Pilots of multi-country, multi-stakeholder consultations in drug development: promoting clarity on sources of medicinal value

Introduction

Healthcare leaders representing multiple roles, institutions and EU member states recently completed the first set of three pilots of multi-country, multi-stakeholder consultations in drug development ("the pilots"). The purpose of the consultations is to improve clarity and alignment among diverse stakeholders regarding what constitutes a medicine's value and what evidence is required to demonstrate that value most effectively. Participating institutions included regulators, health technology assessors (HTAs), payers and pharmaceutical companies; patient advocates and medical experts provided additional input. Tapestry Networks co-designed the consultations with participants, building on experience with existing early-advice processes and in accordance with principles and guidelines for public-private networks. Please see Appendix 1 for Tapestry Networks principles for working with public-private networks.

Table 1 (p. 3) provides an overview of the institutions contributing to the pilots.

Pilot participants were motivated by an urgent need to improve the ability of health systems to provide the right medicines to the right patients at the right time and at reasonable cost. A senior regulator noted the scope of the problem: *"We spend approximately $60 billion every year to put on the market five or six new molecules that are first-in-class ... that means that the cost of drug development is absolutely terrific, and we have to do something about that."* An HTA leader underscored this need by noting that, given current financial constraints, *"effective new agents are appearing that we are unable to fund."* An industry leader concluded, *"The status quo is not working and is not sustainable. If we are going to succeed in the future in bringing effective and cost-effective drugs to patients, then a greater alignment and co-operation will be required between all parties."*

Pilot participants believe that the drug-development process is more likely to deliver medicines and supporting evidence that meet the needs of various stakeholders if they are willing to engage in a dialogue with each other. An HTA participant advised, *"We need to build up a common language between regulators, reimbursers and payers."* Accordingly, the pilots provide a forum for drug developers to receive integrated feedback on the expected value of a medicine under development and how best to demonstrate that value, while encouraging mutual education among all stakeholders.

The pilots also present an opportunity to create a public good in the form of a shared basis of knowledge and experience regarding the benefits and limitations of a multi-constituent approach to informing drug development. This experience can inform and complement other on-going experiments at combined regulatory and HTA advice at the country level and combined HTA advice across multiple countries. These initiatives highlight the increasing recognition among health systems that a more integrated approach can yield benefits to all stakeholders.

The pilots arose from the efforts of the European Healthcare Innovation Leadership Network (the "Network"), which has been on a multi-year journey to address the complementary goals of improving patient health outcomes and enhancing the climate for innovation, while acknowledging pressures to control healthcare costs. Network members have focused on developing more differentiated market access, pricing and reimbursement solutions to reflect – and reward – the true health and economic value that new treatments deliver.[1]

In 2009, the Network launched disease-specific working groups in type 2 diabetes and breast cancer – diseases chosen for their high unmet needs and impact on healthcare systems – to focus these discussions and develop a shared understanding of value across stakeholders. The working groups agreed that both public- and private-sector stakeholders in the drug development system lack sufficient information to support and assess the development of innovative medicines that address unmet needs at reasonable cost. They recommended the creation of multi-country, multi-stakeholder consultations as a way to create greater clarity in value assessment to inform development decisions.

Appendix 2 contains a list of Network members and working group participants.

A pilot participant representing patient perspectives reflected on the importance of this initiative:

> *"It is very important that regulators and reimbursement agencies talk to each other and are both involved in these early stakeholder consultations. It is such a waste of money when, as we have seen so many times, a medicine is registered through [the European Medicines Agency], but then the reimbursement agency concludes that the data is insufficient to show added therapeutic value. It's embarrassing. It is very sad for a company that puts a lot of money into its programme, and it is disappointing and confusing for patients. It was a great added value of this exercise that regulators, reimbursers and payers were in same room and learned from each other to understand how all stakeholders approached the issues."*

This document describes the call to action and rationale behind the pilots, provides an overview of the pilots' design, reports on the outcomes of the first set of consultations and reflects on what has been learned to date.[2]

Table 1. Institutions contributing to the pilots

France
- French Health Products Safety Agency (AFSSAPS)
- Economic Committee on Health Care Products (CEPS)
- French National Authority for Health (HAS)
- Transparency Commission

Italy
- Italian Medicines Agency (AIFA)

The Netherlands
- College of Health Insurances (CVZ)
- Dutch Diabetes Association
- Netherlands Breast Cancer Association (BVN)
- Menzis
- Netherlands Insurance Company (UVIT)

Sweden
- Medical Products Agency (MPA)
- Swedish Association of Local Authorities and Regions (SKL)
- Swedish Breast Cancer Association (BRO)
- Dental and Pharmaceutical Benefits Board (TLV)

United Kingdom
- Medicines and Healthcare Products Regulatory Agency (MHRA)
- National Institute for Health and Clinical Excellence (NICE)
- National Health Service primary care trusts (Derbyshire County, Redcar & Cleveland, Stockton-on-Tees)

Europe
- European Medicines Agency (EMA)
- European Network for Health Technology Assessment (EUnetHTA) *(observer)*
- EUROPA DONNA, the European Breast Cancer Coalition *(observer)*

United States
- Food and Drug Administration *(liaison)*

Industry
- AstraZeneca
- GlaxoSmithKline
- Janssen Pharmaceutical Companies of Johnson & Johnson

The pilots are motivated by a shared sense that the current model of drug development is not meeting society's needs

The pilots represent a milestone in an effort that involves over 200 healthcare leaders from across Europe arising from the European Healthcare Innovation Leadership Network. Participants in this initiative have identified a number of challenges in the drug development process that limit the ability of health systems to deliver the right medicines to the right patients at the right time. These challenges include the following:

- **Scarcity of resources available to develop high-value medicines**
- **Costly failures of development programmes to demonstrate efficacy and added value**
- **Significant number of discrete evaluation procedures for new medicines across the EU that create different evidence and data demands for each stakeholder**

Participating healthcare leaders have concluded that creating a process across institutions to provide better clarity and alignment when measuring the value of new medicines would potentially limit late-stage failures and lead to more efficient and effective medicinal research. This, in turn, would help drive down costs to the healthcare systems and improve the quality of evidence available for healthcare decision-making. Participating healthcare leaders, working with Tapestry Networks, designed the pilots to achieve these objectives.

