Principles for Collaborative, Mutually Acceptable Drug Pricing

Conclusions of the PharmaDiplomacy Dialogue
Meteos is a not-for-profit company that convenes cross-sector, multi-stakeholder dialogues to accelerate solutions to a range of systemic challenges. Meteos uses a highly consultative, research based approach to facilitation. Our dialogues provide a forum for senior figures in the corporate sector, civil society, public sector and investment worlds to share different perspectives on the major trends that will shape market, regulatory and societal outcomes in coming years. The dialogues analyse the speed and direction of these trends and provide an opportunity for those who will determine future outcomes to work together to achieve an alignment of interests.

Meteos dialogues are funded by participant fees on a not-for-profit basis and through the provision of in-kind research and information sharing. As we are committed to ensuring that all relevant stakeholders contribute to the dialogues we provide some spaces on a non-fee basis. Such participants typically pay their own expenses. All participant voices are of equal weight in the dialogues. PharmaDiplomacy is funded on this basis.
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Introduction
from the PharmaDiplomacy Working Group

We, the members of the PharmaDiplomacy Group, have spent the past two and a half years seeking to understand the trust issues between the pharmaceutical industry and some of its key stakeholders, and to identify ways in which this relationship could be improved. Convened by Meteos, we have explored where and how trust is being eroded; and sought practical steps to improve relations, including mechanisms that could hold agreements in place and avert future disagreements.

Drug pricing quickly emerged from our conversations as a major – though certainly not the only – source of mistrust today (sales and marketing techniques, data transparency and access to medicines in developing countries were notable others). We focused our efforts on this critical issue because pricing is becoming the lightning rod in discussions between pharma and healthcare systems in ways that threaten patients’ access to innovative therapies and medicines they need – a priority for all members of the tips for soccer PharmaDiplomacy Group.

Our discussions moved quickly from questions of interpersonal trust – which was strong within the Group – to talk of diplomacy. We came to believe that the use of diplomatic tools as a means of navigating complex relations to achieve mutually acceptable results is the best way of addressing some of the problems inherent in pricing discussions today. Diplomatic tools can elevate the conversation and help overcome the lack of alignment between patients, payers and providers on questions of value and affordability. They can also tackle damaging zero-sum approaches to pricing. Introducing a diplomatic framework permits open, transparent and iterative discussions to begin early in the product-development process and end long after a medicine is launched, making greater alignment of interests of all parties much more likely. Aligning interests leads to earlier access to medicines for patients, faster acceptance for pharma, and sustainable, predictable pricing for payers.

In the course of this work we developed a set of Principles for how such a diplomatic approach could contribute to these goals. We began with a blank slate to which each participant was invited to bring their expertise and to articulate, carefully, how their needs would have to be met in order for such Principles to be of value. We also sought counsel outside the Group, and benefited from a consultation process in which a draft of the Principles (then known as the Checklist) was put out for public comment, online and in person.

The result of our work is this report and the Principles that it sets out for approaches to define mutually acceptable pricing. We believe that the use of these Principles will allow healthcare protagonists to move beyond deeply adversarial engagement to less
antagonistic discussions. Diplomacy is a means of replacing a transactional approach, where missiles are fired from both sides, with a relational, dynamic and negotiated settlement. Not necessarily loved by all, but mutually acceptable.

The Principles alone will not overcome mistrust between healthcare protagonists; our discussions uncovered multiple sources of disagreement and misalignment. However, they could be an important first step. And if they successfully address one of the most contentious issues – pricing – then the principles and approaches that underpin them could be applied to other sources of mistrust. We therefore offer them for use by all stakeholders including pharma, patients, payers, providers, insurers and doctors in the hope that they will be widely used, and that the insights and the approach they bring contribute to building trust between these healthcare stakeholders. This resulting increase in trust is in everyone’s best interest.

The PharmaDiplomacy Group
1. Members of the PharmaDiplomacy Group participated in a personal capacity. While members support the objectives of the initiative, the views expressed in this report are not necessarily fully endorsed by individual members or listed organisations.
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It is in everyone’s interest to improve trust among healthcare stakeholders. Health systems all over the world are changing. Rising demand for healthcare, combined with limited resources, is driving attempts to address affordability concerns by improving efficiency and increasing cost-effectiveness. New technologies and approaches to generating and using data are opening up ways to do this, as well as providing unprecedented opportunities for patients to engage with and shape healthcare delivery. The pharmaceutical industry is generating extraordinary innovations which not only offer the ability to diagnose, manage and treat disease, but also to understand where pharmaceutical interventions can help improve patient outcomes and system efficiency. In this way, its products can not only play a crucial role in patient well-being; they should also – if targeted and used correctly – be able to support successful, outcomes-focused health reform.

The tools exist to achieve the goal of more efficient, better healthcare. But to fully realise this goal will require unprecedented collaboration among health stakeholders. Technological transformation has radically changed how and what we communicate, and has created the ability to monitor and measure progress towards goals.

The potential for greater cooperation is not, however, being realised to the degree possible. This is because the relationship between the pharmaceutical industry and some of its key stakeholders is still characterised by high levels of mistrust. More collaboration relies on people wanting to work together. It requires them to be prepared to cooperate in complex and often siloed health systems and companies. It needs strong leadership to bring people together, and agreement on how to generate and manage information. It calls for mechanisms to improve mutual understanding; and investor acceptance and reward of company strategies that prioritise improved service and responsiveness. Above all it needs trust, which today could be significantly improved.

PharmaDiplomacy began in late 2013 as an attempt by senior health-system and industry personnel to tackle the mistrust that exists between the pharmaceutical industry and its key stakeholders, to improve relations between them and to create a common framework with which to come to agreement on value.

Trust

Trust in healthcare is complex. At a very personal level, people’s interaction with healthcare is often characterised by high levels of trust. Patients trust pharmaceutical companies to produce safe, effective medicines, which they are prepared to put into their bodies to cure or manage disease, and they trust doctors and other healthcare personnel to provide life-saving care. Moving

2. Comments in italics are direct, unattributed quotes from the PharmaDiplomacy Dialogue.
from these very fundamental engagements to a more systemic level, relationships can become more fraught. Patients often trust their doctors, but not necessarily the health system or their insurers. Generally, health professionals and payers trust industry’s medicines, but are less inclined to trust its marketing practices; how it reports trial data; its rationale for pricing; or its lobbying. Pharma, in turn, tends to mistrust government and payer approaches to cost containment. Industry often accuses payers of moving the goalposts when it comes to evidence; of setting unmanageable data requirements; of an inability to recognise the savings pharma offers to the system; and of delaying tactics. The transaction costs – financial, administrative and emotional – resulting from this situation are high and disheartening.

