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THE IMPACT OF HEALTH TECHNOLOGY ASSESSMENT ON DRUG DEVELOPMENT: How Much Does It Matter?

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1. INTRODUCTION

Medical innovation has contributed immeasurably to the health of individuals and the well-being of societies. Resources for financing health care, however, have not kept pace. Public and private payers in every country have adopted measures to moderate spending by containing costs, usually treating each component of spending separately. In many instances, this has created an uncomfortable tension between innovators and payers, and often between payers and their constituents, who naturally want access to promising new treatments.

Disquiet is only increased by payers' lack of direct control over innovation: for the most part, new products such as prescription medicines, devices and diagnostics are conceived, developed and marketed by private industry. Given the tension between innovation and resources, it is not surprising that payers often question whether innovators are focusing on the health issues of greatest import and whether their processes are efficient and cost-effective. For example, the Cooksey Report released in the UK in December 2006 argued that health technology assessment (HTA) 'occurs too late in the drug development process'. It concluded that 'the current way of developing drugs in the private sector is unsustainable in the long-term' and proposed that 'the government, regulators and industry create a new partnership to pilot a new drug development "pathway". . . '[1] Largely ignored, however, was whether and how much government already has affected the drug development process through extensive regulation and fervent cost containment over the past three decades.

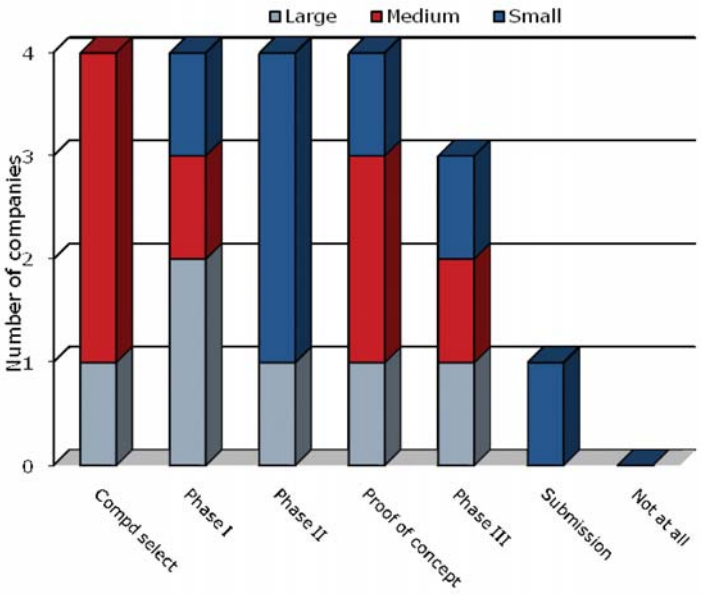
2. ABOUT THE SURVEY

One means for shaping both industry's drug development decisions and the use of prescription medicines in health care is through valuation based on HTA methodologies. Over the past decade, public and private payers have turned increasingly to HTA for guidance on decisions about both access and cost. Although the type and mix of approaches varies by country, HTA has become a critical basis for pricing and reimbursement (P&R) decision-making worldwide. In some countries, extensive requirements for data are set out in guidances or regulation and apply to all new prescription medicines; in others, HTA is required of industry or performed by payers only for therapies expected to be particularly costly.

In late 2007, the Institute for Regulatory Science of CMR International completed a survey to (1) determine whether and how current approval and reimbursement systems are affecting drug development decisions and (2) suggest what changes might be necessary to encourage continued innovation. Nineteen of the Institute's 32 members responded, a sample sufficient to provide an important snapshot of current industry perspectives.

[1] D Cooksey, A review of UK health research funding, December 2006, p. 6

Fig 1. Development Stage When HTA First Considered



Only one of the respondents was a 'biotech' company; its responses on some questions were different from those of the 'traditional' pharmaceutical companies. This is important because both biotechnology and smaller, more specialized companies have become increasingly important as originators of new prescription medicines and as sources of drug candidates for larger pharmaceutical companies. Future research on the impact of HTA should accord greater attention to this increasingly important component of the drug development milieu.

The survey included both close-ended questions and an open-ended narrative section. Most of the close-ended questions focused specifically on HTA, which was defined as 'a cluster of assessment and measurement techniques that aim to assess the relative value of a new medicine and commonly involve some form of economic measurement or measures of social well being . . . going beyond the measures of clinical effectiveness found in the conventional Phase III clinical trial'. Space was provided on the questionnaire for respondents to write in comments for each close-ended question, and many did. The insights that these comments provide into the reasons for respondents' opinions are very valuable.