Resources to develop and fund high-value medicines are increasingly scarce

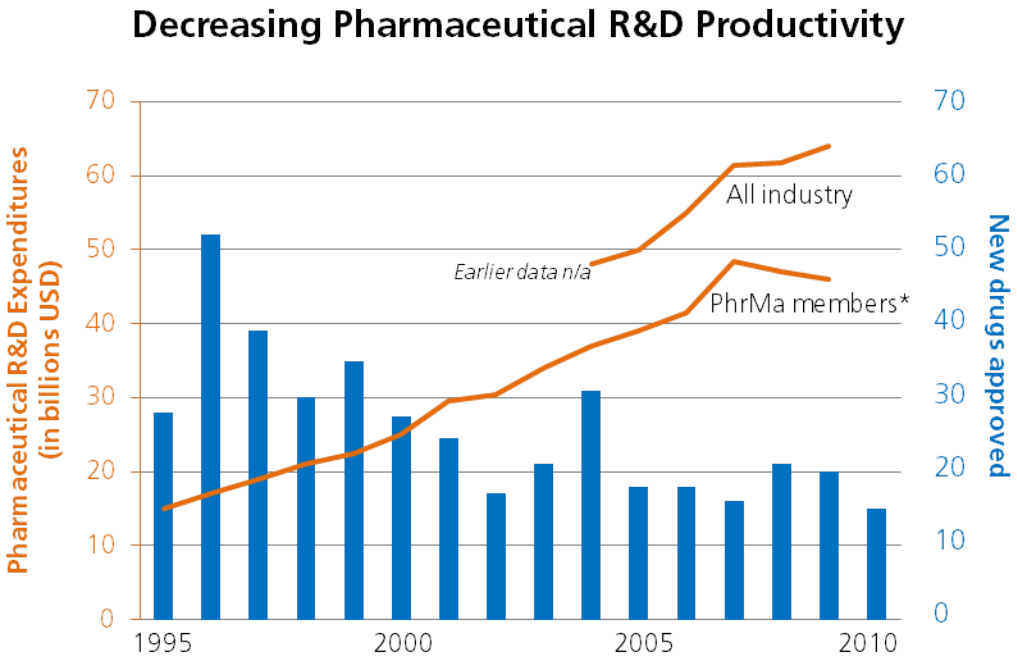
Both public and private spheres are experiencing a scarcity of resources for funding and rewarding innovation. An increase in the cost of developing new medicines, combined with reduced resources to pay for them, has tended to limit patient access to innovative new treatments. Meanwhile, the productivity of research and development (R&D) investment is itself declining.

Public healthcare systems are facing tightening budgets

Many European countries face large deficits and tightening budgets, highlighting the need to prioritise healthcare spending for all stakeholders. For example, the UK's National Health Service has been asked to find £20 billion of savings in the overall health budget by 2014.[3] Similarly, in 2010, Germany began to cut its annual healthcare spending by €3.5 billion[4] and France sought to cut over €2 billion.[5] As a result, one pilot participant said, payers *"face a decision today about how best to use limited healthcare budgets."*

Drug developers are facing tightening budgets

The worldwide recession, coupled with declining R&D productivity and escalating costs, have led pharmaceutical companies to cut back on the development of new medicines. In 2007, it cost approximately €1,059 million ($1,318 million)[6] to develop a new biological or chemical entity, compared with $802 million in 2001 and $318 million in 1987.[7] Despite the considerable investment in the development of new drugs, fewer medicines are being approved. (See graphic below.)



*Pharmaceutical Research and Manufacturers of America (PhrMa)
Sources: Food and Drug Administration; PhrMa; Adapted from the New York Times, *"Fewer New Drugs Gain Approval,"* 7 Mar 2011.

In part because of declining R&D productivity, even the most successful pharmaceutical companies recently have reduced their R&D budgets, closing research facilities and cutting jobs globally. For example, Pfizer is cutting $1.5 billion in R&D by terminating urology and internal medicine projects and closing its research facility in Sandwich UK,[8] and Merck is closing eight R&D facilities globally.[9] Last year AstraZeneca announced plans to save $1.9 billion per year by 2014 by cutting 8,000 jobs, including 1,800 in R&D, and ceasing research in a variety of disease areas.[10, 11] Across Europe, reinvestment of research-based pharmaceutical sales into R&D programmes climbed from 15.6% in 1985 to 20.6% in 2000, but fell back to 17.3% in 2009.[12] In this constrained environment, it is increasingly important for all stakeholders to anticipate which medicines are most needed and to focus scarce resources accordingly.

Development programmes often fail to demonstrate efficacy and cost-effectiveness

Several recent late-stage failures have called attention to the need for greater transparency in the drug development process. Greater clarity would increase the likelihood of success in later stages of clinical development and in obtaining reimbursement, while sending clearer signals to developers to terminate less promising programmes earlier. For example, in 2010, both Eli Lilly and Pfizer experienced late-stage failures in Alzheimer's drugs due to lack of efficacy,[13] and NICE gave negative recommendations for Novartis cancer and asthma medicines because the drugs were deemed not to be cost-effective.[14,15]

Late-stage failures and the difficulty of obtaining reimbursement illustrate the significant risk that companies face when developing new medicines. From the laboratory to the pharmacy shelf, it takes 10 to 13 years to bring a new drug to patients. Aggregate industry data indicate that of every 10,000 compounds that enter the drug-discovery stage, 250 will progress to the preclinical phase, 10 will reach clinical trials, and only one will receive regulatory approval for market launch.[16] Once launched, only three out of 10 medicines generate revenues that match or exceed their R&D costs.[17] Many drugs, particularly those with novel mechanisms of action or less established endpoints, fail because of a lack of demonstrated efficacy.[18] Other drugs gain regulatory approval but fail to demonstrate the significant added value needed for reimbursement. Given the steep odds in drug development, pilot participants have highlighted the importance of ways to *"avoid unnecessary surprises and wastage in development programmes."*

Fragmented requirements lead to delays in getting new medicines to patients

Getting high-value new medicines to the patients who need them is complicated by what one participant described as the *"different responsibilities of reimbursement agencies and the registration authorities,"* which create different evidence and data demands for each stakeholder. A successful new medicine must be supported by evidence to satisfy regulators, HTAs, payers, doctors and patients. Developers regularly cite the lack of transparency of post-registration requirements as a major barrier to patient access. A medical expert involved in the pilots noted in agreement that, *"It has taken an enormous length of time to get the good treatments that are developed into patients, and that process, I hope, will be shortened and made more accurate by better clarity among the requirements of stakeholders."* This delay is due in part to the frequent lack of adequate data for value assessment, as companies focus *"narrowly on the acquisition of data for the purpose of obtaining regulatory approval."*

Healthcare leaders have developed and piloted a process of multi-country, multi-stakeholder consultations to help overcome drug-development challenges

To address shared challenges to effective drug development, participating stakeholders and Tapestry Networks jointly designed a process for pilots of multi-country, multi-stakeholder consultations, informed by existing early-advice processes and input from key European healthcare leaders.

The pilots are defined by an agreed set of design principles

Based upon existing models for consultation in drug development and specific concerns identified by participants, the pilot process incorporates the following guiding principles:

For an overview of existing early-advice programmes, please see Appendix 3.

- **Agree to non-binding outcomes** to increase willingness to experiment, but with an expectation of *"engagement and commitment"* from the parties befitting the importance of this initiative.
- **Ensure multi-country, multi-stakeholder participation.** The novelty of this approach rests in part on the diversity of perspectives it brings to bear on medicine-specific questions of drug development, convened in a setting designed to reduce the complexity of navigating different requirements across health systems.[19] The pilots encourage participation of a full range of decision-makers across Members States and multiple layers of government, along with a diversity of pharmaceutical companies and consumers of new medicines.
- **Foster equal standing and reduce barriers to participation.** To maintain an open dialogue, all parties in the discussion participate with equal standing. To reduce barriers and respect the resource needs of various institutions, the initiative seeks to make participation cost-neutral.
- **Create an environment that supports mutual learning.** Participants designed the pilots not only to deliver insight into medicine-specific development questions, but also to create a body of shared knowledge about how such engagement should be conducted and, potentially, institutionalised. Participating organisations have the opportunity to learn from each other to inform their broader practices as well as their own advice processes. It is the participants' intention for the pilot process to help create a public good through these activities.
- **Encourage transparency while maintaining confidentiality.** This initiative encourages openness and transparency by publishing objectives, the roster of participating institutions and specific consultation dates. The learning from the first set of pilots will be part of the public domain through the publication of this pilot report and other communications. While findings related to the pilot process and non-product specific outcomes are shared, commercially-sensitive information remains confidential.