The PharmaDiplomacy Dialogue began by providing the Group with a conceptual understanding of trust. Trust is the belief that it is safe to make something of value subject to another person’s actions. It lowers transaction costs in any social, economic or political relationship and lightens the burden of providing evidence. It makes people happy – or at least satisfied – about the ongoing relationship. As trust is constantly revisited on the basis of new information, rebuilding trust is more difficult than establishing it from scratch. Furthermore, if a person or organisation is already mistrusted, data that confirm suspicions tend to be over-emphasised. Of all the factors that might predict levels of trust, perceived past trustworthiness is the greatest (see Appendix C for a full bibliography on trust).

Trust relies on confidence in three things: that the other understands and is committed to one’s needs; is capable of delivering on the commitments they make; and can be relied upon to be consistent and honest. The PharmaDiplomacy Group reviewed the conditions needed to rebuild trust: honest and respectful communications; transparency; mechanisms for mutual accountability; redress of past wrongs; and consistent demonstration of new and better behaviours.

**Diplomacy**

It became clear early in the PharmaDiplomacy discussions that rebuilding interpersonal trust is a necessary but insufficient precondition for addressing the trust deficit between industry and health-system personnel. The Group therefore explored the possibility of using diplomatic approaches to accomplish our goals. Diplomacy starts with the premise that multiple and competing interests are at play. It acknowledges that this gives rise to the need for active and ongoing relationship management, and for mechanisms to provide oversight and address and resolve disputes. It also recognises the need to combine committed, influential leadership that models desired behaviours, with the taking of concrete actions to build confidence. Its emphasis on early discussion and alignment is particularly useful in creating mutual understanding and common goals.

The project developed a methodology for working together, based on diplomatic tools, to help the Group find common cause and to navigate their differences by adopting transparent and predictable processes.

> There is no doubt we reach a better outcome, faster, where there is trust. Where trust has failed, you often have incredibly formulaic structures where there is no room for negotiation or discussion. We need a framework for less antagonistic conversations.

> We need a technical tool that can align incentives and manage differences. The value of a diplomatic approach is that it can lead to action and it permits a joint narrative to drive a common agenda.
Trust and Drug Pricing in Context

“Doing nothing is not an option. We have to find a solution because what we have now is not sustainable.”

The PharmaDiplomacy Group explored a number of causes of mistrust between health systems and the pharmaceutical industry, including data transparency and approaches to orphan drug designation and promotion, before settling on drug pricing as the major focus of the work. Drug pricing was chosen because it is a highly topical source of mistrust between multiple healthcare stakeholders. In addition, the Group believed that successfully tackling this particularly thorny issue could reveal mechanisms to improve trust on other topics.

“The elephant in the room is pricing, so I think it’s unavoidable to focus on pricing if you want to deal with trust.”

The Problem to be Solved

Divergent Perspectives on Pricing

The lack of trust in drug pricing has multiple causes. From a health-systems perspective, cost pressures arising from drug price inflation are combining with demographic and epidemiological trends and health reform processes to lead to affordability constraints which threaten the very sustainability of healthcare systems. These pressures are exacerbated by broader economic pressures facing many countries, and by the perceived unpredictability of drug price increases. Although they still represent a small percentage of overall health expenditure, pharmaceuticals account for a highly visible and, in many places, growing proportion of health budgets. The annual price increases of specialty medicines are a particular cause for concern. A recent study found that over the past 15 years the average price of new oncology drugs rose from £10,000 to £100,000 per year.” For payers, that rate of increase cannot continue.

From a patient perspective, affordability concerns are increasingly personal. Until recently, patients have been relatively unaware of actual drug prices, thanks to insurance systems – whether public or private. Although this remains largely true, in countries where patients are responsible for financing a portion of their healthcare via insurance premiums and out-of-pocket payments (deductibles, co-payments and co-insurance), this is changing. In some places insurers are responding to the increased cost of pharmaceuticals by shifting costs to patients through these deductibles and higher co-payments, sometimes in the form of co-insurance. This leaves patients paying a greater proportion (up to 40-60 percent on some specialty medicines) of these inflating prices. In the US, for example, patients saw their deductibles on health insurance rise six times faster than wages since 2010, according to a Kaiser Family Foundation report published in September 2015. vi, vii That translates into about an extra $100 each year. The result is greater patient sensitivity to...
out-of-pocket expenditure on medicines and an increase in patient involvement in the pricing debate.

From pharma’s point of view, public rhetoric around pricing is a distraction from health systems’ inefficiencies and limited investment in infrastructure. The industry argues that pharmaceuticals as a percentage of overall healthcare is the same today as it was in 1960, and government projections expect this figure to remain relatively flat. It points out that patients have been asked to assume the financial burden of increased insurance premiums and hospital costs, but that pharma gets the blame for the decisions made by others in the health system. Specifically, it points out that payers make reference to high drug list-price increases, yet fail to acknowledge the significant rebates/discounts they obtain, which they then may not pass on to the patient. Moreover, it argues that pharmaceutical innovation is pushing back the frontiers of medicine, leading to highly effective, targeted treatments and cures that could significantly save money for the system. These developments need to be paid for, not just to cover their costs but, more importantly, to incentivise investors to support future innovation.

Limited Agreement Mechanisms

These divergent views are further polarised by the very limited number of mechanisms to bring people together to resolve them. Stakeholders – patients, payers, pharma and physicians – tend not to be unified in their definition of what constitutes “value” from a drug. For the most part, they do not all come together to agree on meaningful clinical outcomes, nor the evidence needed to substantiate them. Even if they did, there are no formal pathways to identify and negotiate the evidence needed by payers (unlike with regulators) and to link it to price. Sovaldi, a new drug launched in late 2014 to treat hepatitis C, illustrates the point well. Sovaldi cures 95 percent of patients it treats, and as such is highly valued by patients and physicians alike. However, this appreciation does not extend to its initial price of around $84,000 per patient. The cost has since fallen, in part due to the entrance of Viekira, a competitor medicine, launched by AbbVie at a 40-50 percent price discount negotiated with pharmacy benefit manager (PBM) Express Scripts, which started a downward price spiral. Despite this, and the fact that its “cost per cure” is lower than previous, less tolerable medicines, its $1,000-a-day price was met by fierce payer resistance – in part because millions of patients could now tolerate the treatment. Payer affordability concerns arose as a result of timing, and the combination of high price and high volume. Significantly, appreciation of the drug’s value did not translate into acceptance of price.

Poor Understanding of How Prices are Set

The primary cause of mistrust on pricing, however, appears to result from the lack of transparency over how prices for new medicines are set. The way companies come to their pricing decisions is poorly understood, giving rise to a health-systems view that prices are based on a calculation of what the market will bear. This means of determining price does not sit well with patients, payers and physicians.