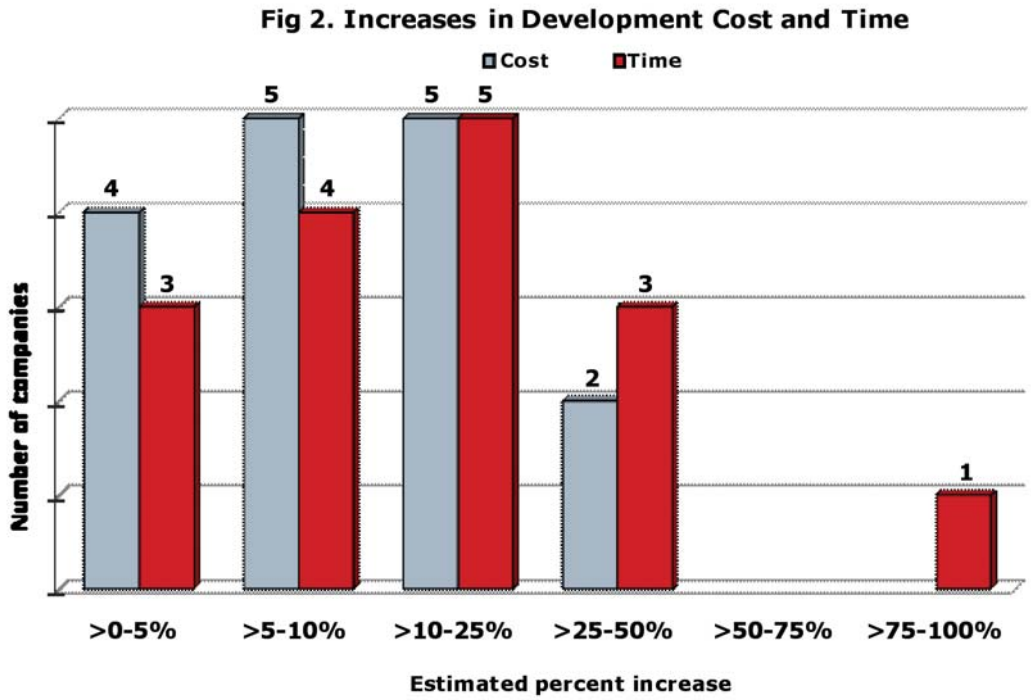
To determine what intervening factors might have affected responses, the analysis for this Briefing took into consideration two characteristics. First, companies were classified as small, medium or large based on pharmaceuticals sales data collected from 2006 annual reports; sales outside the pharmaceutical division of a company were excluded. Seven companies had sales of USD $9 billion or less ('small'); six had between $10 and $19 billion ('medium'); and six had $20 billion or more ('large'). Second, to determine whether daily exposure to country events might affect respondents' attitudes, the country base of respondents was considered. Six respondents each were based in the United States, the United Kingdom, and continental Europe (France, Germany and Switzerland), and one in Canada.

3. THE IMPACT OF HTA AND P&R DECISIONS ON DRUG DEVELOPMENT

Since HTA techniques first made their appearance in prescription medicine evaluation two decades ago, their importance in decision-making within pharmaceutical companies has burgeoned. To provide a glimpse into their current use in the drug development stage, the survey asked when HTA is first taken into consideration in decision-making about a compound.

As **figure 1** shows, over half the companies evaluate compounds before proof of concept, although smaller companies acted somewhat later than medium and large companies. These tallies should be viewed with some caution, however; in their remarks, respondents noted that timing often varies by compound.

Comments also indicated that, for some companies,



including HTA in development programme assessments is relatively new; one large company noted that this has been common practice only for about the past three years. Several respondents stated that their companies intend or are preparing to interject HTA considerations earlier in the process.

The survey asked respondents to quantify the extent to which changes in the overall HTA environment have affected cost of development and time to market. As **figure 2** shows, with respect to costs, 14 of 16 respondents estimated a cost increase of up to 25 percent, a significant sum. Time increases were estimated to be slightly more extensive, with one respondent estimating the increase at over seventy-five percent.

The survey did not specifically ask what aspects of HTA or P&R were most responsible for increases in development costs and time. The open-ended narrative portion of the survey, however, confirmed the cause has been research and analyses needed to meet data requirements for HTA and P&R. Several aspects were identified by the respondents as particularly challenging including, for example, variations in requirements from one country to another and differences of opinion about appropriate methodologies.