Multi-stakeholder consultations promise to address drug-development challenges

The pilots can help health systems overcome the challenges that participants identified. In so doing, this initiative adds to other experiments that are demonstrating the benefits of greater engagement among and between constituencies that share a role in evaluating the benefits of new medicines.

More effective use of limited resources

Multi-country, multi-stakeholder consultations can help encourage the best use of limited public healthcare funds by improving the evidence available for HTAs and payers to assess the value of new medicines. By clarifying their requirements to drug developers, these stakeholders, as one participant said, *"can get better data on which to base their decisions."* Similarly, developers can improve their decisions when HTAs and payers act on *"[their] responsibility as representatives of society to help industry choose what society really needs and what health systems will value."* Reflecting on the benefits of such consultations, an industry representative summarised, *"We think this process will allow us to focus the resources and better manage the risks for all the parties involved."*

Fewer late-stage failures to demonstrate efficacy and added value

The consultations being piloted can help reduce failure rates of efficacious drugs by enabling sponsors to design development programmes that demonstrate the value of new medicines to their stakeholders' satisfaction (where the underlying science supports such a conclusion). As one HTA participant has noted, early-stage multi-stakeholder consultations can help avoid a situation in which *"the notion of medicinal value is insufficiently defined, or the evidence is insufficiently suitable or strong, to support positive reimbursement decisions."*

Understanding different stakeholder perspectives early in development, one Network member added, *"will increase the probability of success in confirmatory trials [by facilitating agreement on parameters such as] the right dose and the right target population."* Participants agree that *"good input from regulators and payers prior to Phase III"* is needed for industry to develop medicines that require long-term outcome data to demonstrate value. Participants are aware, of course, that even the best-designed clinical trial will demonstrate a medicine's value only if it performs well along the agreed measures of clinical benefit.

Conversely, early understanding of varying requirements may influence the termination of programmes that are less likely to be successful. As a senior R&D leader stated, *"The most valuable aspect of the pilots is the opportunity to understand the different views of stakeholders ... If the difference between the stakeholders' views is very large, it will probably cause us to consider whether development is even feasible."*

Integrated perspective on evidence requirements

Multi-country, multi-stakeholder consultations enable participants to understand how evidence requirements differ across member states and stakeholder groups. Such transparency can, in turn, *"be helpful in defining the common set of objectives ... so that, at the time of regulatory authorisation, relevant data has been generated for health technology assessment as well."* Another participant noted that the pilots are also designed to encourage *"regulators and HTAs ... to pose questions to industry and each other so that everyone can understand any concerns associated with a new compound."* This process should provide an *"understanding of common areas among participant stakeholders and of where the gaps or differences remain."*

The first set of pilot consultations has been successfully completed

Between September 2010 and February 2011, healthcare leaders, supported by Tapestry Networks, tested the multi-country, multi-stakeholder process by completing three pilot consultations, each involving a pipeline medicine being developed by one of the initiative's sponsors. The first two pilots involved a drug for type 2 diabetes, the first being developed by AstraZeneca and the second being developed by GlaxoSmithKline; the third involved a breast cancer medicine under development by Janssen Pharmaceutical Companies of Johnson & Johnson.

Participating institutions included the European Medicines Agency (EMA), HTA agencies from France, Italy, The Netherlands, Sweden and the United Kingdom, a German academic HTA centre, and regional payers from The Netherlands, Sweden and the UK. Because medicines for oncology and diabetes must gain market authorisation through a centralised procedure, the EMA provided advice through its Scientific Advice Working Party, with the involvement of the Committee for Medicinal Products for Human Use. Medical experts and patient advocates completed the consultation groups.

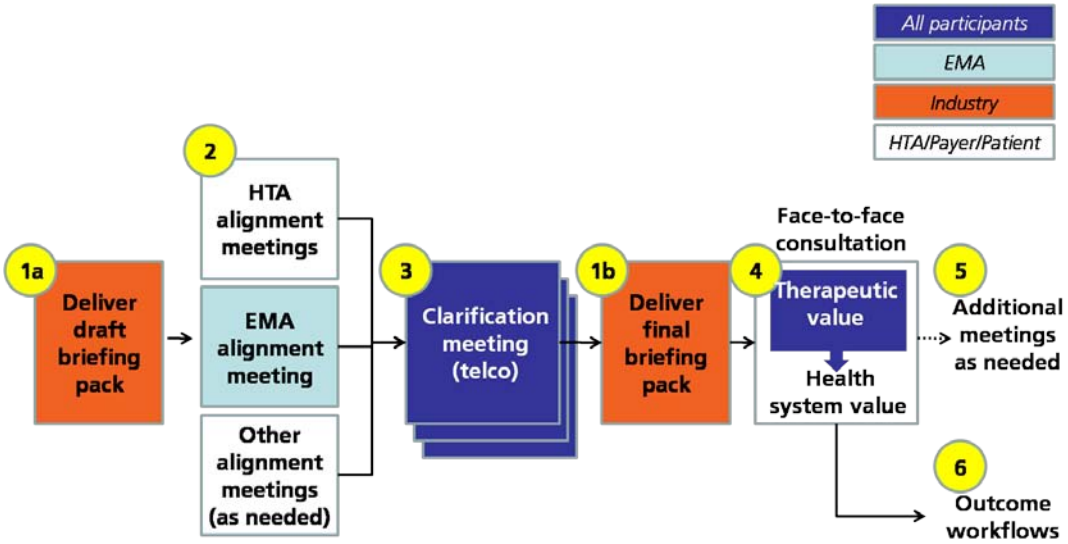
Please see Appendix 4 for an EMA press release describing the pilots.

Each consultation was co-chaired by a regulatory participant and an HTA participant, rotating across Member States. The first set of consultations took place at the EMA headquarters in London.

The pilot consultations employed a design developed jointly by participants. At the start of each pilot, the sponsoring company presented participants with a briefing document that described a medicine under development and raised a number of questions regarding its value proposition and development plan (figure 1, step 1a). Participants then held internal meetings (step 2) to understand and clarify industry questions, in preparation for a series of multi-institutional teleconferences (step 3) designed to give participants the opportunity to request additional information and to help the sponsoring company sharpen its questions. After distribution of the revised briefing pack (step 1b), the process culminated in a face-to-face consultation (step 4) at which the stakeholders engaged in a discussion with company representatives and with each other, guided by the questions raised in the briefing document. The pilot process provided an option to convene additional meetings (step 5) for advice or clarification of issues identified during the face-to-face consultation.

Tapestry Networks debriefed pilot participants following each consultation (step 6) and used the resulting information to refine the process and distil findings. Participants received a set of informal minutes after each consultation.

Figure 1. Overview of multi-stakeholder consultations process in drug development



The first set of pilots highlighted the potential benefits and limitations of multi-country, multi-stakeholder consultations

The pilots resulted in substantial insight for the participating companies, which will have tangible impact on their development programmes. The pilots also enabled participants to gain a better understanding of other stakeholders' perspectives on the specific medicine as well as the key challenges of drug development in the particular therapeutic area. The consultations have demonstrated the need to balance depth and breadth of discussion, as well as the challenge of seeking clarity among stakeholders despite the substantial uncertainties that drug developers face. Participants have also identified alignment and mutual education among participating stakeholders as an important – yet ephemeral – measure of success.