“Is it about price, or is it about affordability? The two things are different. The affordability point I get, but the point is that current health systems are inefficient and no one feels they can change them because it is politically difficult.”
Furthermore, negotiations with payers tend to be opaque, with little understanding beyond the belief that those with greater bargaining power get the best (undisclosed) discounts on the list price. In the US, the situation is further compounded by the complex role of intermediaries, which means that the public is often bewildered by the relationship between drug prices, formularies and what they are obliged to pay out of pocket. Furthermore, the lack of transparency in the contracts between drug companies and payers and providers further obscures pricing, as does the fact that PBMs themselves benefit from high prices. These concerns have led to drug transparency legislation being filed in Massachusetts, California, North Carolina, New York and Pennsylvania, which requires pharmaceutical firms to disclose their development costs to justify rising prices.

"It's totally non-transparent. We have no idea what discussions happen between payers and companies. We don't even know what we don't know."

**Stakeholder Responses**

**US Payer Activism**

Payer activism in the US is increasing. Pricing concerns have provoked large US payers into outspoken criticisms of the increase in specialty drug prices. It has also led them to raise existing hurdles to physicians’ prescribing of innovative, expensive new treatments through, for example, renewed vigour in the application of formulary management tools. Payers continue to negotiate hard to maximise discounts on new drugs. They have also – for the first time – begun introducing exclusionary policies, limiting the number of available therapies per therapeutic area and requiring companies to bid against one another. Such policies are being applied to hepatitis C, chronic obstructive pulmonary disease, erectile dysfunction and diabetes treatments. Some are also setting limits on the drug price increases they will allow in order for treatments to remain on formulary (so-called “inflation protection”), and some are introducing onerous new prior authorisation conditions. Some US states are introducing measures to limit patients’ monthly out-of-pocket expenditures.

It has long been thought that the US is the one market in which explicit rationing will never be acceptable. Yet payers’ actions already amount to rationing, of sorts. US payers are increasingly willing to expand the number of equivalent or substitutable medicines on the formulary. They are able to do so because consumers do not really understand what is happening, and employers are willing to accept less choice on behalf of the beneficiaries of their health plans.

Health Technology Assessment (HTA) methods used in many countries to negotiate prices and rationalise use are gaining prominence in the US. One significant initiative is the Institute for Clinical and Economic Review (ICER), an independent, privately-funded, not-for-profit organisation which assesses a drug’s cost-effectiveness and budget impact, and sets what it refers to as a value-based price. ICER uses the NICE-style cost per QALY (Quality Adjusted Life Year) metric and is promising 15-20 reviews of high-impact drugs in 2016-18. The National Institute for Health and Care Excellence (NICE) does not have a direct role in pricing.
US State and Federal Government Involvement

Pricing debates also affect the public purse and are driving US political discourse. State legislatures are demanding greater transparency about how price is linked to development costs, and drug price reform is an electoral issue in the US. In late 2015, it was also the subject of debate in Senate and Congressional Committees, which stated their intention to engage in “meaningful action to combat the skyrocketing costs of pharmaceuticals”. In early 2016 the White House proposed testing a range of new payment measures for drugs covered as part of Medicare Part D as a way to contain costs.

However, in recognition of the need to maintain a balance between attracting innovation and managing health expenditure, European Ministers of Health have called on national governments and the European Commission to cooperate more closely on a “life cycle approach” for new innovative medicines. The industry has responded by supporting the adoption of new voluntary measures to improve access to medicines in Europe in order to ensure that the single market results in equal access and fair prices, based on ability to pay.

Patients

Concerns about drug pricing have also made it onto the political agenda in Europe, where in recent years the European Council has linked the economic crisis to healthcare spending, and called for cooperation between the European Commission and national governments to develop “strategies to manage spending on pharmaceuticals and medical devices, ensuring equitable access to effective medicines within sustainable national healthcare systems”.

For government to take a more overt role in price negotiations would be complicated. Despite this, the continued high media and political profile given to drug prices creates an environment in which legislation (state or federal) that seeks indirectly to contain prices becomes more likely. Early indications of this are already visible and include, amongst other things, demand for transparency on retail mark-ups and how research and development (R&D) costs are linked to end price.

Europe: Politics and Moves to Multi-Country Buying

Concerns about drug pricing have also made it onto the political agenda in Europe, where in recent years the European Council has linked the economic crisis to healthcare spending, and called for cooperation between the European Commission and national governments to develop “strategies to manage spending on pharmaceuticals and medical devices, ensuring equitable access to effective medicines within sustainable national healthcare systems”.

There is a paradigm shift, with less attention now being paid to the science of a drug and more on how it will economically affect health systems.

There is increasing acknowledgement about the need to involve patients, and also that they need training and clear information about different processes, regulatory affairs and science to be properly engaged.
arena. HIV advocates, for example, have fought to ensure that at least one drug per class is included in treatment options and have been successful in ensuring that the protected classes remain in Medicare Part D. Problems still remain. Prescription drug benefit plans traditionally include a three-tiered drug formulary, with co-pay limits for each tier, but health insurers are increasingly moving treatments to “specialty tiers”, with a 40-60 percent co-pay. Additionally, insurers, for example, are using their discretionary powers to block third-party, non-profit assistance programmes that cover high-cost medicines, in ways that result in the exclusion of people with expensive conditions.

Legislative efforts are underway at the state and federal levels to limit these practices.

Physicians and the Creation of “Drug Valuation Tools”

These developments have been aided by the growth in drug valuation tools. Dr Peter Bach of the Memorial Sloan Kettering Cancer Center is one of a handful of physicians and other experts pioneering the development of tools to help clinicians choose the most appropriate and cost-effective therapies. Bach’s DrugAbacus, which evaluates cancer therapies against six criteria to determine cost-effectiveness, is specifically designed to trigger a wider debate about what factors should influence drug pricing. Physician associations and clinical guideline-setting authorities also began weighing in. The American Society of Clinical Oncologists (ASCO) launched a Value Framework that compares new cancer therapies on the basis of their clinical benefits and toxicity. Alongside this “net health benefit” score, listed drug purchase costs are presented, helping clinicians and their patients to choose wisely.

Meanwhile, the National Comprehensive Cancer Network (NCCN), widely recognised in the US as the standard-setter for clinical guidelines in oncology, has become the latest institution to introduce cost into its assessments. A compendium of drug costs – not just the price of the medicine, but associated costs as well, including for administration, hospital costs and/or toxicity monitoring, was published in October 2015 as one of its “Evidence Blocks”: the so-called “Affordability of Regimen” block for evaluating therapy choice.

To be fully effective, however, any value framework should also be informed and guided by a systematic inclusion of patient perspectives throughout its development and implementation. Patients will have unique – and vitally important – knowledge, perspectives and experiences that are different from those of clinicians, researchers, payers and pharmaceutical companies.

