-based MEAs could have been further developed in the draft opinion.</p>
Page 20 574ff	<p>“MEAs undermine the current system of international price comparison (External Price Referencing EPR) since MEAs usually contain confidential information on discounts, while EPR is only referenced to list prices since the discounted confidential prices are not known”.</p> <p>The real problem is that external price referencing prevents differential pricing, that is to say the possibility for prices to be set according to the characteristics and the ability to pay of a country. External reference pricing and transparency of net prices push for a convergence of prices, which can deter access to medicines in some countries, especially those with a lower ability to pay. Confidentiality of net prices is important to</p>

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Patricia M. Danzon & Adrian Towse. Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents. In International Journal of Healthcare Finance and Economics, 3, 183-205, 2003.

	<p>enable differential pricing.</p> <p>One area of concern in external reference pricing discussions is the failure to compare “like with like”. The current external reference system is flawed in a world of drugs with multiple indications. It is not good practice to expect the price of a vial in country A, where many indications are approved, to be comparable to the prices in country B, where only 1 indication may be approved. Confidential MEAs help to normalize the issues of comparability of conditions between two countries where the breadth of indications and / or patients may not be equivalent.</p>
<p>Page 20ff (Areas of innovation) 588-623ff</p>	<p><i>“Another one is that current incentives reward companies to develop mainly medicines of little advantage rather than developing superior medicines as long as having a new product brings with it the implicit promise of high price. Only 1 in 10 drugs brought to the market is considered a true innovation and important therapeutic gain defined by clinical advantages for patients. Vice versa 9 in 10 drugs have no or only marginal clinical advantages for patients [...]”.</i></p> <p>It is not clear why these paragraphs are here. The various claims about the lack of real innovation have nothing to do with innovative payment models (or at least the draft opinion does not make such a link). Moreover, there are many categorisations of whether products are innovative. There is much wider literature that the draft opinion could draw upon. Roughly four out of every five new cancer medicines licensed in the US and EU between 2003-2013, and evaluated by English, French and Australian HTA agencies, demonstrated some evidence of an overall survival, quality of life, or safety benefit over alternative treatments.⁵⁸ Therefore, for the most part, innovation in the oncology drug market appears to be bringing real value to patients and society.</p> <p>By May 2017, the European Commission had granted 1,868 orphan designations, and 133 Orphan Medicinal Products (OMPs) had obtained marketing authorisation across the EU since the implementation of the EU Regulation on Orphan Medicinal Products (OMP).⁵⁹ In addition, long-lasting transformative effects of treatments such as cell and gene therapies are likely to provide hope to patients who have no treatment today and to reduce ongoing costs of patient support and management of chronic comorbidities, thereby offsetting higher lifetime costs.</p>
<p>Page 20 589ff</p>	<p><i>“Additional to the higher growth of medicines expenditure relative to income growth and overall health expenditure growth, other concerns are present”</i></p> <p>As noted above, lines 97-98, recent data from the OECD shows that retail pharmaceutical spending per capita is more contained than growth in other parts of the health care system (2009-2015).⁶⁰ The share of total health expenditure attributed to medicines has remained broadly consistent over the last fifteen years, though with year-to-year variability in some countries.</p>
<p>Page 20 585ff</p>	<p><i>“However, they (MEAs) are administratively complex and may be difficult to negotiate and their effectiveness has yet to be evaluated. Moreover, they are designed to address the issue of uncertainty about the value of the effectiveness of the drug and not the (high) price tag or the rising pharmaceutical expenditure”.</i></p>

⁵⁸ Salas-Vega S., Iliopoulos, O. and Mossialos, E. (2016) Assessment of Overall Survival, Quality of Life, and Safety Benefits Associated with New Cancer Medicines. *JAMA Oncology*

⁵⁹ Analysis of data from the EMA website

⁶⁰ OECD, *Health at Glance*, 2017.

	<p>MEAs can also be used by governments and payers to address budget uncertainty through financial agreements (e.g. price-volume) or outcomes-based agreements (e.g. payment per results). Therefore, MEAs can be an appropriate tool to manage pharmaceutical expenditure.</p>
Page 20 590-591	<p><i>“The (lack of) development of medicines for small groups, which may raise fairness issues, is one concern”.</i></p> <p>The draft opinion here seems to suggest that there is a lack of R&D on orphan medicines. However, elsewhere in the draft opinion, the current patent and market exclusivity rules are regarded as a problem as it encourage “orphanisation”.</p>
Page 21 608-610	<p><i>“New payment models that reward any new drug irrespective of the therapeutic value they bring can, in fact, be detrimental to the social value of R&D efforts compared with alternative discoveries”.</i></p> <p>It is unclear which new payments models are referred to here. It would have been beneficial if the draft opinion elaborated more on which innovative payment models are best at optimizing these objectives, rather than making general statements.</p>
Page 23 671-674ff	<p><i>“As elements such efficacy and safety are measured along the way, a different problem emerges – the use of products that have an efficacy level that under normal conditions would not lead them to be approved”.</i></p> <p>It is unclear if the term “approved” here refers to Marketing Authorisation (by the EMA/Commission) or reimbursement (by a national authority). Efficacy is normally assessed by the EMA, either fully at the time of Marketing Authorisation or through Post-authorisation efficacy studies.</p>
Page 24 685ff	<p><i>“There is an element of exercise of market power present in the high prices asked that is not addressed by MEAs by design”</i></p> <p>This sentence is unclear. The draft opinion does not indicate which prices and kinds of MEAs it is referring to. MEAs are concluded by the manufacturer and the payer who also benefit from some market power due to the fact that they represent all the patients from their countries. The reference to high prices is not backed up by any evidence.</p>
Page 24 680- 684ff	<p><i>“From a literature perspective there seems to be a general agreement that MEAs can, under certain conditions, help to address post-licencing uncertainty and enable patient early access to innovative treatments. In general, MEAs offer flexibility in dealing with new and often expensive technologies, which are characterised by significant levels of uncertainty about their effects”.</i></p> <p>MEAs contain a range of tools, which offer flexibility for payers and companies to solve certain issues regarding the uncertainty of clinical outcomes, and the budget impact related to the introduction of new innovations. Different types of MEAs can be best suitable for different situations (e.g. depending on product type, disease area and patient population), and there is therefore no “one size fits all”. Furthermore MEAs should not be considered the general rule for access, but an option when certain issues cannot be resolved through the normal P&R process.</p>
Page 25	<p><i>“Opportunities identified range from use of additional information on real-use</i></p>

708- 713ff	<p><i>characteristics of new products (ranking high in health care payer perspective) to faster access (ranking high in patients’ perspective) and to public image benefits (ranking high in companies’ perspective). From these, it has become clear over time that information obtained is smaller than expected, and opportunities related to it were hard to materialize”.</i></p> <p>Many of the opportunities offered by MEAs, especially concerning the collection of information on the real world performance of medicines, could be further developed to the benefit of many stakeholders, including for the purposes of R&D and the improvement of healthcare quality and efficiency. This does not mean that MEAs have failed to deliver up to this point, but that all stakeholders are still learning how to best set up these systems.</p>
Page 25 728 – 764ff	<p><i>On Health System Performance (section 3.2.2)</i></p> <p>Health system performance should not only be assessed from the perspective of use of pharmaceuticals, but in a holistic perspective taking into account all products and services and organizational aspects of the healthcare system. Medicines constitute an element of a care pathway in combination with other products and services (including diagnostics), and where the delivery of care, the role of healthcare professionals and factors such as follow-up services and patient adherence are important for the final outcome of the treatment. It is important that all elements of a health system are assessed and improved in order to cut waste and inefficiencies, and improve outcomes.</p>
Page 26 738ff	<p><i>“The accepted association between value and prices has led to a practice of indication-slicing to secure higher prices, as once a price set for an indication, typically the more cost-effective to command a larger price, an umbrella extension of prices is beneficial to manufacturers and non (...)”</i></p> <p>Contrary to what is argued in the statement above, the purpose of indication-based pricing is to reflect better the clinical value provided by a medicine across indications. Indications-based pricing seems more adequate than a single price for a medicine for all indications to address the access challenges caused by the increased use of medicines in multiple indications and in combinations. Indeed, today the price of combining molecules for a given patient is usually set at the level of the sum of the prices of the respective monotherapies, irrespective of the added clinical benefit provided by the specific combination. When both medicines in the combination come from the same manufacturer, current tools such as MEAs may allow for tailored pricing approaches. When products from multiple manufacturers are combined however, anti-trust laws and current pricing and reimbursement systems hamper the ability to negotiate on the basis of the clinical profile of the combination. As a consequence, patient access to these innovative combination therapies may be delayed or not granted at all.</p>
Page 26 758ff	<p><i>“The impact of medicines on health care costs occurs through three main channels: prices, quantities (consumption level) and cost off-set (when spending more in pharmaceutical products implies spending less in other types of care. The difficulties of the current payment models to health systems performance became apparent with the first case of a high volume – high price drug (sovaldi) which was a pre-announcement of forthcoming drugs asking for a very high price and not restricted to a small number of patients.”</i></p> <p>It is unclear what is meant by Sovaldi being a pre-announcement of forthcoming drugs. This assertion is not supported by any evidence in the draft opinion.</p>