Each sponsoring company involved in the initial pilots offered a different approach to the process: AstraZeneca suggested a new strategy to create value in a disease area in the context of global risk with multiple risk factors; GlaxoSmithKline submitted a drug with a new mechanism of action with proposed novel endpoints to assess value; and Janssen Pharmaceutical Companies of Johnson & Johnson presented two alternative development strategies focused on targeted subpopulations with accompanying diagnostic and an absence of clear precedents.

The pilots were successful in promoting clarity on value

The consultations were successful in providing increased clarity to drug developers about the potential value of their medicine and how to demonstrate that value most effectively. An industry leader commented that *"it is not obvious for everybody to see that what is a value for one stakeholder group is not necessarily a value for another."* Industry participants described the pilots as *"an excellent exchange and certainly worthwhile," "a unique and needed process*

resulting in genuine and constructive discussions" and a *"highly beneficial opportunity to seek advice from a group representing different stakeholders on the decisions to be made early in pharmaceutical product development."* Research and development leaders whose teams participated in the pilots agreed that *"getting feedback early to prioritise our compounds and even prioritise our research and development is paramount."* They reported that the consultations *"will have a concrete and practical influence on the way we continue our development"* with *"tangible consequences for the development programme"* which *"is likely to be different than before the asset team went into the consultation meeting."*

One clinical development team listed three aspects of the programme that the company would approach differently in light of the advice received: the scientific basis for demonstrating the medicine's mechanism of action and link to biomarkers; the approach to patient segmentation; and the proof-of-concept study design. A team representative concluded, *"[The consultation showed] how to develop novel molecules that have different clinical profiles and address different endpoints from other molecules."* Conversely, the consultation influenced a different clinical development leader to terminate part of his programme. He concluded, *"I have no problem saying that we don't need this study because it is not valuable to stakeholders."*

The pilots created opportunities for mutual learning

The pilot process demonstrated that candid consideration of specific drug-development questions provides opportunities for mutual learning that can inform participating organisations' internal decision-making processes. For an HTA participant, the pilots presented *"a learning curve on all sides and a two-way flow of information between the institutions present."* From a payer's perspective, the *"pilots provided an opportunity for better cross-stakeholder understanding and really evolved my views."* An EMA participant added that *"arguments flowing from the other groups ... will make some sort of impact of the regulators' thinking."* One participant noted that multi-stakeholder consultations make reimbursement requirements *"more transparent for other stakeholders and the company,"* even if there are differences among the Member-State HTAs represented.

The continuation of this dialogue across stakeholder groups, to build opportunities for learning and the potential alignment of evidence requirements, is an area of interest for future pilots. One participant noted that, across the pilots, *"we can build some level of trust that we can work together in a multi-stakeholder way."* As an industry participant concluded, *"The true value of this consultation would be the inter-stakeholder debate and the growth of advice that comes out of it, [not just] the stakeholders educating the company."*

Moreover, in some instances participation in the pilots lead to fruitful internal debates. A payer participant commented that *"deliberating inside my agency [about the consultation] and trying to understand the differences in requirements between my department as a payer representative and other departments has been really important because we want to have a clear understanding of the questions posed by the company. We want to be sure that as a national authority we will be able to give a specific answer to each one of the questions."* Enabling institutions to use the

consultations as an opportunity for learning is an important objective that will carry over to the second round of pilots.

The consultations have shown the need to balance depth and breadth of discussion

Experience from the first three pilots suggests that, to encourage robust discussion among stakeholders, it is important to balance broad participation with the in-depth engagement of experts. This was evident in the third pilot, which was the most-attended meeting, with thirty-two participants at the table.[20] The large number of attendees, combined with the significant level of detail and many questions raised by the sponsor, resulted in a tension between addressing the breadth of the questions and the need to consider each question deeply.

Despite the challenge of having so many perspectives in the room, the majority of pilot participants felt that this diversity was a crucial differentiator of the initiative and important to preserve. *"It is absolutely key,"* an industry participant stated, *"to have this interaction not with one single body but with everyone in the same room to understand the best strategy for developing a new drug."* A colleague agreed, emphasising that *"The thing to keep, going forward, is the diversity of the opinions [and] the goal to gather people from across Europe at the same table."* Patient representatives also valued the diversity of the consultation, adding, *"We learned a lot from the perspectives of others, so we would be very happy to take part again."*

Please see Appendix 5 for a first-hand patient advocate perspective on the pilot experience.

Noting the time required to surface each stakeholder's view, however, one HTA representative observed that *"The more institutions that are represented, the less depth you can have."* The second set of pilots will provide additional opportunities to clarify how best to achieve this balance.

Overall, the experience of the first three pilots indicates the importance of balancing a number of factors – including diversity of stakeholders, represented regions and constituencies, and the total number of participants and their expertise – so that a multi-country, multi-stakeholder consultation can achieve an appropriate balance between breadth and depth of discussion.

The pilots have highlighted the uncertainty that drug developers face

Another challenge that surfaced in the consultations is the difficulty in addressing the uncertainty and ambiguity inherent when discussing new, early-stage medicines. Consultation participants confronted this dilemma because the first two medicines on which developers sought consultation raised open-ended questions that were not yet grounded in a substantial body of clinical data. While some participants accepted the speculative nature of this discussion as an inherent part of drug development, others considered it a limited basis upon which to offer their perspective.

Industry participants noted that the *"preliminary nature of the discussion"* in fact reflects the degree of uncertainty they confront in making development decisions. An industry representative recounted that his company's asset team entered the pilot consultation *"having to make decisions in 2011 with a view to a potential launch in 2016."* For them, *"the most*

difficult part of the process … was getting participants to consistently put their heads in 2016 and give them advice in the context of predictions about what the standard of care would be five years later." Thus, the need to be predictive and make assumptions about data required consultation participants *"to go out of their comfort zones."*

An HTA leader acknowledged that, to the extent that the pilots involve early-stage medicines, they will require participants to confront the same uncertainties that developers face. He noted, *"I recognise the problem we have as assessors to look into the five-year future … We have to learn."* An HTA colleague added, *"We have to get used to making assumptions at this stage [of development] because you want the advice early and at that time you cannot have all the data. Yet somehow it has got to be real enough that people can respond to it."* A different HTA representative concurred: *"Reimbursers have to learn to think about how value should be demonstrated in advance, not just when [the data] is already there."*

Several other HTA participants, however, expressed scepticism about the value to the company of advice on early-stage assets without a substantial body of data or established experimental design. One wondered, *"Does the company value having a vague discussion on some very early ideas or do they want something more specific?"* Another HTA representative said, *"[Regarding the future,] everyone is just guessing; it's a thought experiment and that is not helpful for the company."* A regulator added, *"I think it's impossible to pre-empt scientific evolution, especially because there are so many factors influencing what will become the standard of care."*

Structured follow-up to the pilots has helped to distil lessons for all stakeholders

As an element of the pilots' design is to facilitate learning, Tapestry Networks completed debriefing teleconferences with pilot participants following each consultation and used the commentary to integrate lessons learned and evolve the pilot process. Participants also received a set of informal minutes of each consultation. Regulators, taking part through the Scientific Advice Working Party, followed their institutional protocol by also providing a written report to the company. Other stakeholders generally limited their participation to verbal comments, either because they do not have an existing framework for providing written advice or because they preferred a more informal approach (consistent with the pilot design principles discussed above). AIFA, the Italian Medicines Agency, provided a written response to the company following the third pilot consultation.