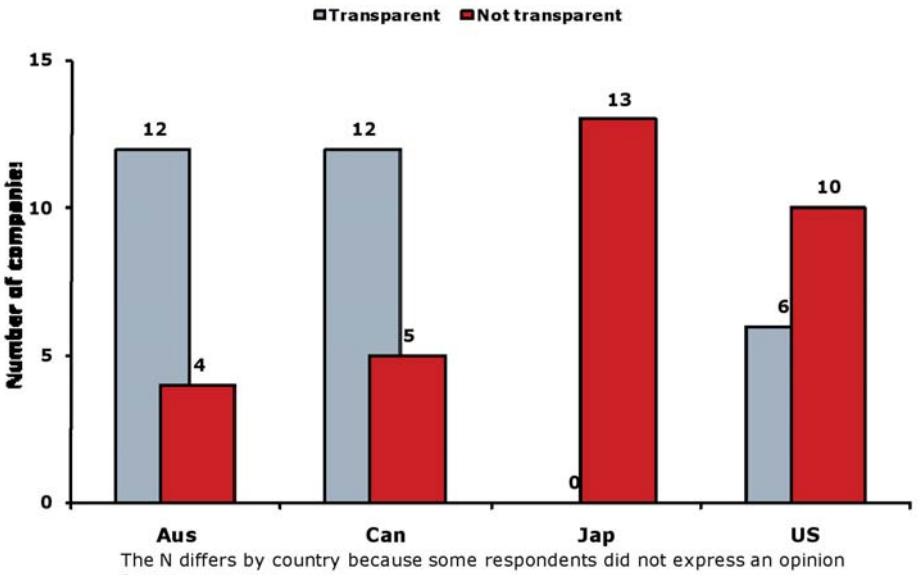
Delays in marketing or reimbursement often result from uncertainty about just what studies and analyses will be required when application for P&R finally is made. Respondents were asked whether they view as transparent current HTA requirements in Australia, Canada, 'Europe', Japan and the United States. Because countries in Europe vary importantly in transparency, as respondents pointed out, scoring for 'Europe' has been omitted from **figure 3**.

Assessment agencies in both Canada and Australia have issued detailed sets of guidelines for HTA assessments and some US payers are comparatively transparent about expectations; Japan's requirements, however, were viewed by this sample as not at all transparent. With respect to Europe, respondents' comments indicated that France, The Netherlands, Sweden and the United Kingdom are relatively transparent, but that Germany, Italy and Spain are not transparent in their HTA requirements. One respondent also noted that, in some countries, even though technical HTA requirements are transparent, decision-making may not be.

Countries vary not only in degree of transparency, but also in specific requirements. Medical culture, societal expectations and health care budgets all vary, creating differences in the information that decision-makers seek. Still, some efforts have been made in recent years to begin to harmonise requirements. An emerging literature is exploring the extent to which harmonisation is possible or appropriate and the feasibility of using evidence and analysis from one country in another.

The survey asked 'whether the needs and requirements of HTA groups around the world are harmonised'. All respondents disagreed or disagreed strongly, although comments pointed out that decision-makers are interested in similar kinds of information. Some remarked that HTA methodology still is evolving and consensus is not yet sufficient to support, or warrant, harmonisation. One respondent

Fig 3. Transparency of HTA Requirements



The N differs by country because some respondents did not express an opinion for every country.

pointed out that the differences across countries go beyond methodology, noting that HTA agencies vary in their ability to evaluate sophisticated models and in the resources available for staffing and training.

Added to issues of transparency and harmonisation are differences in opinion about the HTA models themselves. The survey asked whether 'models used by HTA groups for assessing cost and clinical effectiveness are well validated and accepted' by pharmaceutical companies. Eleven respondents disagreed or disagreed strongly; six were indifferent and two agreed. Several comments qualified 'indifferent' choices by noting this varies by country and HTA group, making the answer more complex than 'yes' or 'no'. One respondent echoed remarks made at other points in the survey, explaining that the cause of differences and debate often are the study assumptions—input parameters, extrapolations methods, and the like—and not the models themselves.

The survey asked whether companies use 'generic' HTA models to assess cost and clinical effectiveness or develop their own models. Responses indicate that companies do use generic frameworks when available, but tailor these to fit the particular product or therapeutic area. All but two respondents indicated that their companies are developing or have developed their own models[2].

From the perspective of these respondents from the pharmaceutical industry, then, HTA and reimbursement requirements have added importantly to development costs and, through delayed marketing, to opportunity costs. Imperfect methodologies, disagreement on appropriate methods, variations in requirements across countries, and lack of harmonisation complicate the process and undoubtedly increase costs and delays.