The Role of Investors

Investors play an often-overlooked role in drug pricing. Investors in pharmaceuticals are heterogeneous. They include hedge fund and private equity investors; large, short-term programme traders who may hold stocks for days or less; as well as longer-term asset managers and asset owners, and bond holders. Despite this diversity, pharma, in common with other equity classes, is feeling pressure to perform against short-term imperatives by investors who see pharma stocks as a trading opportunity rather than a long-term investment option. This puts pressure on pharma to seek the maximum possible price at launch, even in the face of concerns about public and payer backlash.

Following a period of low R&D productivity, investors are feeling more optimistic about pharma innovation than they have for a while, but they realise that the growing societal disquiet about drug prices needs careful monitoring.

“When the smoke clears around these drug valuation tools there will be a variety of sources from which to draw for more informed negotiations.”

“I still think that innovative drug discovery is an exciting place to invest money. Opportunity for innovation has more potential than ever before.”
Some remain phlegmatic, arguing that innovation will always command a premium. Others are watching pricing developments with a warier eye, and hoping companies will convincingly distinguish between breakthrough and incremental innovation, creating headroom for premium prices. In this case, though, some argue that even breakthrough innovation should be priced more judiciously, cautioning against the risk of payer backlash posed by the year-on-year increase in average price of specialty pharmaceuticals, of 25 percent in 2014 and 16.8 percent in 2015 according to Express Scripts.\textsuperscript{xiii}

Still others are watching developments with more concern about their longer-term consequences. These investors are fearful that extreme pricing behaviour is introducing extreme risk to the pharma market. This group argues that the current pricing models are not sustainable and want a new equilibrium. They point to developments such as pooled European procurement, growing patient activism, the politisisation of pharmaceutical pricing and the increased interest in real-world evidence as early signals of more profound changes in the pricing environment. As a result, they are increasingly looking for evidence that companies are taking active steps to address societal concerns.

It is not only this group of investors that is concerned about the impacts on the rest of the industry of the highly publicised, egregious price inflation applied to decades-old treatments undertaken in 2015 by Turing Pharmaceuticals and Valeant Pharmaceuticals. Investors are now largely united in the belief that this business model, which, according to the Financial Times, some experts described as “a toxic mixture of outrageous price increases and unorthodox sales tactics”, has had its day. Therefore they were relieved that industry’s associations were quick to distance themselves from these approaches.

\textit{Capital markets really want a soft landing on pricing; we don’t like the uncertainty. The ideal is for pharma to find a self-regulating equilibrium. If not, they’re inviting regulation down the line.}”

**Conclusion**

**Pricing Pressures Not Going Away**

Investors have every reason to scrutinise developments carefully. Pricing pressures are not going away. In the US, mainstream medicine prices are rising by 5-6.5 percent a year according to CVS and Express Scripts.\textsuperscript{xxiv} Biosimilars are yet to make a big difference to the upward pricing pressure of specialty medicines, though they may do so when there are more on the market. Meanwhile, generic savings from the most recent wave of patent expiries – which should provide headroom for innovation – have for the most part already been realised. As a result, throughout the US and Europe health systems are taking matters into their own hands, and in ways that could, if poorly managed, further increase antagonism.

**Unstoppable Healthcare Trends**

Pricing pressures are not going away because healthcare is transforming. Under pressure from stuttering economies, squeezed budgets and ageing populations, healthcare systems are focused firmly on sustainability of current provision and therefore cost-effective outcomes. At the same time, pharmaceutical
innovation is blossoming, offering more targeted treatments and cures than ever before. Technological advances now offer unprecedented opportunities to dramatically improve diagnosis and management of disease, but not necessarily at reduced costs in the process.

Under these circumstances the relationships between pharma and health systems is changing. Payers now have the will, the tools and the ability to forge a new relationship with the pharmaceutical industry. Patients, for whom technology has also proved a game-changer, are set to become more engaged as they are burdened with higher co-payments or lack of access to the medicines they seek. They too are redefining their relationship with pharma and with the health systems that serve them. Further, others engaged at the delivery end of healthcare reform are focusing on health outcomes and the patient’s experience with care.

The pharmaceutical industry is well aware of these trends. Companies are engaged in new arrangements, including risk-sharing, and pay-for-performance and outcomes-based pricing. This trend needs to be consolidated, because if not, and the majority of stakeholders continue to define value unilaterally, they risk clashes when their definitions are challenged by others. A more collaborative attitude offers the prospect of agreement on what is wanted, needed and will therefore be paid for. The following Principles attempt to outline how this might be achieved.
The PharmaDiplomacy Principles for Collaborative, Mutually Acceptable Drug Pricing
Introduction to the Principles

To respond to the challenging pricing landscape, the PharmaDiplomacy Group sought to outline a process for the negotiation of drug prices that would go some way to recognise the multiple and competing interests of different healthcare stakeholders.

Aims

At the outset it was agreed that to support healthcare stakeholders to come to agreement on the value of medicines, which is reflected in price, any Principles for such a process would need to:

- Provide more targeted and better outcomes for patients and providers
- Address payer concerns about affordability and budget impact by providing greater certainty and control on price, data and volume
- Support and encourage innovation within the drug industry

Overarching Principles

In addition, they would need to be guided by a number of principles:

- Patient-centred: aligning incentives of all stakeholders to focus on patient outcomes
- Patient-inclusive: appropriately and systematically consultative of patient views
- Pragmatic: acknowledging stakeholders’ differing goals and biases while being simple enough to be useful
- Flexible/adaptive: sufficiently iterative to be adjusted and applied across many different systems (health, regulatory and geographic) within a highly dynamic therapeutic landscape
- Transparent: making discussions and data visible to and measurable by other stakeholders and, where there are feedback loops, to data providers

The Principles

The Principles, drawn up by the PharmaDiplomacy Group, outline the concepts, data and compromises required from payers, pharma and patients in order to move towards mutually acceptable drug pricing.

They build on the concept of value, while realising that it is a moving target. The value individuals in different parts of the system place on a drug will vary (as indeed “value” will be perceived differently across geographies and cultures).

The Principles are intended to allow users to adjust, or at least see, the input variables. They are presented as a list, but are in fact iterative; many items appear in more than one place, and should be cross-referenced when being read and applied in practice.

“Pricing” refers throughout to net prices, not list prices; the Principles accommodate but do not specifically seek to address individual systems’ discounting or rebating customs. They use outcomes and therapeutic area (TA) costs to help determine how to reach mutual acceptance of that pricing. They identify three principal “touchpoints” along the drug development timeline where discussions could make the most difference: (Pre) Phase II Dialogue, Around Launch, and On-Market Price Review. These are important indicative touchpoints but they are not exclusive and can be adapted. For example, initial contact could be established even earlier, or discussions could extend post patent expiry.