Comments on Section 3.3: Properties for payment models of innovative medicines

Page	Comments
Page 27 776 – 789ff	<p><i>“A first consideration is that new payment models should implicitly direct R&D efforts to development of breakthrough products that can be considered disruptive innovation, and not just incremental innovation”.</i></p> <p>One type of disruptive innovation which is not discussed very much in the draft opinion is the shift from treatments to cures or near-cures that e.g. can be seen in new cell- and gene therapies for a range of diseases and conditions (e.g. hemophilia and leukemia). Moving from a pattern of regular treatments dispersed over a long time (maybe the entire lifetime of a patient) to a singular, high-cost intervention requires new ways to pay for healthcare products and services. This should have been discussed more in the draft opinion, and examples given of good practices and innovative models which can support the introduction of these types of innovations.</p> <p>The EXPH concludes “in sum, new payment models need to reward more innovative and disruptive products than incremental ones”. This suggests that incremental innovation is not valuable. In reality, incremental innovation is highly valuable in terms of improving efficacy of products, improving administration that improves adherence, providing competition in the market and creating the foundation for the next breakthrough innovation.</p> <p>Not all innovation can be disruptive, and it would be a mistake to neglect the so-called “incremental innovation” as this is how most healthcare products and services normally evolve and the incentives for innovation must reward also these types of innovation.</p>
Page 28 798 - 802	<p><i>“Payment should be made for products that are worthwhile. In this assessment, the value-based health care approach provides a methodology to measurement of results that matter to patients that should be pursued. Note that identification of relevant dimensions of benefits and the definition of measurement approaches do not force a particular mechanism for price determination to be adopted”.</i></p> <p>EFPIA supports the concept of value-based healthcare models as the most appropriate way to design healthcare delivery and reward innovation with the focus on delivering the best possible health outcomes for patients. However, it is important to adopt a value-based approach on the healthcare system as a whole, not just for medicines, as all parts and elements of the system must function in coordination in order to deliver these results.</p> <p>This has also been supported by many academics and policymakers alike.⁶¹</p>
Page 28 809 –	<p><i>“Taking the principle that payment models need to be related to “outcomes that matter” for patients, it follows that no general pricing rule can be set ex-ante. The</i></p>

⁶¹ Office of Fair Trading. The Pharmaceutical Price Regulation Scheme. An OFT Market Study. London: OFT, 2007. Available at http://www.offt.gov.uk/shared_offt/reports/comp_policy/oft885.pdf (accessed 27/03/2007)

815ff	<p>payment model must then establish a procedure that will lead to a price. Such procedure may involve sophisticated methods to define “what matters” for patients and which payers are willing to pay for, and may involve price adjustments over time, as information about the true value of the product is revealed”.</p> <p>Making these models work at scale requires more alignment upfront on which outcomes that should be measured across the healthcare systems for different diseases and conditions, as these metrics would not only be important for payment models but also for outcomes research, identification of best practice and optimization of patient pathways. The implementation of standards for outcomes measurement, such as the International Consortium For Health Outcomes Measurement (ICHOM) standard sets, should therefore be encouraged.</p>
Page 28 803ff	<p>“Another principle to consider is that new payment models should not be based on paying for R&D incurred. Payment models that are solely based on costs incurred provide an incentive to companies to inflate costs as a way to secure higher payments. A “cost plus” approach to pricing would not respect the principle above of providing incentives for new products with high benefits to patients. As it will be argued below, cost transparency is important though not as a way to build the price that rewards innovation”.</p> <p>We agree with the draft opinion that the “cost plus” approach will not create incentives for new innovations and will be inefficient.</p>
Page 28 809-815ff	<p>“Taking the principle that payment models need to be related to “outcomes that matter” for patients, it follows that no general pricing rule can be set ex-ante. The payment model must then establish a procedure that will lead to a price. Such procedure may involve sophisticated methods to define “what matters” for patients and which payers are willing to pay for, and may involve price adjustments over time, as information about the true value of the product is revealed. The use of contracts for payment may replace a simple price announcement.”</p> <p>The industry would agree with this conclusion and that if products are able to show greater value to patients and society, then the price paid should be adjusted to reflect this value. However, in European markets prices often are adjusted downwards and rarely is it possible to put prices up. For example, mandatory price decreases are common. This is well illustrated by a survey conducted by OBIG (Austrian Ministry of Health) and the WHO European Regional Office, which documented all of the policy interventions related to medicines made by the health authorities over the period 2010-15 in 32 European countries.⁶² Of the 557 measures reported the vast majority consisted of austerity interventions to cut prices of medicines, to limit levels of reimbursement, increase levels of patient co-pays, or introduce new forms of external reference pricing with other EU countries that may be used to enforce further price reductions in the future. Indeed, it can be argued that the number of ad hoc price reductions in some markets increases the pressure on prices when a product first enters the market.</p>
Page 29 843-857	<p>“One popular theme in the discussion on access to new pharmaceutical products is the call to drop the “silo mentality”.”</p> <p>We support the EXPHs discussion on breaking down silos across elements of the health</p>

⁶² Vogler, S., Zimmermann, N. and de Joncheere, K. (2016) Policy interventions related to medicines: Survey of measures taken in European countries 2010-2015. *Health Policy*

	<p>care budget and their view that this would increase efficiency. Spending on prevention or medicines should not only be viewed as a cost but also as an opportunity to save money in other parts of the healthcare system. Current budgeting practices are often too short-term, not taking into account future benefits. This is a significant issue and one that the EXPH has not given enough consideration too. This could lead to different payment mechanisms that allow spending to reflect evidence that future costs are offset. However, the EXPH concludes: “these arguments, however, do not call for a particular system of price determination for new pharmaceutical products”. This appears to be a missed opportunity for a useful discussion on innovative payment models.</p>
<p>Page 30 862-870</p>	<p>“The use of generics and biosimilars is often regarded as a contributing element to lower the financial pressure on health care payers. In that line of argument, they open budget space to pay the new innovative products. All these areas for public policy interventions have merit though they arguably do not address the fundamental tension on the pricing of new pharmaceutical products between access and innovation incentives”</p> <p>The EXPH draft opinion has asserted that there is a tension in the current pricing models because the system is unsustainable. This does not appear consistent with the evidence. However, they then argue that policies that can improve sustainability (generics and biosimilars) do not address the fundamental tension. It would appear that different authors of the EXPH draft opinion have very different understandings of the problem they are trying to solve. These contradictions mean that the policy recommendations are often inconsistent and illogical.</p>
<p>Page 31 875-876</p>	<p>“This brings competition to the market, and lowers the price of drugs”.</p> <p>The authors assert that competition only applies after patent expiry. However there is competition also in the on-patent segment. For instance, in the Hepatitis C market, competitors to the first-on-market drug (Sovaldi) have significantly driven down prices. As new, competing treatments entered the market, net prices of Hepatitis C drugs decreased significantly in the US and in Europe, and the widely discussed high prices of these treatments is estimated to be 50% lower in 2016 after negotiated rebates.⁶³ For instance, in France the price of Sovaldi dropped from €41,000 euros to less than €28,700 euros in April 2017.⁶⁴</p>

⁶³ QuintilesIMS (2017) Medicines Use and Spending in the U.S.: a Review of 2016 and Outlook to 2021

⁶⁴ IP Watch website [last access 27 November 2017]: <https://www.ip-watch.org/2017/03/31/france-reaches-agreement-gilead-drop-prices-hepatitis-c-treatment/>

Direct-acting Antiviral Drugs for HCV in the US⁶⁵

Drug	FDA- Approved Indication
Daklinza- daclatasvir	Genotypes 1 - 6
Epclusa - sofosbuvir/velpatasvir (Gilead)	Genotypes 1, 4
Harvoni - sofosbuvir/ ledipasvir (Gilead)	Genotypes 1, 4, 5, 6
Olysio - simeprevir (Janssen)	Genotypes 1, 4
Sovaldi - sofosbuvir (Gilead)	Genotypes 1, 4
Technivie - ombitasvir/ paritaprevir/ ritonavir (Abbvie)	Genotypes 4
Viekira Pak, Viekira XR - dasabuvir/ ombitasvir/ paritaprevir/ ritonavir (Abbvie)	Genotypes 1
Szepatier - elbasvir/ grazoprevir (Merck)	Genotypes 1, 4

Page 31
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Another intertemporal effect is associated with too much current use of products leading to antimicrobial resistance, resulting in higher treatments costs for future generations.

The authors suggest that two types of intertemporal effects are important. The first one is that today's patients pay for innovation that future patients also receive. This is true but given on-going innovation in the pharmaceutical industry, this should not be seen as a problem but rather as a gain for society. They also highlight anti-microbial resistance (AMR) and over use. This is also true but is a very specific problem, and hardly relevant for other classes of pharmaceuticals. There is a considerable amount of work being undertaken on AMR and this should be perhaps left to other experts.