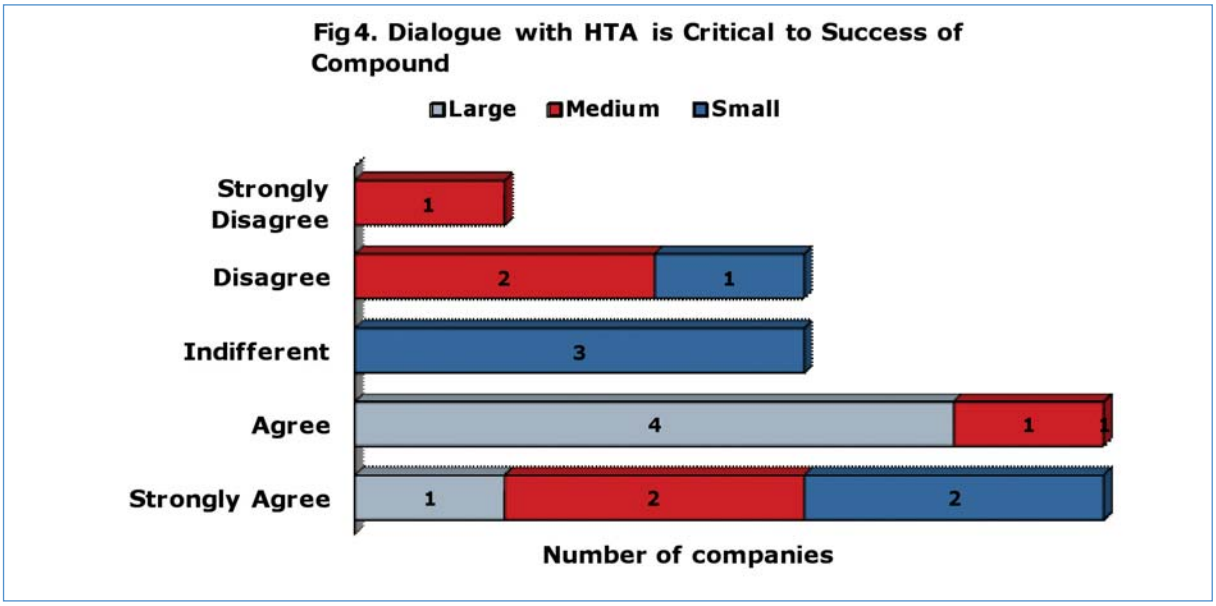
4. THE EVOLVING USE AND APPROPRIATE ROLE OF HTA

The popularity of HTA as a means for making decisions about trade-offs in the health care system is likely to grow in the foreseeable future. Several survey questions asked for opinions about what changes are likely to occur and what important issues will arise. These include the appropriate role of HTA assessment groups, the relationships between HTA and licensing agencies, and the effect of HTA on P&R and market access.

Interactions with HTA groups during the development process

As noted above, companies in this sample are evaluating the HTA profile of a compound early in the development process; four of 19 did so as early as compound selection and another four did so in Phase I. Going a step further, some companies may wish to consult early on with the HTA assessment groups that are likely to either issue recommendations for reimbursement or provide information that will be used to determine initial market price. The survey asked whether and when during the development process companies meet with HTA groups. The

[2] The two "disagree" answers, based on comments provided by the respondents, appear to have been based on a misunderstanding of the question.



responses showed that ten companies do hold meetings during the development process, with each stage receiving roughly the same number of responses. Nine of 19 companies, however, do not meet with HTA groups at all. Respondents' comments provide important insight into why meetings do not occur. Two respondents note that their market planning focuses on understanding the payers and that only a very few HTA groups in Europe are involved formally or directly in P&R decision-making. One reported that a request to a national HTA review group for input at Phase III had not received a reply, suggesting perhaps that HTA groups are not enthusiastic about such interactions. Other respondents noted that a single answer to this question is not possible because the particular product determines whether and when meetings occur.

A companion question asked whether HTA groups *should* be involved earlier in the development process 'to accelerate assessment of clinical and cost effectiveness'. Although 13 of 19 respondents agreed, comments suggest that some were thinking of HTA groups *within* the company and that interpretations of 'involvement' varied. For example, one comment suggested that 'earlier involvement' meant clearer information about the decision criteria applied by HTA groups, not necessarily direct or sustained interaction. The four respondents who disagreed about earlier involvement noted that although HTA should be taken into consideration early on, involvement of external HTA groups is not necessary to achieve this. One comment pointed out that requirements of HTA groups are very different from country to country; to be useful, then, consultations would need to occur with several groups, although differences among them might make the process more confusing than helpful.

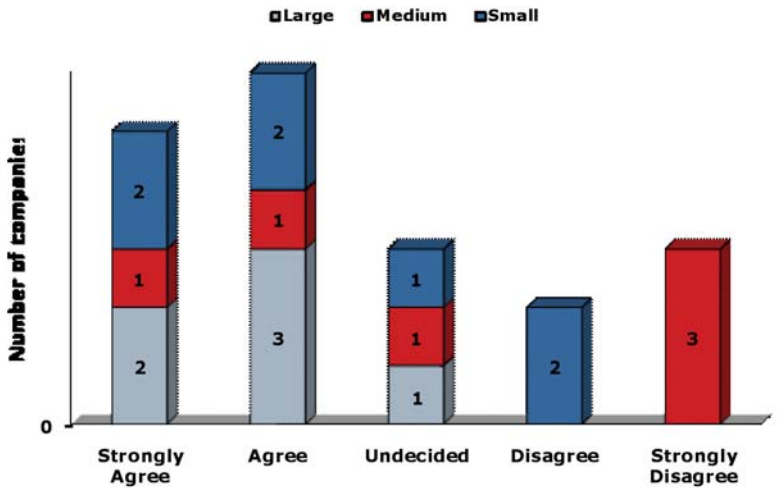
Probing further, the survey asked whether 'dialogue with HTA [groups] during development is critical to the success of a compound reaching the market'. As **figure 4** shows, ten of the 18 who responded to this question agreed, but one respondent noted that opportunities have been too limited to date to demonstrate how important this may be. Of the three who were indifferent, two noted that formal dialogue probably is not necessary as long as companies have a good understanding of the HTA environment in general and apply that to their development plans. One realistically pointed out that the usefulness of engaging in dialogue would be limited by the large number of such groups across countries and the disparities in their data preferences and requirements. Of the three who disagreed, one commented that dialogue would be 'nice to have', but not essential.