At each point along this timeline, the Principles identify items for discussion and agreement among stakeholders that could lead

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3. See Glossary for definitions of terms used in PharmaDiplomacy Principles.
to fairer and more acceptable pricing – generated less by who has the upper hand in negotiations today, and more by agreeing what is beneficial for all parties in the future. They acknowledge the importance of the patients’ views and concerns, and outline possibilities for engagement in the process. Some therapy areas have more established patient-group representation than others, making this kind of patient engagement more straightforward (but also giving rise to the risk that the needs of some patient groups may be unfairly advantaged). These discussions encourage continuous engagement among stakeholders in ways that, ultimately, help to build trust.

The Principles are designed as a tool, more likely to be applied to individual (high budget/impact) drug candidates, and in the process may build trust more broadly. Indeed, the Principles can be applied across portfolios or therapy areas. They require a common baseline agreement on aims, but do not stipulate that all items be addressed, in all cases, in order to reach mutually acceptable pricing. Discussions around a drug or drugs’ impact and perceived value require time and resources, from all sides. The goal is to provide a concrete tool to help initiate and guide this process with the expectation that this could help to develop trust and greater understanding on all sides, independently of specific products, thereby avoiding inflammatory pricing situations in future. To be truly sustainable the Principles would need to lead to sufficient agreement on outcomes and how they are measured, to make them applicable by multiple payers across different geographies.

Each item in the Principles is colour-coded to reflect the fact that some requirements will be tougher to meet than others, and that the level of challenge will vary depending on the health systems and pharma players involved as well as the particular drug or therapy area under discussion. Some discussion items may not apply to certain drugs or therapy areas at all.

**Green items** are proposals that face minimal hurdles and thus could, in theory, be implemented immediately. On their own, these are not enough to achieve mutually acceptable pricing, but they could contribute to rebuilding trust among stakeholders. In many cases, they simply involve protagonists meeting, engaging and addressing the topics.

**Amber items** are proposals that face some challenges, but surmountable ones, at least under certain circumstances. Different stakeholder groups may choose to tackle one or more of these items as confidence builds, and/or as a function of the particular drug or drugs under discussion. Some amber items may require green items to be underway/completed in order to succeed.

**Red items** are the most challenging issues and are likely to demand buy-in from a wider range of stakeholders (e.g. regulatory or legislative authorities) and/or significant cultural change within particular groups. These items are aspirational today, but could become more tractable as green and amber items are addressed in a widespread fashion. Many red items are predicated on some degree of discussion already having taken place among stakeholders – and on most green and some amber items having been addressed.
(Pre-) Phase II Dialogue

Dialogue, involving pharma, payers (public or private depending on market), patients and potentially HTA as well, should occur during Phase II or even earlier; ideally before Phase III trials are initiated. It would complement the current “early scientific advice” offerings from European Medicines Agency (EMA) and US Food and Drug Administration (FDA), and parallel the Adaptive Pathways initiative.

**MINIMAL HURDLES**

- Pharma, payers and HTA discuss extent/limitations-validity of existing therapy area costs (including whether they are based on appropriate care) and how potential drug may influence/impact them.
- Patient representatives provide views and experiences on access to existing medication, outcome expectations, and limitations of existing therapies.
- Stakeholders agree to maintain open dialogue as data emerge.

**SURMOUNTABLE CHALLENGES**

- As permitted by law or within regulatory frameworks, pharma, payers, patients, prescribers and physicians discuss planned/meaningful Phase III endpoints; the drug’s purported added-value; potential real-world outcomes; and position relative to existing therapies.
- Determining the meaningful outcomes patients care most about will require consideration of how to fairly and practically take into account patient and (where possible) societal views at this stage.
- Pharma and payers agree current therapy area cost range and how, broadly, to define costs for certain areas, such as hepatitis C and/or certain cancers, allowing reasonable adjustments/margin of error.
- Pharma, payers and patients discuss possible approaches to a situation where the drug’s impact on therapy area costs may not be apparent for several years (e.g. pay for performance, annuity funds). Given the portability of patients between payers in the private market in the US, this may most feasibly be done first in the Medicare system, where there is greater incentive to take a longer-term view.
- Pharma and payers assess competitive landscape and the implications of similar innovative therapies reaching the market within a similar period.
- Pharma, payers and patient groups explore feasibility of appropriate risk-sharing and adaptive pilots (outcomes-based, adjustable, pay-for-performance agreements). Agreements are made known within participating organisations.

**MOST CHALLENGING**

- Pharma, patients and payers agree scope of costs (e.g. social care/economic productivity/patient quality of life) and timeframe for calculating them for key TAs, including chronic diseases with co-morbidities.
- Pharma, patients, payers, providers and politicians determine how drug-related cost savings are calculated and can be shared across different parts of the healthcare system (e.g. via an accumulating savings “fund”, or annual re-distribution).
- Pharma, patients, payers and HTA address how to deal with drugs used across more than one therapy area where costs/outcomes may differ.
Around Launch

These discussions take place in the lead-up to regulatory approval. The items below are designed to help pharma, payers (public or private, depending on market) and providers (where appropriate) with patient input, to agree on a price range and pricing strategy that is mutually acceptable, affordable and sustainable.

**MINIMAL HURDLES**

- Pharma, payers and patients agree on a process for improved collaboration, and for defining outcomes of primary interest and standardised metrics; this should include analysis of budget impact, structures for data capture and sharing associated costs.

- Pharma, payers and patients agree that the price of innovations should take into account some combination of standard of care (SoC), existing therapy area costs (and calculations of the drug’s impact thereon), unmet needs and outcomes.

- Pharma and payers, in consultation with patients, consider and test shared payment set-ups that measure outcomes, e.g. pharma contributing funding to feasibility stage of aligning and agreeing outcomes of primary interest.

- Pharma, payers and patients jointly take into consideration current and future competitive landscape and its implications for pricing.

**SURMOUNTABLE CHALLENGES**

- Pharma, patients and payers engage to more frequently align the clinical value and volume levers (e.g. appropriate patient segments via severity, characteristics, etc.) in appropriate therapy areas: i.e. higher volumes/lower price predicated on appropriate payers being involved.

- Pharma, patients and payers agree on a reasonable margin for error and timeframe for calculating drug’s impact on therapy area costs, considering new and emerging data sources and methodologies as appropriate.

- Patients, payers, pharma and providers come to data-sharing agreements which commit to providing patients with analysis and feedback.

- Pharma, payers and providers exploit new technologies to facilitate outcomes data capture and to track volumes.