The paper does not acknowledge the tremendous scientific⁶⁶ and regulatory⁶⁷ challenges facing antibiotic developers, nor industry's partnerships⁶⁸ and ongoing work to both call attention to AMR and develop new medicines to combat it.⁶⁹ Industry appreciates the urgent need for a sustainable business model for these critical medicines, without which any interventions to develop new medicines will be limited.^{70 71 72}

⁶⁵ The Medical Letter (2016) In Brief: Hepatitis B Reactivation with Direct-Acting Antiviral Drugs for Hepatitis C. (24 October 2016) [Last Accessed 15 June 2017]: <https://secure.medicalletter.org/w1506b>

⁶⁶ Silver, L. (2011) Challenges of antibacterial discovery. *Clinical Microbiology Reviews*

⁶⁷ Gupta, S. and Nayak, R. (2014) Dry Antibiotic pipeline: Regulatory bottlenecks and regulatory reform. *Journal of Pharmacology and Pharmacotherapeutics*

⁶⁸ IFPMA (2017) New Alliance to Drive and measure industry progress to curb antimicrobial resistance
⁶⁹ Review on Antimicrobial Resistance website. Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. [Last Accessed 28 July 2017] <https://amr-review.org/industry-declaration.html>

⁷⁰ O'Neill, J. (2015) Securing New Drugs for Future Generations: The Pipeline of Antibiotics. *Wellcome*

Trust

⁷¹ OECD, WHO, FAO, and OIE (2017). Tackling antimicrobial resistance: Ensuring sustainable R&D. Note prepared for the 2017 G20

⁷² EU One Health Action Plan against AMR (2017)

	<p>Despite the enormous technical challenges and “no incentives for private capital,” there were 34 antibiotics and infection preventing vaccines in our global pipeline last year, with industry spending around \$6 billion on R&D on anti-infective treatment alone.⁷³ Moreover, industry contributes as part of local, regional, and global partnerships to combat AMR, including through the Innovative Medicines Initiative and as emphasised by the most recent G20 Leaders’ Declaration in Germany.⁷⁴</p>
<p>Page 31 895-896</p>	<p><i>“The traditional payment model based on defining a single price per unit of drug, linear price model, has only one instrument to achieve the several objectives”</i></p> <p>The EXPH draft opinion in this section appears to argue that medicines have a single linear price. In reality, MEA commonly mean that the price of a product differs if the volume changes, or varies by indication or patient population or based on new evidence and information about the product. It is not a linear system today. Other sections of the draft opinion, perhaps written by other authors recognised this.</p>
<p>Page 32 902ff</p>	<p><i>“Although intellectual property protection has been the cornerstone to foster innovation by private companies, in medicines as well as across the economy it can be questioned whether it can or should be replaced or complemented by other ways to reward innovation in the health care field (say, prizes for discoveries, followed by a immediate generics strategy)</i></p> <p>The “international prize initiative (for discovery)” is an idea to be considered, in particular in the area of treatments where there are no incentives to R&D, e.g. Antimicrobial resistance.</p> <p>However, intellectual property and market incentives remain as important as ever. IP provisions have created the preconditions for a sustained commitment to innovation over the last two decades. With over 7,000 products currently under development, we are seeing the fruits of that effort and of a stable incentives framework⁷⁵. Far from diminishing, the role of IP and market incentives therefore remains as important as ever to foster innovation including in unmet medical needs. The competition for R&D infrastructure and skills is increasingly global, requiring countries to adjust to remain attractive for investment. China and several other emerging markets are deliberately investing to create the right incentives to attract global R&D funding and to create competitive, world-class innovation leaders. In 2005, investigators sites involved in pivotal trials outside of the US and Europe accounted for less than 10% of all sites; the share has now grown to 28% by 2011, testament to quality of clinical research and testing now being conducted in emerging markets and the increasing importance of these markets in investment decisions⁷⁶. While Europe has many strengths, in encouraging biotech investment and the formation of Small and Medium sized Enterprises, the reality is that the gap with other markets is narrowing, with centres like Singapore and Shanghai increasingly seen as more attractive than Europe for investment. In that context, it is important that Europe remains at the forefront of global standards for the use of incentives to drive socially productive innovation.</p>

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Pisani, E. (2016) Stepping up to the plate on antimicrobial resistance. *OECD Insights*

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Berlin Declaration of the G20 Health Ministers. [Last Accessed 21 July 2017]: https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/G/G20-Gesundheitsministertreffen/G20_Health_Ministers_Declaration_engl.pdf

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Health Advances analysis; Adis R&D Insight Database.

⁷⁶

EMA. Clinical trials submitted in marketing-authorisation applications to EMA. Overview of patient recruitment and the geographical location of investigator sites (accessed 2017).

	<p>We agree with the EXPH that prices should not be the single way to reward innovation. However, this is unrelated to the need for a stable IP system that encourages innovators to invest in costly and risky investment programmes.</p>
<p>Page 32 915ff</p>	<p><i>“Pharmaceutical companies have proved to be quite adaptable to the economic environment they face. They have adjusted to the new incentives to develop orphan drugs. Some may argue they adjusted too much, as many drugs are now presented initially as indicated for a few number of patients in which they are highly effective (and thus command a high price), benefiting from orphan drugs’ special treatment. Later, expansion on indications to use of the product brings scale to activity”.</i></p> <p>Rare diseases are serious, often chronic and progressive diseases.⁷⁷ The orphan medicines designation has successfully encouraged investors to enable the development of essential therapies for patients in need. This success resides in the fact that the legislation has created an ecosystem, which includes designations, interactions with regulators, and some protection of revenue through market exclusivity rights regardless of the patent or new chemical entity status. Even so, the cost of orphan medicines accounts for a small share of the overall prescription medicine (in 2015, IMPs accounted for some 4% of total medicine cost across the EU5),⁷⁸ and is expected to remain sustainable.^{79,80}</p> <p>In terms of prices, evidence demonstrates that the median cost of more than 70 orphan drugs approved by the European Medicines Agency up to 2014, was GBP 30,000 per annum. The study shows that 24% of all orphan drugs considered had an annual cost less than GBP 10,000, while only 18% had an annual cost of more than GBP 100,000.⁸¹ Orphan drugs with more than one indication are not common.</p> <p>An analysis of the 93 orphan designated medicines with marketing authorisation as of September 2016, found that following initial marketing authorisation:⁸² Only 11% of orphan medicines expanded license to include a new indication (new disease), only 16% of orphan medicines expanded license within initial indication. Furthermore, the benefits of orphan designation do not apply to the non-orphan indication. If medicines with orphan and non-orphan indications wish to retain an OMP designation, they will be commercialised under different trade names and have separate marketing authorisation.</p> <p>Orphan drug regulation supports the development of medicines in areas of great unmet need. In the EU, the EMA Committee on Orphan Medicinal Products only approves orphan designation to medicines indicated for a rare and serious condition for which there are no existing treatment options, or where the product brings a significant benefit over existing options.⁸³</p>

⁷⁷ Orphanet website. [Last Accessed 12 July 2017]: http://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN

⁷⁸ IMS Institute Data September 2015

⁷⁹ Schey C. (2011) Estimating the budget impact of orphan medicines in Europe: 2010 - 2020. Orphanet Journal of Rare Diseases

⁸⁰ Hutchings, A., Schey, C., Dutton, R., Achana, F. and Antonov, K. (2014) Estimating the budget impact of orphan drugs in Sweden and France 2013–2020. *Orphanet Journal of Rare Diseases*

⁸¹ Onakpoya I.J., Spencer, E.A., Thompson, M.J. and Heneghan, C.J. (2015) Effectiveness, safety and costs of orphan drugs: an evidence based review. *BMJ Open*

⁸² Dolan analysis of EMA statistics

⁸³ Giannuzzi, V., Conte, R., Landi, A., Ottomano, S.A., Bonifazi, D., Baiardi, P., Bonifazi, F. and Ceci, A. (2017) Orphan medicinal products in Europe and United States to cover needs of patients with rare diseases: an increased common effort is to be foreseen. *Orphanet Journal of Rare Diseases*