Regulatory approval and HTA

To achieve market access in some countries, a prescription medicine must receive regulatory approval and a pricing and/or reimbursement decision, often based on HTA review. For the most part, moreover, the same clinical trials provide the data for each type of assessment. Both time to market and the costs involved in research potentially could be reduced if the two processes were to occur simultaneously and if, for example, regulatory and HTA groups agreed to accept the same clinical endpoints.

The survey asked whether 'there is a role for parallel joint review models' that would allow companies to submit dossiers for new prescription medicines 'almost simultaneously to HTA and regulatory agencies'. Comments suggest that 'parallel joint review' was interpreted by some respondents as *combined* review and by others *simultaneous* review. Six agreed that there is a role for parallel joint review,

Fig 5. Companies Should Seek Clinical Endpoints Acceptable to Both Approval Authorities and HTA Reviewers



six disagreed and four were undecided. Those who agreed urged caution, however, noting that the approval and HTA review processes have different objectives and so should be kept separate. Comments from those who disagreed expressed similar concerns; one also pointed out that licensing approval should be granted first in any case because HTA review only will be necessary for prescription medicines that gain approval.

Responses to this question did seem to cluster according to the country base of the respondents. Five the six who agreed were based in Canada, France and the UK, each of which has a national focal point for HTA review that would facilitate a joint review process.

Opinions were strong about the desirability of companies working with approval agencies and HTA review groups to define clinical endpoints acceptable for both reviews, as **figure 5** suggests. One respondent who agreed noted that discussions with the two groups should be kept separate, not occur jointly. Others who agreed noted that the process should improve transparency, help set realistic expectations, and make clearer any issues that might prove troublesome later on. Those who disagreed noted in their comments that this is not yet feasible because most HTA groups still have insufficient experience and capacity, particularly for some therapeutic areas. Others comments pointed out that requirements vary so much across countries, particularly for HTA, that agreement on endpoints applicable globally would be impossible to conclude. This question also evoked comments about regulatory harmonisation that urged that agreement be reached first on endpoints for clinical trials for regulatory review.

The importance of keeping regulatory approval and P&R decision-making separate is a recurrent theme in respondents' comments throughout the survey. One

Fig 6. Cost-Effectiveness Inevitably Will Be Required for Regulatory Approval by 2015-20

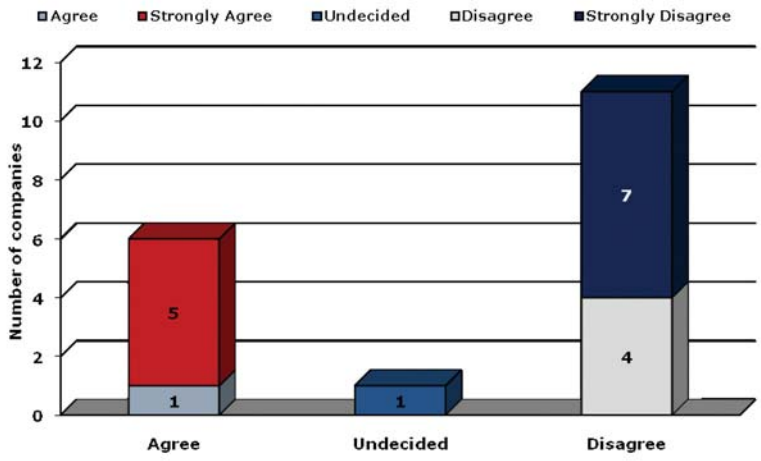
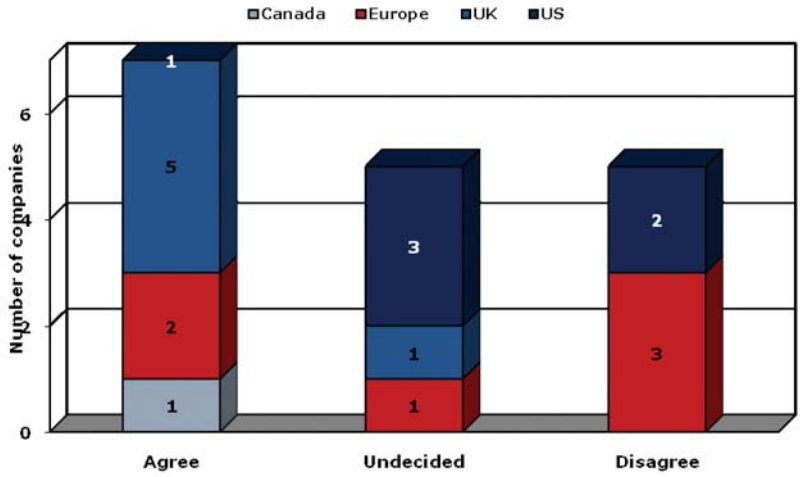