Some participants suggested that the multi-country, multi-stakeholder consultations could develop into an iterative process, wherein participants could arrange additional meetings with the company once it had more data about a medicine under development. One regulator noted that, *"follow-up discussion is quite important."* An HTA representative agreed, explaining that he *"would love to see further down the road the same molecule coming back with new data [and to] compare early potential to what really happens later."* A medical expert added, *"Another round would be helpful for looking into the potential for added value."*

Upcoming pilots will refine approaches to multi-stakeholder consultation

Participants view development of a multi-stakeholder process as a public good

It is clear to participants that, as voiced by a senior regulator, *"The experience of the pilots should be a benefit not only to industry but to all participants around the table."* An industry leader affirmed the need for clarity about *"what the consultations deliver in a broader sense for everybody that is part of it."* Moving beyond immediate participants, another industry representative framed the initiative's overall objective, explaining *"we would like to see whether we can achieve a new process that delivers improvements and better medicines for patients with unmet needs."*

Healthcare institutions seek a pragmatic model for participation

Further developing the multi-country, multi-stakeholder model requires pragmatic issues to be addressed. Participating companies are eager to conduct a second set of pilots to refine the consultation process and gain additional insight about specific medicines in their pipelines. Non-industry participants generally also would like to continue their involvement while managing the resource implications of doing so. An HTA participant explained, *"The question is not whether this is a good activity, because the experience is positive for most ... The question is how to develop a business model that supports it."*

A key objective for the second set of pilots is therefore to develop a model that enables sustainable participation from a range of stakeholders. An HTA representative explained, *"It is about capacity; it is about money; it is about independence; it is about confidentiality ... We need some kind of organisation to make that easy for the participants to handle these things."* For the time being, Tapestry Networks is providing that organisation, with the objective of developing an approach that can eventually operate independently. An important element of this evolution is identifying the highest-impact use of multi-country, multi-stakeholder consultations as a complement to other forums.

Future pilots will explore the most appropriate uses of the multi-country, multi-stakeholder forum

Participants agree that the multi-country, multi-stakeholder consultation process should be applied in selected drug development situations. Such a process can be more resource intensive than meeting with any individual stakeholder, but can provide the benefit of *"the total picture of the best strategy for developing a new drug."* As such, the pilots have a unique, but by no means exhaustive, contribution among emerging initiatives to improve health systems' ability to deliver needed treatments. A participant involved in multiple consultation formats suggested that *"you may see a menu of single country – single stakeholder forums, single country – multi-stakeholder forums, single stakeholder forums, and multi-country and multi-stakeholder forums, with the choice of forum being up to the needs of the company."*

The pilots are testing the most appropriate application of the multi-country, multi-stakeholder forum. Participant feedback suggests that these applications are areas that require integrated

engagement to achieve progress in attaining *"clearer measures to ensure that innovators are rewarded and to make the environment less risky to innovative companies."*

Participants have suggested that a multi-country, multi-stakeholder consultation may be most appropriate in the following applications:

- **Evaluating novel and strategic development questions in early-stage assets.** As an HTA participant suggested, multi-country, multi-stakeholder consultations will offer the best advantages *"when you have real novelty. The novelty can be in the source of the value that is being explored, the approach to collecting the evidence to demonstrate it and the way in which the evidence is being synthesised."* This type of engagement would minimise the risk of pursuing an otherwise uncertain development programme without *"a well-defined pathway"* by shaping the value proposition and trial design of a novel medicine to provide the data that stakeholders need to evaluate it. In this case, the multi-stakeholder process provides *"an early perspective"* across constituencies and geographies that could be later refined as needed through more regular early advice processes once further evidence support develops.
- **Clarifying how current methods of value assessment differ in their approach to a new medicine.** Regulators, HTAs and payer decision-makers all apply somewhat different methodologies to value assessment. Participants agreed that it would be valuable to explore more in depth *"the amount of variation there was among the HTA agencies and also between HTAs collectively and the registration authorities."* Clarifying those differences and having stakeholders co-develop a path forward with the company would be a potential goal of this consultation. This type of consultation would likely fit a later-stage asset with significant proof-of-concept data already available.
- **Addressing requirements for post-launch data to evaluate effectiveness.** The length of time needed to demonstrate outcomes in a number of therapeutic areas suggests that a medicine's value should be followed and assessed after initial marketing and reimbursement authorisation. One pilot participant commented *"What we need is the level of evidence required for post-launch assessment."* Consultations on late-stage medicines involving multiple stakeholders and member states could provide the kind of integrated perspective necessary to develop a post-launch data development programme that meets the needs of a range of health systems. This approach could complement and inform other ongoing initiatives that address post-launch issues.

Future pilots will test new approaches to accomplish pilot objectives

In the second set of pilots participants will consider how to evolve the consultation process to better support pilot objectives. To clarify each organisation's perspectives on a company's questions, a regulator suggested that participants *"set down in writing the discussion of the various points to be shared with other stakeholders."* The written documentation would help ensure that the company correctly interprets comments made during the consultation and help to

clarify areas of agreement and disagreement among participating institutions. This document could take the form of a *"common document"* that would be circulated among participants.

Additionally, pilot participants suggest expanding the pilot process to demonstrate applicability to other therapeutic areas, new geographic regions and additional medicine developers. Tapestry Networks is engaging with healthcare leaders in Germany and Spain in an effort to expand institutional participation across member states. Countries outside Europe, including Canada and Australia, have also been proposed as potential new regions to be included in the initiative.

Participants have also noted the importance of broadening participation to include *"not just new member states, HTAs and regulatory participants but also new company participants"* so that the value from multi-country, multi-stakeholder consultations as a public good can accrue more broadly and the scalability of these pilots can be tested by including broader industry representation. Talks to bring new drug developers into this process are ongoing.

Conclusion

The pilots of multi-country, multi-stakeholder consultations in drug development serve as a concrete demonstration of a new model of governance and leadership that supports the collective interest of multiple distinct institutions. In so doing, they join other experiments at bringing multiple perspectives to bear on the assessment and demonstration of medicinal value.

Today, a single clinical development programme must address the varied evidence requirements of regulators, reimbursement agencies, providers, patients and payers. In this era of complexity and interdependence, the development of high-value medicines to address critical unmet patient needs calls out for individual and collective leadership. As one participant observed, *"There is something immensely powerful about payers, HTAs and companies all accepting that there is a common problem that they are all required to gather around a table to solve."*

Participating companies and most non-industry participants are eager to move this initiative forward, both to refine the process of multi-country, multi-stakeholder consultations and to identify the highest-impact uses for them in the drug-development system. In so doing, they are joining a growing group of healthcare leaders who see success as the ability to *"align commercial and public interests to result in affordable innovation that meets medical needs better than existing treatments."*

End notes

[1] European Healthcare Innovation Leadership Network, "Setting the Agenda for Healthcare System Performance," *ViewPoints*, 11 December 2006.