<p>Page 32 922-928</p>	<p><i>“Companies are able to set attention of payers into the logic of paying ever more under the approach that any price that guarantees that cost-effectiveness is below a pre-defined threshold is fair”</i></p> <p>In this argument, the EXPH claims that by setting a threshold in the cost-effectiveness system, payers have been invited to pay higher prices. The industry does not support artificial rigid thresholds and has argued against them. Where countries use thresholds, the HTA process is an input into the price negotiation process, and therefore does not determine prices. Moreover, if we look at ICER for products that go through a system with a threshold you find a range of products above and below the threshold. The argument advanced by the EXPH does not make sense.</p>
<p>Page 33 929-933</p>	<p><i>“The focus on incentives to R&D investment (and thus higher prices for better, more valuable innovation) should not lead automatically to the highest price possible as chosen by companies. The approach of unchecked pricing behaviour for products under patent (meaning not being assessed as exercise of market power by competition authorities), common in most industries, breaks down here”</i></p> <p>Prices are not chosen by companies but based on a complex value assessment process and then a process of negotiation. This process involves competition between companies with competing products.</p>
<p>Page 33 933-938</p>	<p><i>“The limit on very high prices for innovative products in other industries results from sensitivity of consumers’ demand to price – at very high prices some, or many, consumers will stop using the service or consuming the product. In health care, the existence of health insurance protection (public or private) eliminates, or decreases considerably, the role of demand sensitivity to price (at the gain of the value of insurance protection).”</i></p> <p>The panel argues that because patients are covered by national health insurance schemes, and hence are not responsible for paying the price of the medicines, this reduces the price sensitivity of the market, contributing to higher prices. On the contrary: first, patients as consumers would be in a weak position to negotiate price in a context of a life-saving medicine (notwithstanding that this would be unethical). Second, delegating the negotiation to a payer de facto increases the negotiation power in two respects: a) monopolizing the negotiation power to a single agent representing multiple consumers, b) making the procurement more objective since the payer is not affected by the respective disease/ health situation and can make a neutral judgment about value. Third, payers have developed a sophisticated value assessment, which would not be possible for patients. In conclusion, patients may be less price-sensitive in terms of health resource use because of the insurance system; however, in today’s environment the price is determined by the payer who is much more powerful than the individual patient.</p>
<p>Page 33 946-948</p>	<p><i>“One example of the importance of adequately framing the price determination process is given by the rule that if a product meets a certain criterion (a certain threshold for incremental cost-effectiveness) then it must be approved for reimbursement”</i></p> <p>This repeats the argument set out in 922-928. In addition to the criticism we have set out, it is also not the case that products adjudged to be cost effective are automatically reimbursed. Sovaldi is a good example of that. Indeed, while the product was considered</p>

	to be cost effective, there were significant delays in the effective reimbursement.
Page 33 953-955	<p><i>“The direct implication is that defining payment models for high-cost innovative medicines is an issue of health system design, not an issue of finding a particular contract for prices of a particular drug”</i></p> <p>We agree that health system design is important and there needs to be a framework for contract that brings benefits to patients, the health care system and innovation. To a large degree this already exists in many markets. MEAs have been used extensively by a range of countries. Other countries are changing the regulatory rules to allow MEAs to be used in the future (their value was also recognised by the OECD).⁸⁴</p> <p>For example, in France, pharmaceutical pricing relies on an ex-ante evaluation of the medical value of drugs. Prices are negotiated on the basis of an industry-wide contract between drug manufacturers and the Health Products Pricing Committee (Comité Economique des Produits de Santé). Together the Committee and the drug companies sign a number of contractual agreements, which give the national health system a variety of flexible means to monitor prices and drug use, also ensuring that public resources are properly allocated.⁸⁵ Confidential clauses are essential for these to work effectively.</p>
Page 34 967-970	<p><i>“The “uncertainty motive” for using MEAs should, statistically lead to some products being delisted.”</i></p> <p>The definition of delisting used by the EXPH is unclear. The conditions required in MEAs varies from agreement to agreement. In some cases, this restricts the use to particular patient populations and in some cases affects the price of the medicines. It is unclear why delisting is as important as EXPH concludes it.</p>
Page 34 980-981	<p><i>“Some health systems, the ones not based on a single (or major) health care payer, face an additional issue of coordination across payers, which can eventually be accused of collusion if information about payment models and values is shared and alignment of models is coordinated.”</i></p> <p>This analysis is confusing. Where there are multiple payers they can conclude their own agreements. Indeed, this is exactly what we observe with sick funds in Germany or hospitals.</p> <p>Equally, payers often work together as in joint negotiation and in sharing information. The EXPH raises an important issue of potential collusion. This is not consistent with their recommendation on joint negotiation in other parts of the draft opinion.</p> <p>It is true that innovative payment mechanisms require important changes in the legal and institutional settings of health systems. However, this is a national competence and it is unclear why the EXPH is advising DG Santé on this issue.</p>

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OECD (2017) New Health Technologies: Managing Access, value and sustainability

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Carlson, J.J. Gries, K.S., Yeung, K., Sullivan, S.D., Garrison and L.P. (2014) Current Status and Trends in Performance-Based Risk-Sharing Arrangements between Healthcare Payers and Medical Product Manufacturers. *Applied Health Economics and Health Policy*

Comments on Section 3.4: The instruments

Page	Comments
Page 36 1019ff	<p><i>“The combination of existing products may have extra value to patients (from convenience or from an increase in treatment compliance, for example). Costs of production do not change considerably by setting a joint product and as individual products’ prices are already rewarding innovation, having a higher price for the bundle of products is a mere transfer of value to companies”</i></p> <p>Combination therapies are not the “sum of two or more innovative products”. Bringing a combination therapy to the market implies research costs to demonstrate their benefits and safety for patients. In general, EMA says that “sponsors must show data to support the pharmacological and medical rationale for the combination. To do so, sponsors must establish the evidence base for the contribution of all active substances included in the combination to the desired therapeutic effect and demonstrate a positive benefit-risk balance for the combination.”⁸⁶</p> <p>In addition, this statement assumes that the price of a medicine should somehow be linked to the cost and not to the value delivered. If combination products are to be developed, the price should reflect the value they deliver.</p>
Page 37 1062ff	<p><i>“Monopoly pricing has the same relative price structure as the one selected by a regulatory entity but goes for higher prices”</i></p> <p>The statement ignores that prices of pharmaceuticals are not the result of a monopolistic decision but the result of negotiations between the manufacturer and the monopsonist purchaser. This is only noted below in the draft opinion (1080-1081: “The automatic rule of the incremental cost-effectiveness ratio (ICER) where “costs” are set by the prices asked to the payer gives bargaining power to Governments”) but fails to consider that all the single-payer systems, regardless of the rules to control prices, are characterized by monopsonistic purchasing power.</p>
Page 37 1070- 1071	<p><i>“But the use of RWD has its own shortcomings”.</i></p> <p>The meaning of this statement is unclear. This observation should have been expanded upon.</p>
Page 38 1085ff	<p><i>“The justification of high prices based on the high underlying R&D costs is often unchecked (as none or very little information is released by companies on the costs of R&D, which include opportunity costs of investment and failed attempts to obtain the innovation).”</i></p> <p>Medicines provide great value to society and this value is not measured solely by R&D costs, but rather in terms of societal benefits. Assessing the overall cost of R&D investment in an industry (with many diverse business models therein) is not likely to produce information that is applicable to inform price decision. Moreover, payers understand that the costs of development are significant and cannot be directly associated to individual products. This explains why we have progressively moved away from cost-based approaches over the last thirty years.</p>

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Raps website [last access 24 November 2017]: <http://www.raps.org/Regulatory-Focus/News/2017/04/03/27253/EMA-Adopts-Updated-Guideline-on-Fixed-Dose-Combination-Drugs/>

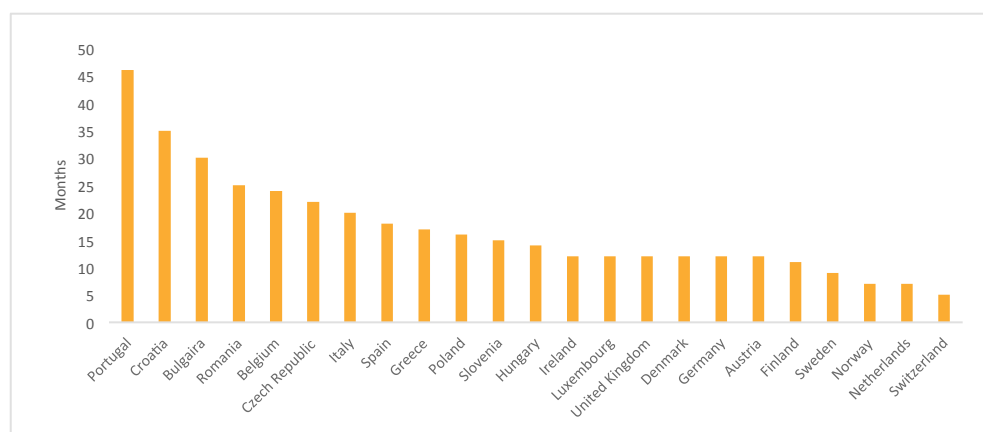
<p>Page 38 1089ff</p>	<p><i>The pharmaceutical industry alleges that high prices are unavoidable given the expense of R&D to bring new medicines to the market</i></p> <p>The price of a medicine is based on the value it brings to patients, healthcare systems and society. It provides the appropriate incentive for companies to invest in new therapy development. Pharmaceutical companies take a look at a number of factors when pricing drugs including the level of innovation, the availability of other medicines to treat the same condition, the level of added benefits over existing treatments, induced changes to the care pathway like reductions in hospitalisation or the need for surgery or other procedures. All these factors are taken in to account by companies in setting a price, that is then subject to rigorous value-assessments and negotiations with healthcare systems.</p>
<p>Page 39 1101ff</p>	<p><i>“Knowledge of R&D costs would help to scrutinize the extent of exercise of market power. A simple hypothetical example illustrates the relevance of this element.”</i></p> <p>The example provided is oversimplifying the reality and not capturing any of the complexities of the pharmaceutical business model. In its simplicity, the only point made by the example (revenues should be compared to R&D costs) is again wrong: the price of a medicine is justified by the value delivered (which is assessed by payers) and cannot be linked to the R&D costs. Moreover, the revenue/cost comparison made in the draft opinion is conceptually wrong: R&D costs are borne in the past and revenues are accrued in the future AND even such a simplistic calculation should recognise the need of discounting cash flows.</p>
<p>Page 39 1123- 1124</p>	<p><i>“There are several claims that price setting should be more transparent and should not be left to industry alone.”</i></p> <p>The price of a medicine should reflect its value as well as other economic, cultural, institutional and epidemiological specificities of a country. Confidentiality of net prices is a way to ensure that medicines deliver value for money based on the individual characteristics of each country.</p> <p>Moreover, the uniform price outcome is not desirable: not all countries should pay the same price as the poorer countries. An effective negotiation process enables each government and pharmaceutical company to match price, value and ability to pay on a product-by-product basis. Factors that guide markets for medicines differ greatly from one nation to the next and even within nations. The following factors should be taken into account:</p> <ul style="list-style-type: none"> • healthcare priorities • healthcare financing and the deficits and revenues in health budgets • the population covered (rural vs. urban, younger vs. older, chronic vs. ambulatory care, etc.) • treatment pathways • the evaluation of technologies (methods and endpoints, comparators, etc.) <p>Price comparisons by third parties using publicly available data will likely yield inaccurate conclusions as each healthcare market is unique in the pricing it makes available in the public domain. Reasons for this might include the fact that some reported prices might be inclusive of local taxes and/or distribution costs that are unique to a specific country and not controlled by the manufacturer, while other countries reported prices might not</p>