Fig 7. Payers and Companies Should Risk-Share if Data to Provide an Informed View of Cost-Effectiveness Are Not Available at Launch



survey question addressed this issue directly, asking respondents whether 'it is inevitable' that by 2015-20 regulatory approval of all new prescription medicines will be based not only on safety and efficacy, but also on cost-effectiveness. Twice as many disagreed as agreed. Several of those who disagreed commented that this is neither feasible nor likely. In Europe, for example, EU licensing approval is valid in all Member States. Adding a cost-effectiveness requirement would mean satisfying the needs of P&R decision-makers in all Member States—difficult, if not impossible, within seven to twelve years. Unfortunately, those who agreed did not provide comments.

Conditional reimbursement and HTA

As the findings discussed above make clear, the HTA data required to satisfy P&R decision-makers can be a moving target. Not only is it difficult to know with certainty which clinical endpoints will be of greatest relevance when the HTA assessment actually is made, but the data needed to make decisions vary by country and payer as well as over time. Although companies compile 'master' dossiers that contain core analyses, meeting specific requirements still can be a lengthy and costly process. In countries that base access to the market on P&R decisions—several important European markets, for example—this can mean a delay of several months, sometimes more, between licensing approval and marketing. A recent study has shown that for those new medicines that became available to patients across Europe between January 1, 2003 and December 31, 2006, average time between marketing authorisation and patient access was between 74 and 478 days, depending on the country[3].

Conditional reimbursement is being discussed in some circles as a means for shortening the time between approval and marketing—and perhaps allowing monitored marketing at the end of Phase II. This would allow a new prescription medicine to appear on the market before all HTA data are available, with the understanding that price and access would be adjusted later (up, down or not at all) based on studies in conditions of actual use. The advantage is not only earlier access for patients, but also important research on the value of the prescription medicine in use in the 'real world', rather than only in the closely controlled environment of pre-approval clinical trials.

The survey asked whether data usually are available at the time of launch to allow an 'informed view on cost-effectiveness'. None of the respondents was indifferent; eleven agreed and eight disagreed. Those who agreed did not provide additional commentary that could illuminate the reasons for their opinions, although two did note that only preliminary data are available at this point and are based on pre-approval research. The comments from those who disagreed were similar, suggesting that 'informed view' was interpreted differently by respondents. All those who provided comments, no matter what their opinion, agreed that the value of the prescription medicine in actual practice is unknown at launch because data available then can reflect only pre-approval clinical trial experience.

The desirability of risk-sharing, or conditional reimbursement, was a separate question in the survey. Specifically, respondents were asked to agree or disagree that 'if data are not available at the time of launch to take an informed view of cost effectiveness, then payers and companies should risk-share until enough data are available'. As **figure 7** shows, more respondents agreed than not. Looking at the respondents' country base, the idea had greater

[3] EFPIA, The PATIENTS' W.A.I.T. Indicator, Phase 8 Report – November 2007 http://www.efpia.eu/

popularity among those based in the United Kingdom where the option has been under discussion recently.

Comments from respondents who were undecided or disagreed shared common themes: 'risk-sharing' is a misnomer since the burden of risk for a new prescription medicine already has been shouldered by the manufacture by the time the product reaches the market; conventional P&R agreements *are* risk sharing; a myriad of details would need to be explored before an informed opinion could be made; what sounds like a good idea on its face may not be so on further exploration. In the narrative portion of the survey, respondents added that conditional reimbursement must allow prices to rise based on valid research, not just stay the same or decline.

Smaller companies were more likely to favour the idea of conditional reimbursement than medium or large size companies, possibly because delaying market access is financially more onerous for them. Two respondents who agreed strongly were from the 'small' category (sales less than USD 10 billion). Three additional small companies agreed; one was unsure and one disagreed.

5. INCENTIVES AFFECTING DRUG DEVELOPMENT DECISIONS: HTA IN CONTEXT

The discussion thus far has been limited to survey questions specifically about HTA, including its influence on decisions about compounds in development and its impact on development costs and times. The survey also sought to define the impact of a broader range of factors on research and development.

Respondents were asked to indicate which factors influenced decisions at four stages in the drug development process: compound selection, entry into man, late stage development and submission. The factors, identified by industry representatives as those of greatest interest, are scientific opportunity, expected market size, expected P&R, resources for development, and medical need. **Figure 8** shows how each factor ranked in each of the four stages of development. Not surprisingly, scientific opportunity and medical need ranked highest in the earlier stages, with market size and reimbursement dominating in the latter stages. This table, however, must be interpreted with caution. The survey data upon which these rankings are based are imperfect: not all respondents provided estimates for every stage of development and some assigned influence to an 'other' category, which was not always explained in written remarks.