[2] This paper reflects the Network's use of a modified version of the Chatham House Rule, whereby names of participants and their affiliations are a matter of public record, but comments made during meetings are not attributed to individuals or organisations. Quotes in italics are drawn directly from comments made by members and guests participating in the initiative.

[3] Randeep Ramesh and Denis Campbell, "NHS Cuts to Run Deep as Spending Goes Up," *The Guardian*, 17 October 2010.

[4] "Germany to raise state healthcare charges by 6bn euros," *BBC News*, 6 July 2010.

[5] "French government to tackle surging health care deficit," *Reuters*, 7 September 2009.

[6] "A Highly Regulated Industry," European Federation of Pharmaceutical Industries and Associations, accessed 24 March 2011.

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[8] Pharmafeed, "Pfizer Carving $1.5B from R&D Budget, Dropping Diseases," 2 February 2011.

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[10] Rachel Cooper, "AstraZeneca to Double Share Buybacks but Cuts Sales Target," *The Telegraph,* 2 March 2011.

[11] John Carroll, "AstraZeneca Outlines Deep Cuts in Global R&D Ops," *FierceBiotech*, 2 March 2011.

[12] "The Pharmaceutical Industry in Figures."

[13] Elizabeth Lopatto, Michelle Fay Cortez and Meg Tirrell, "Lilly Alzheimer's Setback Threatens Rivals' Prospects," Bloomberg Businessweek, 2 March 2011.

[14] The Telegraph, "Kidney cancer patients denied drug that can extend their lives," 29 March 2011.

[15] ThePharmaLetter, "UK's NICE reaffirms decision to deny use of Novartis' asthma drug Xolair for children," August 2010.

[16] PhRMA, "What Goes Into the Cost of Prescription Drugs?" June 2005.

[17] PhRMA, "What Goes Into the Cost of Prescription Drugs?" June 2005.

[18] Maria A. Gordian, Navjot Singh and Rodney W. Zemmel, "Why Drugs Fall Short in Late-Stage Trials," *McKinsey Quarterly*, November 2006.

[19] Participating member states for the pilots included France, the Netherlands, Sweden, the United Kingdom and Italy.

[20] Participants included HTA representatives from five member states (France, Italy, the Netherlands, Sweden and the UK), payers representing three member states (the Netherlands, Sweden and the UK), recognised medical experts in the field from the UK and Italy, patient advocates from national organisations in the Netherlands and Sweden, regulators including the new head of the Scientific Advice Working Party, and nine Janssen Pharmaceutical Companies of Johnson & Johnson representatives, including senior leadership. This level of attendance approached reasonable limits for all participants to have the opportunity to make substantive contributions to the discussion.

Appendix 1: Tapestry Networks principles for working with public-private networks

Public-Private Networks

- Tapestry Networks is an independent business that specialises in the creation of exclusive, leader-to-leader networks. Our networks set the agenda for economic, social and organisational change.
- The networks that we produce may include a cross-section of private sector leaders, non-profit experts and public officials uniquely equipped to advance a common set of interests. These public-private networks create a context for dialogues that define issues and develop multidisciplinary projects to advance shared interests.

Ethical and Legal Considerations

- There are four broad areas of the law that may apply to the management of public-private networks with which Tapestry Networks complies. They are election law, the body of laws governing gift giving, lobbying law and competition law.
- Equally important, our networks are guided by a set of ethical rules and considerations that protect both the interests of network members and the constituencies they represent.
- Tapestry Networks has adopted principles and guidelines for all public-private networks it produces which reflect these areas of the law and the ethical obligations and responsibilities of its sponsors and members.
- Tapestry Networks, its sponsors and members do not engage in directly or indirectly offering or promising any benefit to a public official or any other person or otherwise exercise any undue influence on such persons which may influence these persons in the exercise of their duties.

Election Law

- Members and networks are non-partisan in composition and disposition and do not engage in any election-related activities.
- While our networks engage in meaningful dialogues on important social, global and economic issues, Tapestry Networks does not actively seek to influence any election-related activity; in particular, Tapestry Networks does not contribute to the funding of any political party or representatives of any political party in the European Union.

Gift Giving Law

- Tapestry Networks, its sponsors and members adhere to the laws and rules governing gift giving, including but not limited to meals, travel and entertainment.
- Public officials and individuals working for a public entity or carrying out a publicly funded project participating in any network event pay all related meals, travel and entertainment costs.
- No gifts or indirect gratuities are given by Tapestry Networks, its sponsors or members.

Lobbying Law	▪ Our networks, as unique public-private entities, may discuss topics related to public policy and may determine to take action based on those discussions. ▪ In the course of these discussions and associated actions, network members may engage in activities that could be considered lobbying contacts with covered officials. In these cases, network members are subject to the requirements and regulations dictated by their positions and organisational affiliations. ▪ Tapestry Networks is not a registered lobbyist in any jurisdiction. We do not attempt to influence public policy or legislation on behalf of our clients, our networks, or our own corporate interests. ▪ Our networks make their papers, meeting summaries, and other deliverables freely available to the public upon request. All network conversations are protected by a modified version of the Chatham House Rule, whereby participants' names are a matter of public record but no comments are attributed to any individual.
Competition Law	▪ Tapestry Networks, its sponsors and members adhere to the relevant competition and antitrust laws. ▪ Tapestry Networks, its sponsors or members will not exchange or facilitate the exchange of commercially sensitive information, including but not limited to prices, terms of sale, costs, customers, suppliers, strategy plans, investments, marketing, or technology. ▪ Tapestry Networks, its sponsors or members will not agree on or take commercial actions.
Pharmaceutical Sector	▪ Tapestry Networks, its sponsors and members adhere to the laws and rules governing the indirect or direct offering or promising of any benefits, incentives, premiums or gifts to any organisation or individual active in the medical or pharmaceutical sector.
Ethical Considerations	▪ Tapestry Networks provides a unique service that advances both the interests of our sponsors and contributes to broader social and economic advancement. Although not required by law, our networks also strive to uphold the highest ethical standards including: ▪ A commitment to candid, non-partisan dialogue ▪ A willingness to accept accountability and transparency of action ▪ A shared sense of a greater good that transcends the interests of any particular organisation represented in the network

Appendix 2: Membership in the European Healthcare Innovation Leadership Network and Breast Cancer and Type 2 Diabetes Working Groups

Network

Member States

France

- **Eric Abadie** | Director General | French Health Products Safety Agency (AFSSAPS)

Germany

- **Rainer Hess** | Impartial Chairman | Federal Joint Committee (G-BA)

The Netherlands

- **Bert Boer** | Executive Member of the Board | College of Health Insurances (CVZ)
- **Leon van Halder** | Director-General for Curative Care | Ministry of Health, Welfare & Sport
- **Martin van Rijn** | CEO | Pension Fund for Care and Well-Being (PGGM)

Sweden

- **Sören Olofsson** | Chief Executive Officer | Region Skåne

United Kingdom

- **Mike Farrar CBE** | Chief Executive | National Health Service – North West
- **Sir Michael Rawlins** | Chairman | National Institute for Health and Clinical Excellence (NICE)
- **Sir Mike Richards CBE** | National Clinical Director for Cancer & End of Life Care | National Cancer Action Team