include some/any of these elements.

Price disclosure and reference pricing also have the potential to reduce or slow down patient access to new medicines.

One example is access to the breast cancer medicine, Trastuzumab, where lower income countries had an access delay of more than 4600 days (Latvia) compared to higher-income countries like Austria with 34 days.⁸⁷ Those differences in access to oncology medicines have been confirmed by Glynn (2013) over a 12- year time horizon with a nearly 40-month difference between those countries with fastest and slowest access.⁸⁸

Average launch delays for in-patent oncology drugs: 2001-2013



In addition, it may lead to higher prices as shown by Glynn (2013).⁸⁹ While for some types of markets price transparency can lead to more competition and subsequently lower prices, in other types of markets as is the case for medicines it can lead to higher prices for some countries which may be unaffordable.⁹⁰

In some cases, forced disclosure of net price and reference pricing may lead to a greater number of products not being launched in certain markets. If prices are driven too low in a key market, companies may not be able to sell their products at the value those products offer patients and the health system (this is the case of Korean companies, which are unable to sell their products abroad, or may not opt to sell there because they cannot gain sufficient return on investment (ROI) because they have to reference their home country price, which is too low for other markets).

Page 40
1152ff

“More elaborated payment structures, like two-part tariffs, is mentioned in Jonsson et al. (2016) “A two-part tariff, including price volume agreements and different prices for different uses is common in many markets characterized by large investments (for instance, transport, energy and telecoms) and could potentially improve the situation”.”

In practice, medicines are priced using non-linear pricing. The use of MEAs introduces payments based on volume and taking into account evidence on outcomes. It is unclear whether elaborate payment structures envisaged by the EXPH are implementable in practice. For example, the mentioned two-part tariff would require that the price of a

⁸⁷ Ades, F., Senterre, C., Zardavas, D., de Azambuja, E., Popescu, R., Parent, F. and Piccart, M. (2014) An exploratory analysis of the factors leading to delays in cancer drug reimbursement in the European Union: the trastuzumab case. *European J Cancer*

⁸⁸ Glynn, D. (2013) External Reference Pricing. *Europe Economics*

⁸⁹ Ibid.

⁹⁰ Glynn, D. (2015) The case for transparency in pricing. *Competition Law*

	<p>medicine in each market consists of a fixed part (i.e. a sort of “access fee”) and a variable part (linked to the number of patients). The calculation of the fixed part would require too many assumptions and too much coordination across different countries, making it unfeasible.⁹¹</p>
Page 41 1172ff	<p><i>“Whenever neglected areas can be detected and be consensual on the opportunity to have innovation, using available instruments (soft ones, as joint horizon scanning discussions, or hard, as price or reward commitments) can be improve innovation value.”</i></p> <p>There should be more arguments to support this statement. For instance, it is unclear how joint horizon scanning discussions can support research in neglected areas.</p>
Page 42 1198ff	<p><i>“A major issue to be explicitly recognized is that exercise of market power (meaning that prices are well above a benchmark of “fair return” on investment, including R&D investment) is present and it is a result of the current institutional framework. Some relevant proposals will not solve the issue.”</i></p> <p>The authors have not shown that returns excessively high or defined what they mean by fair returns. In addition, if value is not rewarded, incentives for R&D of new medicines will be limited. Any assessment of the returns of the successful innovator needs to take into account all the failed investments and that first in class products are facing competition from second and third in class products much more rapidly than in the past, with the result that returns to an innovative medicine can be very short lived. There is also a point about who determines what ‘fair’ is? And is it “fair” to determine Return on Investment (ROI) for one specific industry, but let other industries remain open to market forces? Some would argue this is the opposite of fair - it is discriminatory, creating an artificial market.</p>
Page 42 1212ff	<p><i>“Value-based pricing does not mean that providing price signals (economic incentives) to true therapeutic added value equates to prices allowing companies to capture all possible surplus.”</i></p> <p>The authors have not shown that, under the current pricing structure, the industry is capturing all possible surpluses. On the contrary, under the current pricing rules of European payers, most of the value is delivered to the patients and the healthcare system. There is a large amount of literature showing that the industry is only rewarded with a small share of consumer benefit.</p>
Page 43 1215ff	<p><i>“Many references to excessive prices, but no reference to indicate how this is measured or even to which products we talking about?”</i></p> <p>There is no evidence for this assertion.</p>
Page 43 1227ff	<p><i>“Paying more for higher value drugs provides an incentive for investment in such drugs compared with lower price drugs. The target left behind will likely to be affordability, and consequently access to the new pharmaceutical discoveries”.</i></p> <p>The draft opinion contains many statements implying that sustainability considerations</p>

⁹¹ Towse, A., Pistollato, M., Mestre-Ferrandiz, J., Khan, Z., Kaura, S., & Garrison, L. (2015). European Union Pharmaceutical Markets: A Case for Differential Pricing?. *International Journal of the Economics of Business*, 22(2), 263-275.

	<p>are not considered within value-based pricing, which is not correct. Indeed, to address existing inequalities in patient access to medicines, pharmaceutical companies are already differentiating the price of a medicine according to a number of criteria, such as:</p> <ul style="list-style-type: none"> • Level of the country’s GDP per capita • The population’s health needs and local disease burden • Availability of alternative treatments • Government pricing regulations and health economic evaluations • Economic conditions of patients and payers • Society’s health resource priorities <p>Companies are considering the total cost of care with a medicine versus the standard of care. Attention is also being paid to the potential total budget impact, based on the prevalence of the disease in the population.</p>
<p>Page 43 1241ff</p>	<p><i>“Under a rule that says that a product is accepted to coverage by a health care payer as long as it meets a threshold for (incremental) cost-effectiveness, the power to set prices is with company and the “demand” decision is basically an “all or nothing decision”</i></p> <p>The draft opinion presents the threshold as a problem that company’s abuse. This is not a problem of a given threshold but a problem of the value assessment. If a given medicine is at or below a threshold this should be taken into account in determining if the products represent value for money. The threshold itself is defined by the health system or the payer.</p>
<p>Page 44 1266ff</p>	<p><i>“Since bargaining is about division of value generated, it is also necessary to know, at least to the bargaining sides, the costs of obtaining and producing the new product.”</i></p> <p>As already argued, it is unfeasible for companies to calculate the cost of a new product. This would also require defining a rule to attribute the share of indirect costs to each single product in a company’s pipeline and portfolio.</p>
<p>Page 45 1281ff</p>	<p><i>“The use of mandatory licensing (with royalties for patent use being determined by judicial decision) is another way to leverage negotiation powers to payers”</i></p> <p>There have been very few cases of governments issuing compulsory licenses historically and globally; most incidences were in connection to HIV/AIDS in the early 2000s. Encouraging compulsory licensing undermines the incentive system in a manner that is disruptive and extreme and therefore threatens future investment in medical R&D. It is not an effective solution to address healthcare challenges.</p> <p>Policy options such as “last resort mechanisms” do not serve patient access in the long term, but would result in increased unpredictability with significant implications for innovation in medicines. Companies have incentive to create access, and have used a variety of approaches to improve access for different countries. Danzon and Towse (2003) note that <i>“in the absence of clear criteria to define which drugs and countries/ populations should be eligible, the compulsory licensing approach is at risk of undermining the function of patents over broad markets and therapeutic categories. This approach may seem to offer cheap drugs to needy people in the short run, but at the risk of undermining incentives to develop new drugs in the longer run.”</i>⁹² In addition, this</p>