Respondents also were asked to evaluate countries with respect to the incentives they provide for both (1) innovative medicines targeted at diseases and conditions currently not treatable and (2) safer and more effective therapies for diseases and conditions that can be treated currently. As **figure 9** shows, Canada ranked worst, overall. The US generally ranked best, followed by Japan. Europe ranked

Fig 8. Ranking of Factors that Influence Go/No Go Decisions

	Compound selection	Entry into man	Late stage development	Submission
Scientific opportunity	5	4	1	2
Market size	3	3	5	5
Market reimbursement	1	1	4	4
Development resources	4	2	2	2
Medical need	5	5	4	3

5 = greatest influence 1 = least influence

Fig 9. Comparisons of Country Incentives for Developing New or Better Prescription Medicines

	CANADA	AUSTRALIA	UK	EUROPE	JAPAN	US
New therapy approval	2	5	4	1	3	6
New therapy reimbursement	1	2	3	NA	5	4
Better therapy approval	1	5	4	6	3	2
Better therapy reimbursement	1	2	3	NA	4	5

6 = most likely to provide incentives 1 = least likely

lowest on new therapy approval; unfortunately, respondents did not comment on this ranking so the reasons are unclear. Europe's least favourable ratings came from the four small companies that responded to this question.

The rankings[4] presented in figure 9, however, can provide only a general impression. Three respondents did not complete any portion of this section and some completed evaluations only for some countries. The difference between one ranking and the next, moreover, often was small. Europe is not included in the reimbursement rankings reported in figure 9 because the substantial variation in P&R approaches across Europe makes assessing 'Europe' as a single entity impossible.

6. THE 'IDEAL LANDSCAPE' – HTA AND DRUG DEVELOPMENT IN THE FUTURE

As this survey demonstrates, HTA has added to both the cost and time required to develop and market new prescription medicines. In efforts to contain health care costs, public and private payers are relying increasingly on HTA reviews to support informed P&R decisions. Very few payers, however, are transparent about what data they require. Moreover, decision-makers' specific data needs and methodological preferences differ from one country to another, often substantially. The uncertainty and complexity of the current environment make it particularly difficult for pharmaceutical companies to develop solid, comprehensive HTA dossiers in a cost-efficient and timely manner.

Various options for improving the overall process were explored in the close-ended questions in the survey, discussed above. In the open-ended portion, respondents were asked to describe their visions of an 'Ideal Landscape' of regulation and reimbursement. The description that follows amalgamates the sample's comments into a single vision.

The Pharmaceutical Industry's Ideal Landscape of Regulation and Reimbursement

1. Health care systems are better integrated, including the financial aspects. All aspects of care are assessed using the same sets of value or cost-effectiveness criteria, allowing more accurate trade-offs. Assessments, moreover, are multidimensional, focusing not on health care costs alone, but also on the economic and social importance of maintaining health.

2. This broader perspective is accompanied by a better understanding of the pharmaceutical R&D process, including greater appreciation of the complex relationships between innovation incentives and market characteristics. The importance of predictable pricing regimes is understood, and the harm from unexpected unilateral price cuts or sudden and extensive revisions of reimbursement schemes is recognised. The importance of specific innovation incentives also is more obvious, producing additional measures targeted specifically towards smaller companies.

3. A fuller understanding of the drug development process and the pharma/biotech industries has produced a number of changes. First, data requirements for both approval and reimbursement have evolved. Data requirements for HTAs, for example, are tailored to specific diseases or conditions and have moved away from a uniform reliance on a single standard, such as QALYs. Both patient preferences, which can be important for outcomes (through, for example, convenience and tolerance), and unmet medical need are integral to cost-effectiveness valuations.

4. Dialogue with regulatory agencies and payers earlier in the drug development process leads to agreements on what studies and data are necessary for licensing and reimbursement of a particular compound in development. Data requirements are more transparent and as realistic as possible with respect to amount, type and precision of data required. As a result, data submitted for evaluation match agencies' and payers' requirements fully, avoiding costly new studies or re-analyses thereby shortening the elapsed time for decisions.

[4] The rankings were calculated by taking the average responses for each country and each incentive, then ranking incentives across countries. Those countries with the highest average for the incentive categories received a six and those with the lowest received a one.

5. With respect to reimbursement decisions, earlier and more transparent interactions produce clear expectations about whether a compound in development, for example, ultimately can be considered 'innovative'. Licensing and P&R decisions stay within the time limits specified in legislation and other published or agreed timetables. P&R decisions are consistent from one company and compound to another and across time. (Some respondents also foresee binding, formal consultation processes whereby payers commit in writing to their decisions.)

6. The processes for licensing approval and reimbursement decisions remain separate, but take place concurrently. Data requirements for the two processes are as coordinated as possible, reducing unnecessary duplication and promoting efficient use of both company and agency resources. Conditional approval is supported by regulatory and reimbursement authorities. Payers agree explicitly that prices may be adjusted upward – not just remain the same or be lowered – based on new studies and data after the product is available on the market.