- Pharma, patients and payers discuss and determine how a drug’s estimated impact on therapy area costs, its HTA-determined added benefit related to SoC, and eventual outcomes should relate to price range, taking volumes into account where practicable (and establish any exceptions to this framework).

- Pharma and payers consider how changes in SoC may influence price; and explore potential compromise pricing options, e.g. in case of genericisation.

- Pharma and payers engage creatively in risk-sharing deals and/or incentive-based deals which reward certain outcomes over given timeframes. Savings accrued should benefit payers/insurers, and patients should be informed of how clinicians and providers are being incentivised.

**MOST CHALLENGING**

- Pharma and payers, with patient input, agree on relative weighting and influence on price of a drug’s: a) estimated short- and longer-term impact on TA costs; b) HTA-determined added benefit related to SoC; c) eventual patient-centred and other clinically relevant outcomes.

- Pharma, payers and patients should consider impact on pricing of additional indication approvals during drug’s life cycle, perhaps building on early experience of indication-specific pricing, and ensuring metrics are appropriately aligned. Alternatively, they could consider price adjustment based on averaged weighted use or a treatment “package” involving more than just medicines.

- Explore price “banding” or advice-price parameters for certain product categories and/or for individual drugs whose use is likely to expand, allowing greater predictability for both payers and pharma. This may draw on aspects of existing tiered (usually added-value-linked) reimbursement systems (US, EU). Such arrangements would need to permit changes to dosing/indications.
On-Market Price Review

On-market price review may take place at agreed intervals for certain drugs, e.g. high-budget items, drugs whose efficacy/cost-benefit is questionable, and/or where external circumstances change (e.g. disease prevalence, competitive landscape changes, etc.) It may also allow adjustments to take into account drugs’ value accruing over time (e.g. new indications or improved data sets), and/or additional evidence (or lack of evidence) of effectiveness. Ideally such a process would replace price increases that appear unsupported.

MINIMAL HURDLES

- Payers, pharma and patient groups confirm (or reiterate) meaningful outcomes (contingent on earlier discussions having taken place), having identified and agreed enabling technology for the collection of outcomes data for the purpose.
- Formalise inclusion of patient voice in review process; establish criteria that patient organisations and representatives must meet to ensure independence and representation.
- Pharma, payers, providers and relevant patient groups state their commitment to the principle of on-market price adjustment, in both directions, according to outcomes, and taking into consideration premiums, deductibles, co-pays, insurance, etc. In the US, this may require changes to mandated price requirements.

SURMOUNTABLE CHALLENGES

- Pharma and payers embrace wider use of volume lever in some therapy areas as a substitute for price increase in case of positive outcomes.
- Pharma, payers and providers engage more frequently and creatively in risk-sharing deals and/or incentive-based deals which reward certain outcomes over a given timeframe. In the US, this may require changes to mandated price requirements.
- Pharma, payers and providers agree practicable review timeframes and structures for sharing cost of data review/collection across key therapy areas and/or for specific high-impact products. Patients should be engaged to understand potential impact on access.
- Pharma and payers discuss appropriate price adjustments (and/or the practicalities of indication-specific pricing and alternatives) if a drug is approved for further indications.

MOST CHALLENGING

- Payer, provider and pharma work to improve the frequency and minimise the resource/implementation burden of multiple on-market drug reviews; e.g. priority review for certain drug types and/or therapy areas; grouping certain drug classes for review.
- Pharma, payers and patients agree on a price-adjustment plan for when SoC goes generic, and/or implement interim price plan in the face of inconclusive outcomes data.
The PharmaDiplomacy Principles are intended – by systematically and iteratively acknowledging the changing perception of value the longer a medicine is in use – to foster agreement on fair value and price. They seek to be a guidance tool to come to mutually acceptable pricing. The creation of the Principles themselves – a collective effort of different stakeholders with, at times, competing interests – demonstrated this potential. In the process understanding, was increased, negotiating skills were honed and much common ground was identified. The Principles can be applied today and, through similar processes, trust between pharma and its stakeholders can be built. However, the Group was also conscious that changes to the external operating environment could make collaboration significantly faster and easier. They identified the following key enabling factors that could achieve this:

**Leadership**
Leadership is needed to ensure that the right people are at the table; that they are empowered to negotiate; that they model the desired behaviours; and take actions to build confidence. In a conflicted environment the leadership of a sufficient number of healthcare organisations will have to be prepared to call for aligned incentives, credible data-sharing plans and risk-sharing agreements, and to require their staff to deliver these. This leadership needs to demonstrate the value of cooperation to others in the system.

**Policy Guidance**
A strong policy steer on healthcare priorities would also help. Though controversial, and challenging to achieve, a clear articulation of public healthcare goals would enable a more rational approach to mutually acceptable drug pricing. The definition of desired outcomes by disease state, and the inclusion of reference to the need for a longer-term (e.g. ten years or more) perspective on the value and cost-saving potential of new drugs, are vital for true estimation of drug value.

**Regulatory and Legal Adjustments**
In some places – the US in particular – regulatory and legal adjustments are needed to permit different stakeholders to adopt a diplomatic approach to their negotiations. For example, it is currently prohibited in the US for pharmaceutical firms to discuss potential drug outcomes with payers before such outcomes have been demonstrated in clinical trials. Neither are multiple drug firms permitted to engage in appropriate and constructive dialogue around the principles and boundaries of mutually acceptable drug pricing. The regulatory system also needs to continue to develop its initiatives to better recognise patients’ voices and to better define how patient inputs influence the system. Such regulatory changes would allow – and indeed encourage – payers, patients and industry to discuss unmet needs, the limitations of existing therapies, and the potential value of new types of innovations.

**Enhance Patient Group Capacity to Engage**
For the Principles to reach their full potential, the confidence, engagement and participation of patient groups will also need to be enhanced. To meaningfully participate in such processes, patient groups will need to be resourced and supported. They will also need independent funding to build their research and advocacy capacity as well as to allow them to better capture and
use patient-reported data. This need is growing as patient involvement in the definition of acceptable outcomes becomes increasingly influential.

**Differentiation between Companies**

PharmaDiplomacy revealed a desire amongst payers to find a way to legally and fairly differentiate between pharma companies. Some argued that payers should be permitted to opt for medicines produced by companies that help them address patient outcomes and their budget constraints. This “reward” for good behaviour could take the form of being able to opt for medicines produced by such companies over others – in situations of clinical equivalence – or more systemically, by awarding companies with a stamp of approval, like that received by “Authorised Economic Operators” who trade goods with the EU. At the moment, neither payers nor the market reward companies for seeking better alignment with patient and health-system needs.