⁹² Danzon, P.M. and Towse, A. (2003) Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents. *International Journal of Health Care Finance and Economics*

	<p>initiative could create future disincentives to launching innovative drugs in countries that have exhibited a propensity to resort to compulsory licensing (CL).</p> <p>Rather than use of last resort methods, working in partnership has improved access. The biopharmaceutical industry is working with governments to promote sustainable and affordable access to healthcare, while securing the future of medical innovation.</p>
Page 50 1411ff	<p><i>“An important aspect is that price cannot be the single consideration, as ensuring competition and availability of supply is important. [...]”</i></p> <p>We share the view of the EXPH that price cannot be the single consideration. Unfortunately, the draft opinion focuses only on technical criteria such as supply etc. and does not take into account the lack of interchangeability (except for identical medicines), patients’ needs, physicians freedom to prescribe etc., in short, the clinical perspective when procuring medicines.</p>
Page 51 1432- 1474 ff	<p>3.4.7 Adaptive pathways</p> <p>It is unclear why this section is in the draft opinion at all, since it does not make any link to innovative payment models. The concept of adaptive pathways is complex and would merit a much more expanded explanation, and many of the statements made in this section feel simplified or misconstrued.</p>
Page 51 1435- 1437ff	<p><i>“Critics have called for a “paradigm shift”, that would allow some products to be approved on the basis of preliminary data, allowing their benefits and harms to be monitored among those using them using what has been termed “real world data”.</i></p> <p>Adaptive pathways do not entail marketing of products that are unsafe – the drugs would still have to undergo clinical trials to confirm their safety for use.</p>
Page 51 1448- 1449ff	<p><i>“There are circumstances where a need for special measures is clear, but they are quite exceptional”.</i></p> <p>What is the basis for this statement? Which exceptional circumstances are referred to?</p>
Page 52 1460ff	<p>Adaptive pathways</p> <p><i>“[...] in the absence of randomization it will be very difficult to determine whether any events (beneficial or adverse) are due to the drug or to other characteristics of the subject.”</i></p> <p><i>“The use of such expedited approaches could see significant numbers of products brought to market despite being unsafe, ineffective, or both”.</i></p> <p>We agree that Randomized Controlled Trials (RCT) are the gold standard. However, in some circumstances, e.g. life-threatening diseases, it would be unethical to put patients on a placebo.^{93,94} In terms of efficacy, more flexible pricing and reimbursement schemes could overcome the risk of uncertainty.</p>

⁹³ Evans, S. R. (2010). Fundamentals of clinical trial design. *Journal of experimental stroke & translational medicine*, 3(1), 19.

	<p>In summary, using RCT as the only criterion for pricing and reimbursement risks preventing patients from access and may be unethical under certain circumstances. Health systems should allow for more flexible approaches, which in turn require closer collaboration among all stakeholders.</p>
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Eichler, H. G., Baird, L. G., Barker, R., Bloechl-Daum, B., Børlum-Kristensen, F., Brown, J., ... & Garner, S. (2015). From adaptive licensing to adaptive pathways: delivering a flexible life-span approach to bring new drugs to patients. *Clinical Pharmacology & Therapeutics*, 97(3), 234-246.

Comments on Section 3.5: Basic principles for new payment models

Page	Comments
Page 54 1531ff	<p><i>“Thus, no single model of payment can be reported as “the solution” to achieve all intended objectives (financial, sustainability of health systems, access of patients to innovation and ensuring conditions for innovation that matters to take place)</i></p> <p>We agree with the EXPH that there is no single solution. Countries have very different healthcare systems and use very different approaches to assess, negotiate and fund innovative pharmaceutical products. Every system has pros and cons. However, some of the solutions suggested in the draft opinion may cause a big threat to innovation such as compulsory licensing.</p>
Page 54 1537- 1539	<p><i>“Current price-setting models are inserted into an institutional framework that is benevolent with market power exercise, exacerbated by financial protection systems (health insurance) that reduce the price-sensitivity of demand.”</i></p> <p>It is a bit unclear what the EXPH intends to say in this section. The pharmaceutical must comply with competition law, as it is the case for every other sector. As such, the industry has been examined in the Pharmaceutical Sector Inquiry.⁹⁵ Regarding price sensitivity, we refer to our response on lines 215 and 1659.</p>
Page 54 1540- 1546	<p><i>“The reporting of cost information to regulatory bodies, even if kept as commercial secrets, will act as an implicit deterrent on very high margins.”</i></p> <p>The EXPH argues that reporting of cost information would act as a deterrent. However, it does not set out what cost information would be required. The cost of developing a medicine includes the cost of successful molecules and the cost of failed potential competitor products, which is not known to any manufacturer. The cost of developing a medicine is a global cost, and there is a set methodology for attributing this to individual countries. The problem of cost transparency is well known.</p>
Page 55 1547- 1549	<p><i>“On the other hand, competition, when feasible, takes place sometimes by way of “secret” price discounts. Such price competition element should not be discarded, and advises against full posting of all prices.”</i></p> <p>In this section the EXPH appears to accept the benefits of competition, which we agree with. This is facilitated by confidential agreements, known between the purchaser and the seller of the product. These are commercially confidential rather than secret. Commercial confidential contracts occur in many other industries and commercial negotiations.</p>
Page 55 1555- 1557	<p><i>“Still, under the current and foreseeable conditions of pharmaceutical markets, greater price transparency can be beneficial to the performance of the health care sector, including the rate of innovation.”</i></p> <p>The draft opinion argues that greater price transparency would necessarily be beneficial. However, this assertion ignores the literature on the negative impact of transparency of</p>

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<http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>

	<p>pricing and price convergence in the pharmaceutical sector, notably in terms of access to medicines in low-income countries⁹⁶. For instance, Glynn (2015) concludes that in the pharmaceutical sector, transparency, in particular European Reference Pricing harms patients.⁹⁷ Price transparency is likely to be harmful to countries with lower than average healthcare spending. Solidarity between Member states, which encourages equal access to medicines for patients in all countries, has not been recognized in this draft opinion.</p> <p>Ensuring the confidentiality of net prices allows prices to be negotiated and adapted based on an individual country's health and economic needs, which is a key criterion for value-based pricing. In the context of external reference pricing (where governments set a price for a medicine based on its price in other countries) and parallel trade (where a medicine is bought in one country with the sole objective of exporting to another country to sell at a higher price), confidential net prices allow companies to adapt the price of a medicine to a country's specific economic and healthcare environment. In this case, governments can get an 'optimal' price arrangement, tailored to the country's needs. Increasing the transparency of net prices puts at risk the shared objective of ensuring that patients across countries get rapid access to the latest, effective and lifesaving medicines. For instance, if the net price is known by wholesalers, they will be tempted to move medicines to countries where they can get a higher price, which could lead to shortages.</p> <p>Overall, the Panel understates the negative effects of price transparency. Increased transparency and disclosing of net prices would lead to lower access to medicines in countries that today get rebates due to their lower income levels/ability to pay.</p>
<p>Page 55 1558- 1560</p>	<p><i>“Use of health technology assessment and economic evaluation works as necessary but not sufficient conditions. It limits too high prices, but does not advocate lower than threshold prices”.</i></p> <p>The EXPH takes a rather simplistic interpretation of HTA. First, many HTAs bodies do not apply a threshold, many focus on relative effectiveness rather than cost-effectiveness. Where they do apply cost-effectiveness they do not apply a threshold. Secondly, HTA bodies are not there to determine prices. Relative effectiveness assessments are a contribution to the price negotiation process. Third, even in markets where the threshold is important, we see a range of outcomes with products near the threshold and with products priced significantly below the threshold. Fourth, there are products that are assessed as below the threshold but are still not reimbursed.</p>
<p>Page 55 1563ff</p>	<p><i>“A possible course of action is that firms submit an estimate of the costs they incurred and its breakdown (R&D, marketing and productions costs) as part of the HTA assessment”.</i></p> <p>This proposition seems to be in contradiction with other parts of the draft opinion, which recognise that a cost plus approach would be detrimental to innovation and therefore inappropriate. Asking companies to submit an estimate of the costs they incurred and their breakdown would likely result in a cost-plus approach. This approach fails to distinguish static and dynamic expenditure, the latter providing the necessary funding for future innovation. See also response to lines 1540-1546.</p>

⁹⁶ De Cock, J. (2013) Access to medicines: can differential pricing be an answer? *Presentation to the European Parliament*