Pharmaceutical Innovators

- **Eddie Gray** | President – Pharmaceuticals Europe | GlaxoSmithKline
- **David Norton** | Company Group Chairman – Global Pharmaceuticals | Janssen Pharmaceutical Companies of Johnson & Johnson
- **Jaak Peeters** | Company Group Chairman | Janssen Pharmaceutical Companies of Johnson & Johnson (Member designate – following David Norton's retirement in September 2011)
- **Ulf Säther** | Regional Vice President – Europe | AstraZeneca

Other Key Constituents

- **David Byrne** | Former EU Commissioner, Health and Consumer Protection
- **Thomas Lönngren** | Former Executive Director | European Medicines Agency (EMA)
- **Anders Olauson** | President | European Patients' Forum
- **Sophia Tickell** | Director | Meteos Limited

Breast Cancer

Medical subject-matter experts

- **Jonas Bergh**, Karolinska Institute, Sweden
- **PierFranco Conte**, Universitaria di Modena, Italy
- **Jindřich Fínek**, University Hospital Plzen, Czech Republic
- **Luca Gianni,** University of Milan, Italy
- **Anthony Howell**, Christie NHS Foundation Trust, UK
- **Christian Jackisch**, Offenbach Hospital, Germany
- **David Khayat**, Pitié-Salpêtrière Hospital, France
- **Jan Lubiński**, Pomeranian Medical University, Poland
- **Larry Norton**, Memorial Sloan-Kettering Cancer Center, USA
- **John Robertson**, University of Nottingham, UK
- **Karol Sikora**, CancerPartners UK, UK
- **Michael Untch**, HELIOS Klinikum, Germany

Payers, regulators, health economists and advisors

- **Johannes Bruns**, German Cancer Society, Germany
- **Karl Claxton**, University of York, UK
- **Pierre Démolis**, French Health Products Safety Agency (AFSSAPS), France
- **Harald Enzmann**, The Federal Institute for Drugs and Medical Devices (BfArM), Germany
- **Pavel Hroboň**, formerly of the Ministry of Health, Czech Republic
- **Bengt Jönsson**, Stockholm School of Economics, Sweden
- **Bertil Jonsson**, Medical Products Agency, Sweden
- **Sören Olofsson**, Region Skåne, Sweden

Patient representatives

- **Els Borst-Eilers**, Dutch Federation of Cancer Patients, The Netherlands
- **Susan Knox**, EUROPA DONNA, European Breast Cancer Coalition (observer)

Industry representatives

- **Jim Baker**, Janssen Pharmaceutical Companies of Johnson & Johnson
- **Alan Barge**, AstraZeneca
- **Paolo Paoletti**, GlaxoSmithKline

Type 2 Diabetes

Medical subject-matter experts

- **Amanda Adler**, Institute of Metabolic Science, Cambridge, UK
- **Jean-François Bergmann**, Hôpital Lariboisière Paris, France
- **Christian Berne**, Uppsala University, Sweden
- **Bernard Charbonnel**, University of Nantes, France
- **Ele Ferrannini**, University of Pisa School of Medicine, Italy
- **Vivian Fonseca**, Tulane University Medical Center, USA
- **Philip Home**, Newcastle University, UK
- **Harald Klein**, Ruhr-Universität Bochum, Germany
- **Mohan Kumar**, NHS North Western Deanery, UK
- **Andrew Morris**, University of Dundee, UK
- **Eberhard Standl**, Munich Diabetes Research Institute, Germany

Payers, regulators, health economists and advisors

- **Andrew Briggs**, University of Glasgow, UK
- **Hans-Georg Eichler**, European Medicines Agency (EMA)
- **Peter Kolominsky-Rabas**, University of Erlangen-Nuremberg, Germany
- **Félix Lobo-Aleu**, Universidad Carlos III, Spain
- **Noël Renaudin**, Economic Committee for Health Products (CEPS), France
- **Michael Schlander**, Institute for Innovation and Valuation in Health Care, Germany
- **Sjaak Verduijn**, CZ Insurance, The Netherlands

Patient representatives

- **Maarten Ploeg**, Dutch Diabetes Association, The Netherlands

Industry representatives

- **Martin Fitchet**, Janssen Pharmaceutical Companies of Johnson & Johnson
- **Gunnar Olsson**, AstraZeneca
- **Carlo Russo**, GlaxoSmithKline

Appendix 3: Overview of existing early-advice processes

The process for multi-stakeholder consultations was informed by existing early consultation models. Existing early advice models include the EMA's Scientific Advice Working Party, the UK National Institute for Health & Clinical Excellence (NICE) scientific advisory process, the new joint early-advice process of the Swedish Dental and Pharmaceutical Benefits Agency (TLV) and Medical Products Agency (MPA), and the US Food and Drug Administration early-advice process.

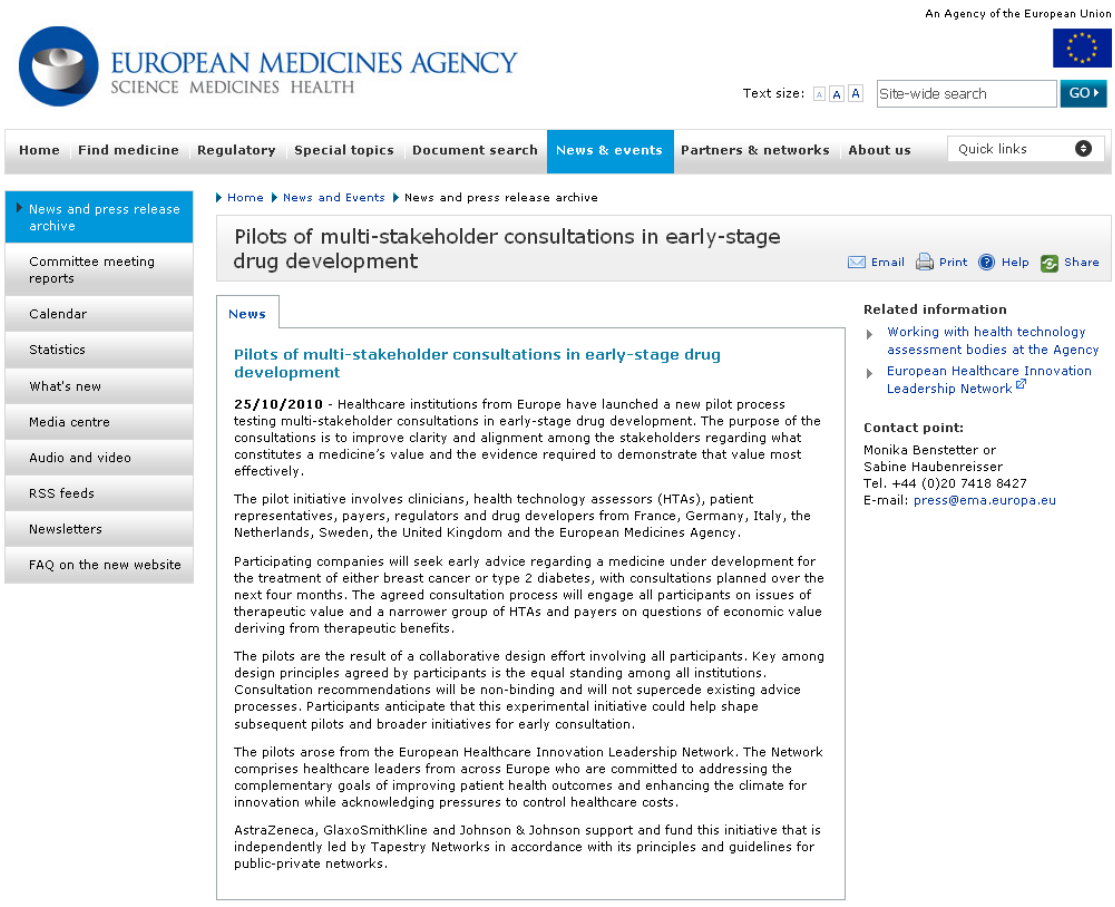
While these organizations were just beginning to test new approaches for early HTA or joint HTA-regulator interactions, stakeholders believed that early consultations were not occurring frequently enough and did not involve the right combination of participants. The few early interactions that did take place tended to be *"bilateral conversations between industry and a regulator"* and *"very rarely involved payers or HTAs, regardless of member state."* The overall view was best stated by one stakeholder who declared, *"Early interactions across Europe between industry and payers are absolutely not happening systematically."*