7. With respect specifically to HTA assessments, methods are harmonised as much as possible across countries with implementation and decision-making left to each country. HTA is not required for market entry, i.e. licensing.

The survey also asked respondents to identify major barriers to achieving this vision and suggest actions that might be taken to overcome them. Responses recognized that change is necessary in a number of areas, within both agencies and payers and the pharma/bio industry itself. For example, in general, both the R&D and commercial units of companies need to be more realistic about what can be considered real innovation and about pricing and access. Regulatory authorities and reimbursement decision makers need to better understand how to work with industry to achieve common objectives. For example, clear agreement on the terms of a conditional reimbursement arrangement, including review and criteria for success and failure, should help assuage regulators' fears that 'conditional' will instead be permanent. Respondents recognised also that decision making bodies themselves are constrained by limited resources for both staffing and training.

Developing and adjusting to new ways of determining value will be a serious challenge that affects all parties. Approaches to meeting this challenge include 'think tanks', comprising all parties, devoted to developing mutually beneficial new strategies; investment in methodological research and centres of excellence will be essential to implementing those strategies.

More immediately, demonstration programs could encourage change with far less investment. For example, this might be collaboration on a specific product(s) or disease area that involves a regulatory agency, an HTA group and a company. The effort would pilot test the feasibility of early communication, input to trial design and joint assessment of the data for both regulatory and reimbursement decisions. If true transparency and honest feedback from all parties about what did and did not work is achieved, industry and licensing and reimbursement decision-makers should be more convinced about the value of such collaboration. Industry enthusiasm would be further heightened if the pilot process reduced development time and eliminated lag between regulatory approval and marketing with P&R agreement.

7. BEYOND TODAY'S CONCERNS

The survey reflects but one corner of the much larger, evolving picture of drug development. Nevertheless, it provides a useful glimpse into how the marriage between HTA and P&R is beginning to influence trends. Responses show that the pharmaceutical industry is adjusting to the realities of today's cost-conscious health care systems by incorporating HTA considerations early on in development decisions. It also suggests some frustration with uncertainties in the current environment that make difficult the most efficient use of development resources. This includes, for example, the perceived lack of transparency in HTA requirements until very late in the process and the need to serve two masters—approval authorities and P&R decision-makers—whose perspectives about clinical endpoints and demands for data often are decidedly different. To meet these challenges, the respondents in this survey appear very willing to collaborate with outside groups on devising and testing new processes. They also are keenly aware, however, that the demands of a global market limit

and define such efforts. For example, several comments pointed out that differences across countries in cultures and values restrict the extent of harmonisation that can be expected. As one survey comment pointed out, countries have not yet managed to fully agree clinical endpoints for regulatory review, an effort that has been underway for some time.

The concern expressed by the Cooksey Review in the UK about the sustainability of industry's R&D model is shared by many–including within the industry. This has to be kept in perspective, however. Just two months before the Cooksey Report's release, the US Congressional Budget Office, a non-partisan research group, published a fact-finding review requested because 'perceptions that the pace of new-drug development has slowed and that the pharmaceutical industry is highly profitable have sparked concerns that significant problems loom for future drug development'[5]. The study takes a long-term view of the evolution of the pharmaceutical industry and the effects of pricing on innovation. Although it draws no conclusions, the study finds no evidence of a serious slowing of the development process but, instead, a quickly evolving drug development paradigm. In other words, market pressures are producing observable change.

Even as the drug development process itself evolves, the existing concerns of payers, regulators and companies need to be addressed and mechanisms found for improving working relationships. The 'Ideal Landscape' outlined by the respondents to the survey highlights important suggestions for change in both the development and marketing milieus. For example, if health care systems were to become financially integrated and assess all health interventions using comparable methods, trade-offs across the entire system would be possible thus minimizing the perceived need to focus as heavily on controlling the cost of one aspect of care. Processes for licensing approval and reimbursement decisions would remain separate, but take place concurrently, involving early dialogue with regulatory agencies and payers and so enabling data submitted for evaluation to better match agencies' and payers' requirements. Where uncertainty remains, or to speed up access for patients, conditional approval could be used by regulatory authorities and reimbursement decision-makers. Prices could go up when evidence supports higher value; pricing and reimbursement regimes would seek to send consistent signals about the willingness to pay for innovation and the type of evidence needed to support a price that rewards investment. The shared goal is innovation that enables constrained health care systems to make patients healthier and able to live more fulfilling and productive lives.

[5] Congressional Budget Office, Congress of the United States, Research and development in the pharmaceutical industry, Pub. No. 2589, October 2006.

As with all OHE publications, this briefing was peer reviewed by its Editorial Board and by other experts in the field and is intended to be a contribution to research and to public policy making. It does not represent the views of the OHE.

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- disseminate the results of this work and stimulate discussion of them and their policy implications.

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