⁹⁷ Glynn, D. (2015) The case for transparency in pricing. *Competition Law*

<p>Page 56 Section 3.5.2</p>	<p><i>“The patent system is out of balance: in the European Union on top of the lengthy protection period, additional market exclusivity, data exclusivity and eventually supplementary protection certificates (SPC) is granted to market authorization holders and delays price-lowering generic competition”</i></p> <p>The draft opinion provides no evidence for such a blanket statement. It also seems that this conclusion comes from Health Action International and not from the EXPH, which is very surprising and puts into question the working methods of the panel. Both this section and the following (“Changing the rules in R&D funding”) seem mostly based on policy messages from one stakeholder.</p> <p>The EXPH draft opinion does not provide any evidence for these assertions. It cites Health Action International’s concerns. Evidence on the role of intellectual property and the need for different incentives regimes should be included. In particular, there is a large literature on the benefits of the patent system and the need for particular forms of incentives.</p> <p>Indeed, the pharmaceutical industry has been subject to a detailed Sector Inquiry. On 8 July 2009, the European Commission published the conclusions of its 18-month pharmaceutical sector, which looked in detail at competition.⁹⁸ This does not support the EXPH recommendations.</p> <p>Effective and predictable intellectual property systems have been identified as one of the key principles for creating and nurturing innovation ecosystems. This was reinforced through the recent B20 Health Initiative, launched in May 2017⁹⁹, which built on the International Chamber of Commerce (ICC) “Principles for Policy Makers” paper for creating and nurturing innovation ecosystems for high-tech industries.¹⁰⁰</p> <p>Companies have an incentive to create access, and have used a variety of approaches to improve access for different countries. Danzon and Towse (2003) note that “in the absence of clear criteria to define which drugs and countries/ populations should be eligible, the compulsory licensing approach is at risk of undermining the function of patents over broad markets and therapeutic categories. This approach may seem to offer cheap drugs to needy people in the short run, but at the risk of undermining incentives to develop new drugs in the longer run.”¹⁰¹</p> <p>Industry is working in partnership with other stakeholders to improve access. The biopharmaceutical industry is working with governments to promote sustainable and affordable access to healthcare, whilst securing the future of medical innovation.</p>
<p>Page 57 Section 3.5.3</p>	<p><i>Section 3.5.3 Changing the rules in R&D funding</i></p> <p>The number of medicines that fail even late in the development process illustrates the risk that the Biopharmaceutical industry takes on. Payers & NGOs only see Pharmaceutical successes, but they typically have limited understanding of the development risks. Public funding of R&D is therefore not a realistic alternative to the commercial development model.</p>

⁹⁸ <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>

⁹⁹ B20 Health Initiative (2017) Stepping Up Global Health: Towards Resilient, Responsible and Responsive Health Systems

¹⁰⁰ ICC Policy Principles Paper (2015) Creating and Nurturing Innovation Ecosystems for High-Tech Industries

¹⁰¹ Danzon, P.M. and Towse, A. (2003) Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents. International Journal of Health Care Finance and Economics

“There is growing consensus that alternative models to finance R&D for actually needed drugs (rather than me-too drugs)”

The EXPH mentions a growing consensus without providing any evidence on this. They also distinguish between actually needed drugs and ‘me-toos’. In reality, significant efforts are already being put into diseases that target unmet need. R&D is correlated with therapeutic areas that have the greatest societal impacts.¹⁰²

- The pharmaceutical industry wants to be able to develop medicines to meet unmet medical needs wherever they occur. However, the return on investment on R&D for diseases disproportionately affecting the developing world is often not viable unless the scientific and financial risks are shared.
- The industry is increasingly working in collaborative Product Development Partnerships (PDPs) with other stakeholders to tackle a range of needs.¹⁰³ An example is the *Project Data Sphere* initiative.¹⁰⁴ Typically, this model involves companies providing technology they have invested in, as well as their development and distribution expertise, to the partnership. Public sector partners help fund development costs and can improve the access of patients to medicines and vaccines by financing implementation programmes¹⁰⁵.
- A number of these PDPs such as the Medicines for Malaria Venture (MMV), the Malaria Vaccine Initiative (MVI), the Drugs for Neglected Diseases Initiative (DNDi), and the TB Alliance have transformed the pipeline of R&D projects for diseases of the developing world. Research programmes are overseen by joint steering committees with representatives from all the partners.¹⁰⁶ Under the terms of the agreements, where sales opportunities exist, priority must always be given to treatments for neglected tropical diseases in the least developed countries.
- The PDP approach is working. A report from Policy Cures published in February 2016 showed that 485 products were in the pipeline for products to fight diseases of the developing world¹⁰⁷ the vast majority being developed in partnerships.

The industry has made a tremendous contribution to diseases, which disproportionately impact lesser resources economies (including neglected disease and diseases such as rare, underserved conditions).¹⁰⁸ The ninth G-FINDER survey report shows that industry is the third largest contributor into research and development (R&D) of new products for neglected diseases (15%) after the US NIH (40%) and the Bill & Melinda Gates Foundation (17%)¹⁰⁹

¹⁰² Catalá-Lopez, García-Altés, A. Álvarez-Martín, E., Gènova-Maleras, R. and Morant-Ginestar, C. (2010) Development of new medicinal products in the European Union. *A.T. Kearney analysis*

¹⁰³ Reddy, D. and Spigelman, M. (2014) Product Development Partnerships: an innovative approach to tackling neglected diseases. *Dev Policy Blog*. [Accessed 20 June 2017]: <http://devpolicy.org/product-development-partnerships-an-innovative-approach-to-tackling-neglected-diseases-20140528/>

¹⁰⁴ Project Data Sphere. CEO Roundtable, Press Release 8 April 2014. [Last Accessed 21 July 2017]: https://www.projectdatasphere.org/projectdatasphere/html/resources/PDF/PDS_PRESS_RELEASESET

¹⁰⁵ Moran, M. (2005) A Breakthrough in R&D for Neglected Diseases: New Ways to Get the Drugs We Need. *PLoS ONE*

¹⁰⁶ Topal, C. (2014) An Interview with Robert Lin: The Value of Product Development Partnerships. *The National Bureau of Asian Research*

¹⁰⁷ Policy Cures Research website. Neglected Diseases. [Last Accessed 23 June 2017]: <http://pipeline.policycures.org/>

¹⁰⁸ Policy Cures Research. (2016) Ninth G-FINDER 2016 Neglected Disease Research and Development: A Pivotal Moment in Global Health

¹⁰⁹ Ibid.

<p>Page 57 1607- 1617</p>	<p><i>“The delinkage of R&D from sales is demanded”</i></p> <p>The EXPH draft opinion refers to prize models and delinkage without any reference to the large literature on this issue. The proposal, which they correctly cite from some NGOs has been discussed for many years.</p> <p>They refer to DNDi (drugs for Neglected Disease Partnerships) Development Partnerships as a potential model (Gerlinger 2017). However, the number of products developed through these partnerships has been limited. The draft opinion also fails to account for the other many challenges (e.g. limited infrastructure) to ensuring patient access to healthcare and medicines in low-income settings.</p> <p>The prize model’s proposal is contradicted by the earlier text on the nature of innovation. On line 792, the EXPH concludes “disruptive innovation is mostly unpredictable in its effects, it is not feasible to define ex-ante a payment model general enough that can be optimal in all future contingencies”. As innovation is unpredictable a prize model would not be possible.</p> <p>The most effective pull incentive is competitive markets that reward innovative products. However, it is acknowledged that there are markets where incentives are insufficient and other mechanisms may play a role. The role of models suggested should be more clearly/explicitly limited to the specific scenarios considered (ND, AMR) i.e. where the inherently unique market dynamics of these markets mean that innovative policy instruments may have a role to play. For example, there are existing AMC for product such as pneumococcal vaccines.¹¹⁰</p>
<p>Page 57 1618- 1620</p>	<p><i>“Other alternatives are also possible, including unbundling phase 3 in development of new products, with trials being performed by independent groups and allowing open access to results.”</i></p> <p>The pharmaceutical industry currently spends about \$157 billion a year on research and development.¹¹¹ There is considerable risk of failure at Phase III. For example, a study of Alzheimer’s disease clinical trials between 2002 and 2012 found that an estimated 72% of agents failed in Phase I, 92% failed in Phase II, and 98% failed Phase III.¹¹²</p> <p>It is unclear how independent research will be funded and who will accept the risk that they require. Finally, there is nothing to stop independent trials being undertaken today, but the number of such trials is exceedingly small.</p>
<p>Page 57 1621- 1624</p>	<p><i>“Other alternative courses of action are discussed in Vandenbroek et al. (2016), including ways of sharing the costs and returns of R&D investment in new products. These options involve a different approach to R&D public funding, with a higher involvement by the public sector in the appropriation of returns from the R&D it funds.”</i></p> <p>The public sector plays an important part in funding basic research. Basic research is</p>

¹¹⁰ Cernuschi, T., Furrer, E., Schwalbe, N., Jones, A., Berndt, E.R. and McAdams, S. (2011) Advance market commitment for pneumococcal vaccines: putting theory into practice. *Bulletin of the WHO*

¹¹¹ Statista website [last access 27 November 2017]: <https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/>

¹¹² Cummings, J.L., Morstorf, T. and Zhong, K. (2014) Alzheimer’s disease drug-development pipeline: few candidates, frequent failures. *Alzheimer’s Research & Therapy*