**Big Data**

For the PharmaDiplomacy Principles to have greatest impact they will need to tap into the ongoing revolution in the collection, organisation and acceptance of patient data. Participants in the dialogue will need to be able to build the use of this data into their consultation and negotiation processes. This new source of information could significantly enhance the nature, quality and quantity of data used to develop or evaluate medicines. These processes are also increasing transparency, which could expose opaque mark-ups and disincentives to reduce price that exist within current healthcare systems.

**Neutral Convenor**

The final enabler of improved collaboration is the presence of a neutral convenor capable of bringing together the relevant parties, and assisting the group to overcome mistrust in order to be able to work through the practical requirements of a negotiated solution. Neutral, trusted convenors will be needed to facilitate ongoing discussions about fair and appropriate pricing, based on agreed definitions of value.
Pricing debates are dovetailing with broader societal discussions about how to allocate health expenditure. These include how to balance demand for high-cost pharmacological treatments that can prolong life by weeks or months with the need for chronic and palliative/end-of-life care centred on patient comfort, and how to invest in treatments or prevention methods that can save future healthcare costs. They are highly politicised, controversial and sensitive issues, which politicians have proved reluctant to tackle. These debates are happening in both Europe and the US. Resolving them in the US is particularly problematic, though, due to the fragmented nature of the markets (with commercial, Medicaid and Medicare segments), served by multiple public and private sector organisations, some of which operate in only a single part of the healthcare value chain: pharmacy benefits managers (PBMs), for example, are primarily concerned with the drug component of healthcare.

The practical and political difficulties in resolving these issues mean that the focus on pricing is likely to continue and, unless action is taken, debates over drug pricing will become increasingly acrimonious. Pharma and payers are taking steps to come to mutually agreed pricing, through risk-sharing and market access agreements (drug-specific payer-pharma access deals, mostly in Europe), and pay for performance. It is vital that these efforts do not remain a minority activity. If the majority of pharma and payers continue to regard drug pricing as a zero-sum game, it will be much harder to achieve mutually acceptable compromises on how to practically quantify value and to ensure that it is appropriately adjusted as usage evidence emerges. This matters. Heightened antagonism is already leading to entrenched positions as a result of which patients are the principle victim.

Despite – or perhaps because of – the growing acrimony, many participants in the conversation were enthusiastic about the opportunity that PharmaDiplomacy offers to engage in a positive conversation, focused on solutions. The PharmaDiplomacy Principles cannot solve all the causes of mistrust between pharma and its stakeholders. They can, however, encourage protagonists – patients, providers, payers and pharma – to build on diplomatic approaches to achieve mutually acceptable results. In demonstrating this approach to compromise and engagement, which accommodates all stakeholders, they point to ways of engaging that could be applied to other sources of mistrust. We hope, therefore, that they are widely used, both as a means of achieving mutually acceptable outcomes on pricing, and also of improving trust. Achieving this will benefit everyone – and patients above all.
References


xiv. Ibid.
Appendices
Appendix A: About the PharmaDiplomacy Dialogue

PharmaDiplomacy was a US/EU leadership initiative seeking to overcome the trust deficit between health systems and the pharmaceutical industry in order to ensure that effective, affordable and innovative medicines get to patients who need them. The PharmaDiplomacy dialogue aimed to:

- Identify where and how trust is being eroded.
- Identify pathways that could be taken to achieve better outcomes, and take practical action to model them.
- Consider the mechanisms that could hold agreements in place and avert new potential flashpoints before they escalate.
- Undertake outreach to engage their peers and colleagues as well as other key stakeholders in taking this agenda forward.

Phase One – Agenda-Setting (November 2013 – January 2014)
- Defined a conceptual framework on trust and diplomacy.
- Identified flashpoint issues that need to be addressed.
- Considered two flashpoints: data analysis and orphan drugs.

Phase Two – Solution-Building (February 2014 – July 2014)
- Continued exploration of underlying causes of mistrust.
- Considered two further flashpoints: pricing and patient engagement.
- Explored the role of investors.

- Focused on pricing as a primary contributor to mistrust.
- Initial development of a value-focused drug pricing framework.
- Considered the leadership requirements of the Group.

Phase Four – Outreach (March 2015 – November 2015)
- Agreement of draft “Checklist for Collaborative, Mutually Acceptable Drug Pricing” (which later became the PharmaDiplomacy Principles).
- Consultation events with organisations and fora in US and Europe.

Phase Five – Conclusions and Dissemination (December 2015 – March 2016)
- Final PharmaDiplomacy workshop to draw conclusions.
- Publication and dissemination of findings of the PharmaDiplomacy dialogue.

Meteos dialogues are funded by participant fees on a not-for-profit basis and through the provision of in-kind research and information sharing. As we are committed to ensuring that all relevant stakeholders contribute to the dialogues, we provide some spaces on a non-fee basis. Such participants typically pay their own expenses. All participant voices are of equal weight in the dialogues. PharmaDiplomacy is funded on this basis.
Appendix B: Glossary of Terms

Drug Development Timeline

Phase I: Small safety trial, usually among healthy volunteers and using low doses.

Phase II: Tests dosing, efficacy and side-effects over a short period among sick patients.

Phase III: Tests efficacy, side-effects and dosing among a large group of patients, over a longer period (sometimes up to a year), and usually compares the treatment to existing standard of care.

Phase IV: Assesses the safety, effectiveness and side-effects of a medicine after it has been approved by regulators and while being used in practice.

Approval: FDA (US) or EMA (EU) authorises the drug to be marketed, sometimes with conditions attached.

Patient Input

Patient views and input into drug R&D and commercialisation is growing, helped by greater awareness, empowering new technologies and an increasingly mainstream debate over pricing, value and access. Yet patient voices are multiple, ranging from the individual to the highly organised group. Fairly taking into account the broadest range of viewpoints isn’t straightforward, but awareness of the broad categories of patient voice may help.

Consumer: Healthy individual who moves in and out of the health system according to need.

Patient: Someone dependent on the health system for a health condition or disease during their life.

Patient groups/unaffiliated communities: Groups of patients with the same or similar conditions who interact, typically online, to share views and information (e.g. PatientsLikeMe).

Patient advocacy organisations: Bodies that seek to represent patients with given condition(s) and provide a unified voice for this community. Advocacy groups seek support for their mission and programmes, which may range from patient education/awareness to support services, influencing health policy issues, and/or funding treatment R&D.

Institutions

Accountable Care Organisations (ACOs): Groups of healthcare providers (physicians, hospitals) in the US which collaborate to provide cost-effective care and are paid by results, not per procedure.

Commercial insurers (aka Private Market): For-profit health insurers, e.g. Aetna or UnitedHealth in the US, and BUPA in the UK.

Employers: Employers often provide health insurance for their employees, using commercial insurers; a few are self-insured.

Government payer (Public Systems): National health payer, e.g. National Health Service (UK) or, in the US, the Centers for Medicare & Medicaid Services (CMS).