The table below provides some details on several of the most widely utilised early-advice processes, such as the EMA's Scientific Advice Working Party (SAWP), as well as newly introduced early consultations with HTA agencies:

Example	Participants	Asset stage	Meeting protocol	Additional details
Swedish joint advice	▪ MPA ▪ TLV ▪ Company representatives	▪ Typically end of Phase II	▪ 90-minute meeting ▪ The company submits written questions in advance. ▪ The company prepares briefing materials.	▪ The MPA coordinates the meeting. ▪ Most advice to date has focused on planning confirmatory trials and health economic modelling. ▪ The company records minutes of the meeting. ▪ Advice is non-binding.
SAWP	▪ SAWP appointees ▪ Company representatives	▪ Varies	▪ Typically 90 minutes ▪ SAWP responds based upon documentation provided by the company. ▪ Some SAWP responses are written, though the company will be invited to a discussion if SAWP disagrees with a company's development plans. ▪ Follow-up consultations may be scheduled if outstanding questions remain.	▪ SAWP experts are bound by strict confidentiality rules. ▪ Company questions should be prospective and concern the future development of a medicinal product. ▪ Advice is non-binding. ▪ The company records minutes of the meeting, which are not endorsed by the SAWP. *continued on overleaf*

Example	Participants	Asset stage	Meeting protocol	Additional details
NICE early-advice process	▪ NICE ▪ Company representatives	▪ Can be late-stage (post-Phase III launch)	▪ Four hours ▪ The company provides initial set of questions. ▪ The NICE interacts with the company prior to the meeting to clarify and pose additional questions.	▪ The NICE records the minutes of the meeting. ▪ Advice is non-binding. ▪ Company receives a written report detailing the proceedings approximately one month after the meeting.

Appendix 4: EMA press release describing the pilots



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Pilots of multi-stakeholder consultations in early-stage drug development

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Pilots of multi-stakeholder consultations in early-stage drug development

25/10/2010 - Healthcare institutions from Europe have launched a new pilot process testing multi-stakeholder consultations in early-stage drug development. The purpose of the consultations is to improve clarity and alignment among the stakeholders regarding what constitutes a medicine's value and the evidence required to demonstrate that value most effectively.

The pilot initiative involves clinicians, health technology assessors (HTAs), patient representatives, payers, regulators and drug developers from France, Germany, Italy, the Netherlands, Sweden, the United Kingdom and the European Medicines Agency.

Participating companies will seek early advice regarding a medicine under development for the treatment of either breast cancer or type 2 diabetes, with consultations planned over the next four months. The agreed consultation process will engage all participants on issues of therapeutic value and a narrower group of HTAs and payers on questions of economic value deriving from therapeutic benefits.

The pilots are the result of a collaborative design effort involving all participants. Key among design principles agreed by participants is the equal standing among all institutions. Consultation recommendations will be non-binding and will not supercede existing advice processes. Participants anticipate that this experimental initiative could help shape subsequent pilots and broader initiatives for early consultation.

The pilots arose from the European Healthcare Innovation Leadership Network. The Network comprises healthcare leaders from across Europe who are committed to addressing the complementary goals of improving patient health outcomes and enhancing the climate for innovation while acknowledging pressures to control healthcare costs.

AstraZeneca, GlaxoSmithKline and Johnson & Johnson support and fund this initiative that is independently led by Tapestry Networks in accordance with its principles and guidelines for public-private networks.

Related information

- Working with health technology assessment bodies at the Agency
- European Healthcare Innovation Leadership Network

Contact point:

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Appendix 5: First-hand patient advocate perspective on the pilot experience

Shared by **Pauline Evers**, PhD, Dutch Federation of Cancer Patient Organisations (NFK) and patient representative on EMA Committee for Orphan Medical Products, and **Arja Leppänen**, Chief Executive Director, Swedish Breast Cancer Association (BRO), patient representative on Consumer Expert Group for Swedish Medical Products Agency (MPA) and breast cancer survivor, who participated in the third pilot of multi-stakeholder consultation on 3 February 2011 on Johnson & Johnson/Janssen-sponsored breast cancer medicine.

"As patient advocates, we found the pilot experience novel, educational and rewarding, even though we faced unique challenges to participating in the consultation.

Key challenges. *The greatest challenge to patient advocate participation was the need for technical expertise to interpret the scientific and economic issues raised, and lack of experience with regulatory and reimbursement processes common to other participants. Conducting interactions in the English language increased these challenges. Thus, we invested a lot of time and resources into engaging experts, organising patient focus groups necessary to incorporate a true range of patient views and translating and educating as needed to bridge the knowledge gaps. Given these challenges, however, we felt that the time invested was not in balance with the final contribution we were able to make to the process.*

Pilot lessons. *Engaging helpful experts and technically-versed patients for the focus groups was critical to overcoming the challenges. These groups enabled us to pinpoint what patients want most from industry; those are the issues we raised in the consultation and consequently we hope that other stakeholders learned about patient needs. In return, we learned a lot about drug development, regulatory and reimbursement issues. Because we were not able to participate in more technical parts of the discussion, we felt that we likely learned more from others than they learned from us.*

Future pilot recommendations. *For a sustainable process, we suggest that not all consultations need to involve patients, but only those that have questions truly relevant to them, i.e., purely technical discussions on clinical design might not need patient views. In the scientific advice working party of the EMA, patients are involved only when considered necessary. Otherwise, patients might be involved at a higher aggregate level, giving input on a disease level instead of on a product level. When patients are involved, however, companies should ensure that the briefing documents highlight issues that are important to them, including side effects and quality of life metrics, and they should pose relevant questions directly to patients. Improved access to technical resources would help us understand scientific issues more quickly. Additionally, because of the learning curve of this process, we suggest that the same patient representatives could participate across pilots, consulting those with a specific disease when needed, similar to the structure of patient involvement with the Orphan Drug Committee and the MPA Consumer Board. Implementing these suggestions will enable more efficient and effective patient advocacy.*

It is too often that patients are disappointed when different stakeholder requirements block access to a new drug. Thus, we were happy to be included in this initiative aimed to make these requirements more harmonious and transparent. We believe that patient representation is critical to this initiative, but questions to and input from patients should be focused on issues relevant to them. We look forward to participating again in the near future."