	<p>often relevant to a very broad range of fields, to have application over many years, and be useful only when combined with other research and therefore it can be considered a public good. Owing to the non-appropriable, public good and intangible character of knowledge, the market does not provide sufficient incentives for private investment in research.¹¹³ For this reason, public funding of basic research is desirable. This is evidenced by the success of the Innovative Medicines Initiative.¹¹⁴</p> <p>It is also not the case that research is only undertaken with public investment. Private investment also targets basic research. For instance, the U.S. pharmaceutical industry is the major driver behind the recent jump in corporate basic research, according to NSF's annual Business Research and Development and Innovation Survey (BRDIS), which tracks the research activities of 46,000 companies. Pharmaceutical company investment in basic research soared from \$3 billion in 2008 to \$8.1 billion in 2014, according to the most recent NSF data by business sector.¹¹⁵</p> <p>In fact, two decades of reliable analyses by academia and government, based on sponsorship, patent, project, and licensing data, as well as considerations of central scientific contribution to applied science, clinical improvement, and the development of manufacturing protocols, consistently demonstrate that 67% to 97% of drug development is conducted by the private sector.¹¹⁶ In particular, the private sector is found to be dominant in the drug discovery stage and the chemistry/manufacturing/controls and drug development phases, relative the public sector.¹¹⁷</p> <p>Where the public sector is directly involved in the development of medicines, there are existing licensing agreements that pay a royalty to the institutions involved.</p> <p>However, it is true that the uncertainty and associated cost in the later phases, is mostly born by the private sector. Approximately 70% of the cost of bringing a product to the market arises after discovery of the compound, and most of this is usually borne by the innovative pharmaceutical industry. Only one in five medicines, which are brought to market is profitable.¹¹⁸</p>
Page 58 1633ff	<p><i>“EMA should be fully funded by public fund rather than by industry generated user fees in order to end the potential risk of “industry’s capture of the regulator”</i></p> <p>This section questions the current role and set-up of the EMA. It is very unclear what this section is doing in the draft opinion, since it does not relate to innovative payment models. The section includes statements such as “EMA should be fully funded by public fund rather than by industry generated user fees” and “it also should be clear that Real</p>

¹¹³ OECD website, Public research policy [Last Accessed 12 July 2017] <https://www.oecd.org/sti/outlook/e-outlook/stipolicyprofiles/competencestoinnovate/publicresearchpolicy.htm>

¹¹⁴ Innovative Medicines Initiative website. Success Stores. [Last Accessed 25 July 2017]: <http://www.imi.europa.eu/content/success-stories>

¹¹⁵ Mervis, J. (2017) Data check: U.S. government share of basic research funding falls below 50%. *ScienceMag*. [Last Accessed 23 June 2017]: <http://www.sciencemag.org/news/2017/03/data-check-us-government-share-basic-research-funding-falls-below-50>

¹¹⁶ Chakravarthy, R., Cotter, K. and Di Masi, J. (2016), Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy, *Therapeutic Innovation & Regulatory Science*

¹¹⁷ Ibid.

¹¹⁸ Vernon J.A., Golec J.H., and Di Masi J.A. (2010) Drug development costs when financial risk is measured using the Fama-French three-factor model. *Health Economics*

	<p>World Data and Adaptive Pathways pose risk” without explaining or elaborating on this any further. On what basis do the authors conclude that Real World Data pose risks, and in what sense?</p> <p>The draft opinion contains quite serious allegations about the governance of the regulatory process, the importance of incremental innovation and the work of the industry, without providing any evidence. The Opinion appears to suggest that because the EMA, is funded by industry fees, it is allowing products onto the markets that are not safe and with too little clinical evidence. However, they have provided no evidence of this.</p> <p>Indeed, the proposal being developed by EMA are similar to other regulators across the world, who are funded differently. Flexible approaches to regulation of medicines are welcomed by patient groups, clinicians and the industry. It appears that the EXPH has based its analysis on a small number of papers by particular authors.</p> <p>The EXPH claims “an “orphanisation” strategy to provide evidence of high effectiveness on a very short number of selected type of patients to support a high price to the product”. Orphan designation is determined by the EMA, so the draft opinion implies that this is being given out in conflict with the rules. No evidence has been produced on this. The panel also seems to imply that because a product achieves orphan status it is free to set prices. This is also incorrect.</p>
<p>Page 58 Section 3.5.5</p>	<p><i>“Develop methodologies to measure the value of pharmaceuticals”</i></p> <p>Measurement of value and outcomes is a key element of realising innovative payment models. It is therefore very disappointing that this topic has merited only three sentences in the draft opinion. The sentence “The important element is that identification of relevant outcomes is made and that measurement can be made in a clear and easy-to-understand way” hardly brings any new information to the reader.</p> <p>It appears that this section was a work in progress and will be completed in the next draft of the draft opinion.</p>
<p>Page 59 (Section 3.5.6) 1659ff</p>	<p><i>“Have an assessment of exercise of market power in each price negotiation” & “That role of prices is much weaker in health care, as insurance protecting patients from the financial hardship associated with healthcare needs also withdraw the natural barrier to very high prices set by providers of care, including pharmaceutical companies”.</i></p> <p>While, patients may be less price-sensitive due to the insurance system, in today’s environment the price is determined by the payer who is much more powerful than the individual patient. Indeed, delegating the negotiation to a payer de facto increases its negotiation power as it represents multiple consumers. Payers have developed a sophisticated value assessment, which would not be possible for patients.</p> <p>Most remarkably, the EXPH argues for a definition of the meaning of the abusive exercise of market power in pharmaceutical markets with help from competition authorities. The pharmaceutical market is already under the competition rules. As referred to earlier, there was a pharmaceutical sector inquiry by the European Commission.</p> <p>This system already exists with purchasers being able to make complaints to the competition authorities. This includes redress when payers have paid a higher price as a result of anti-competitive activity.</p>

Page 59 Section 3.5.7	<p><i>“Set better rewards for higher therapeutic added value”</i></p> <p>We agree with the title of this section. However, this currently only repeats the executive summary and we not accept the analysis of the relationship of price and current cost effectiveness thresholds that is discussed elsewhere in the EXPH draft opinion. See our discussion regarding cost effectiveness in response to lines 392-394 (page 13).</p>
Page 59 Section 3.5.8	<p><i>“Move towards acquisition of service rather than product”</i></p> <p>We agree with the aspiration in this section but currently it only repeats the executive summary providing no further guidance on how this should be done or the degree to which this is a problem today. Again, this would appear to be a work in progress section that should be completed in the next version of the draft opinion.</p>
Page 59 Section 3.5.9	<p><i>“Explore non-linear payment systems, including bundling, differentiation across geographies and across indications”</i></p> <p>The EXPH’s draft opinion repeats the assertion that for price differentiation to work, it is necessary to set an average price cap over the different markets such that all parties benefit. The EXPH should provide arguments or sources to support this position. Many industries have price differentiation without an average price being set (for instance, the electric power and telecommunication industries set different prices for different consumers and different countries but do not require any average price cap to work¹¹⁹). This would suggest significant issues in many different industries.</p>
Page 60 Section 3.5.10	<p><i>“Create dialogue platforms”</i></p> <p>Dialogue is valuable and the EXPH sets out how this involves all stakeholders. This should be supported. However, it is unclear why there are different stakeholders in different platforms. Encouraging collaborative approaches to innovative payment models would be best undertaken with all stakeholders being able to engage actively. This should also involve different stakeholders from government, including those with a health, finance and industry strategy perspective.</p> <p>However, it should also be recognised that there are many on-going discussions between supranational organisations, national and regional governments, third party payers and patients, clinical and industry groups. Any new dialogue should carefully describe these on-going initiatives, explain the need for a further process and set out how they can be coordinated with these other processes. Dialogues between stakeholders and spearheaded by the OECD (Pricing Review), WHO (Fair Pricing Forum), European Commission and others are prevalent.</p>
Page 60- 63	<p><i>“Final remarks”</i></p> <p>The Panel makes some statements that we agree with</p> <ul style="list-style-type: none"> • They accept that pricing to costs would destroy the incentives to innovate. • For neglected therapeutic areas, payment models based on new ways of procuring innovation are an interesting alternative • The use of HTA (relative effectiveness) enables health systems to learn about the

¹¹⁹ Oseni, M. O., & Pollitt, M. G. (2017). The prospects for smart energy prices: observations from 50 years of residential pricing for fixed line telecoms and electricity. *Renewable and Sustainable Energy Reviews*, 70, 150-160.

value of medicines

- When uncertainty exists about the effectiveness of new products, MEAs with a performance component embedded in the payment model and use of real world evidence may be a useful instrument

However, the EXPH suggests a set of unrelated recommendations such as the request for R&D costs, the introduction of a competition policy review of high prices asked by companies with the cooperation of competition authorities and the idea to use mandatory licensing in extreme cases of public health risks. These policies do make sense and their negative consequences would be significant.

In other areas, the expert panel sets out recommendations that already exist. For example, “select one neglected area and launch international prize initiative with patent being retained by the set of countries participating”. There are already Advanced Marketing Commitments for a series of products. The EXPH asks for the “[assessment] of the value of new products of uncertain benefit using sound and transparent health technology evaluation methods” without any discussion of current HTA methods. The development of joint negotiation procedures is currently being tested.

Given the poor quality of the analysis, the inconsistencies of the arguments, and the incoherence of the policy conclusions, the value of this draft opinion is highly questionable.