Health Technology Assessment (HTA): Health Technology Assessment bodies are used by national agencies, e.g. NICE, to systematically examine the safety, clinical efficacy and effectiveness, and cost-effectiveness of a health technology.
Health Maintenance Organisations (HMOs): Organisations that arrange or provide care on a pre-paid basis for insurance plans or individuals.

Pharmacy Benefit Managers (PBMs): Administrators of prescription drug programmes similar to government insurance (e.g. Krankenkassen in Germany, Express Scripts in US).

Statutory health insurers: Non-profit bodies providing legally enforced health insurance in Europe.

**Pricing**

**Differential pricing:** Drug prices adapted to the purchasing power of consumers in different geographical or socio-economic segments. Differential pricing is regarded by some as an effective way to improve access to medicines in low- and middle-income countries. Its use is applied most frequently to vaccines, anti-retrovirals and contraceptives.

**International/External Reference Pricing (IRP):** The use of the price (or prices) of a drug or therapy in one or several countries to set or negotiate a price for the same product in another country. The number of countries included in any nation’s reference “basket” varies widely, from one to more than 30. The most widely-referenced countries are France, followed by Germany and the UK. IRP can result in manufacturers maintaining a high public “list price” (official price, before any discounts or rebates) in commonly referenced markets such as Germany or the UK, and explains why these discounts are often confidential. IRP can affect drug firms’ willingness to engage in initiatives towards fairer, more value-based pricing in particular markets, for fear of a wider, downward price spiral.

**Reference pricing:** A reimbursement system used to control costs, that involves grouping drugs according to some equivalence criteria and setting a reference price for each group. The group criteria may be defined narrowly (e.g. chemical equivalence) or more broadly (e.g. all drugs treating a given condition). Payers then reimburse no more than the reference price for any drug in that group.

**Tiered pricing:** Sometimes used interchangeably with “differential pricing” – e.g. selling the same medicine at a different price in different countries, according to ability to pay. In the US, tiered pricing is used to refer to different levels of patient co-payments required for drugs covered by insurance. Tier 1 drugs generally include generic medicines, and have the lowest co-pay; Tier 2 is a higher co-pay and includes “preferred brands” – e.g. branded drugs that are prioritised due to their effectiveness, a favourable price deal or both; Tier 3 drugs require higher co-payments and may be non-preferred brands or new medicines whose safety and effectiveness are uncertain; Tier 4 require the highest co-payments and include specialty medications.

**Risk-sharing agreements:** An agreement between a payer and a pharmaceutical, device or diagnostic manufacturer where the price level and/or nature of reimbursement is related to the actual future performance of the product in either the research or “real world” environment, rather than the expected future performance.

**Elements that Contribute to Definition of Value**

**Biomarkers:** Traceable substances that provide a measurable indication of disease state or of pharmacological response to a particular drug. A well-known example is Prostate Specific Antigen (PSA), used as a proxy for prostate size. Not all diseases have reliable biomarkers, but where available they can be used as a measure of a drug’s effectiveness.

**Comparative Effectiveness (CE):** The relative effectiveness of two (or more) types of treatment for the same disease. Comparative effectiveness research compares the results of one treatment approach with those of another – e.g. two different drugs, or drug treatment versus surgery, for example.
**Cost-Effectiveness (of a treatment):** The comparison of the cost of a treatment to its health effects. Cost-effectiveness analysis helps find ways to allocate limited resources to achieve maximum benefit in a particular population. It is used to determine whether a drug or intervention provides value for money, including by HTA agencies on behalf of national health systems.

**Efficacy (of a treatment):** How well a drug or treatment works under the best possible conditions – i.e. when taken properly among a pre-selected group of patients.

**Effectiveness (of a treatment):** Whether and how well a treatment works in real life – when taken in normal, everyday-life circumstances as opposed to when part of a controlled clinical trial.

**Incremental Cost-Effectiveness Ratio (ICER):** The ratio of the change in costs to the incremental benefits of a treatment. Cost-effectiveness in the UK is expressed by NICE as “cost-per-QALY”. For instance, the ICER for Sovaldi, as estimated by NICE, ranges from £9,415 per QALY gained to £109,526 per QALY gained, depending on the patient sub-group.

**Quality-Adjusted Life Year (QALY):** A commonly used measure of outcome or effect, the QALY is designed as a gauge of disease burden, including both quantity and quality of life lived. It is based on the number of life-years that a treatment would add, with years weighted according to disease burden (from 1=perfect health to 0=dead).

**Patient Reported Outcomes (PROs):** Information and data about a particular treatment, which are collected directly from a patient, typically via questionnaire or interview. The questions typically cover symptoms, functioning/disability, quality of life, and general health status and perceptions. PROs are used as part of clinical trials. Several validated, reliable PRO tools exist, often covering health-related quality of life and/or healthcare evaluations, and may be included in drug approval submissions. They are increasingly being used to monitor post-market-approval outcomes when the therapy is used in the real world outside of a clinical trial.

**Real World Evidence (RWE):** Data and information gathered from a real-world setting, rather than generated under controlled, clinical trial conditions. RWE encompasses many different types of data, from a variety of sources. It may come from disease registries, insurers’ claims data, electronic medical records, or be generated via pragmatic clinical trials, patient surveys, questionnaires or observational studies. RWE is valuable because it provides information about actual treatment outcomes, and thus can help improve those outcomes.

**Standard of Care (SoC):** A description of the diagnostic and treatment process that a clinician should follow for patients with a particular condition. It varies by country and/or health system and is used somewhat loosely, without a precise medical definition. SoC is typically understood to correspond to (or at least derive from) clinical Principles supported by evidence-based medicine, though the link is informal, and some argue that the term should as a result be used with more caution.

**Surrogate endpoints:** A replacement for clinically meaningful endpoints (such as a major cardiovascular event, or death) when endpoints are difficult to measure or ethically inappropriate. Biomarkers are sometimes used as surrogate endpoints in clinical trials.

**(Trial) endpoints:** Target outcomes that a clinical trial is trying to measure, e.g. reduction (of a pre-defined size) in blood sugar levels or in sustained viral load.
Appendix C:
Trust Bibliography


http://www.amazon.co.uk/Thin-Trust-Essential-Primer-Building-ebook/dp/B001PBEXFQ


The PharmaDiplomacy Dialogue was directed by Sophia Tickell and Becky Buell. Other core team members were Melanie Senior, who provided invaluable research, writing, design and analytical capacity throughout the project, Sarah Cassidy and Zoe Scabbiolo, who provided extremely high quality project management, research, logistics and networking support, and Cassie Painter and Maggie De Pree, who provided further research support.

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Sophia Tickell and Becky Buell