

# Regulating the economic evaluation of pharmaceuticals and medical devices: a European perspective

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## Abstract

Throughout the developed world, economic evaluation of costly new pharmaceuticals and medical devices became increasingly widespread and systematic during the 1990s. However, serious concerns remain about the validity and relevance of this economic evidence, and about the transparency and accountability of its use in public sector reimbursement decisions. In this article, we summarise current concerns in Europe, based on interviews with European health economists from industry, universities, research institutes and consulting firms. We identify five challenges for European policy-makers, and conclude that there is considerable scope for improving decision-making without damaging incentives to innovate. The challenges are: (1) full publication of the economic evidence used in reimbursement decisions; (2) the redesign of licensing laws to improve the relevance of economic data available at product launch; (3) harmonisation of economic evaluation methodologies; (4) development of methodologies for evaluation of health inequality impacts; and (5) negotiation of price–performance deals to facilitate the use of economic evidence in post-launch pricing review decisions, as information is gathered from studies of product performance in routine use.

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## 1. Introduction

European pharmaceutical manufacturers spend more on evaluating their new products than the rest of the European economy put together spends evaluating all other health care technologies,

procedures and policies. Spending on economic evaluation grew particularly rapidly during the 1990s, as pharmaceutical purchasers stepped up their demands for economic evidence demonstrating that costly new products represent good value for money.

The medical device industry currently spends less on clinical and economic evaluation, since clinical trials are not routinely required by European regulators and (partly as a result) product life cycles and payback periods are shorter. How-

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ever, spending on device evaluation is rising, and the larger firms are now starting more routinely to perform clinical trials on new devices for which there are significant concerns over safety and which are likely to have substantial impacts on health care budgets. Rising spending on pharmaceuticals and medical devices, and the prospect of an accelerating pace of innovation due to advances in genetics and biomedical engineering, means that the trend of rising spending on economic evaluation of new health care products looks set to continue for the foreseeable future.

The structures and timescales of pharmaceutical and medical device evaluation activity are determined primarily by licensing regulations, rather than purchaser requirements. Pharmaceutical licensing regulations require evidence of quality, safety and efficacy—known to industry as the three ‘hurdles’ to market. Licensing regulations for devices, diagnostics and implants are similar, except that European authorities generally do not require evidence of efficacy in clinical trials, and are instead satisfied with the evidence of mechanical performance in laboratory tests. In essence, these product licensing laws are designed to ensure that the product is safe to use and fit for its purpose. Neither pharmaceutical nor medical device licensing authorities examine whether, under conditions of routine use, the product is (a) better for the patient’s health than the leading alternatives (‘comparative effectiveness’), or (b) better value for money than the leading alternatives, taking into account the full range of costs and savings for the purchasing organisation and its stakeholders (‘cost effectiveness’). These factors are crucial to any clinical decision to use a drug or device and any policy decision to finance the use of such products in public health care systems.

During the 1990s, however, the evaluation of comparative and cost effectiveness expanded dramatically, and most European countries started to take such data into account on an informal basis in making reimbursement decisions [1]. This was partly in response to demand from purchasers concerned about the rising costs of new technology. It was also partly in response to the organised efforts of clinicians involved in the ‘evidence-based

medicine’ movement and associated organisations such as the international Cochrane collaboration.

More recently, several Member States have started to develop formal procedures for incorporating comparative and cost effectiveness evidence into reimbursement decisions—known to the pharmaceutical industry as the ‘fourth hurdle’ to market. Since 1997, Denmark, England and Wales, Finland and The Netherlands have all introduced official procedures for the use of economic evidence in selected national reimbursement decisions [2]. In addition, Germany is considering such a move [3] and Belgium, France, Italy, Portugal and Spain have all taken the step of introducing methodological guidelines for the conduct of economic evaluation studies [4]. Because the European Union (EU) has a 25.8% global market share for pharmaceuticals in 1998 [5], firms are starting to modify the production of evidence accordingly.

In what follows, we summarise current concerns about the economic evaluation of medical products in Europe. We then identify five challenges facing national- and EU-level policy makers in designing tighter regulations of the market for economic information, which will help channel the efforts of industry into developing and marketing more cost effective medical technologies. Our central conclusion is that there is considerable scope for improved transparency and accountability in the production and use of economic data about pharmaceuticals and medical devices by manufacturers and purchasers.

## 2. Methodology

This article is based on interviews with mainly UK-based health economists, carried out as part of the ASTEC project by one author (Richard Cookson), coupled with the personal knowledge and experience of the other author (John Hutton) from many years, working as a health economics consultant to the European pharmaceutical and device industries.

Interviews were carried out during 1999 and 2000 with health economists working for industry, universities, research institutes and consulting

firms. Most of those who were formally interviewed are listed in *Acknowledgements*, although a small number of industry-based interviewees asked to remain anonymous.

The majority of those interviewed were, like the authors, UK-based. However, many of the UK-based interviewees were capable of providing an EU perspective: in particular, those in industry working for EU or global divisions within their firm, and consultants working for firms that support industry health economics submissions across the EU. Furthermore, to help guard against possible bias towards UK-specific concerns rather than broader EU concerns, interviews and comments on earlier drafts were obtained from ASTEC partners and their colleagues based in a range of other EU countries.

Interviews with health economists from universities, research institutes and consulting firms were largely informal, and secured through the personal contacts of the authors and those of the ASTEC project director, Professor Alan Maynard. This was felt to provide sufficiently broad coverage of these groups of health economists, particularly as Professor Maynard was in 1999 the President of the International Health Economics Association.

Interviews with industry-based health economists were conducted more formally, and were sought by sending letters to the UK chief executive officers of 10 large pharmaceutical and life science companies. This approach succeeded in identifying a range of industry experts from six large pharmaceutical firms and three small medical device firms.

Once firms identified a contact person to coordinate their response, interviews were arranged with experts within the organisation. Care was taken to obtain input from those who could provide an EU perspective as well as a UK perspective, and to obtain input from science managers who could talk about the use of economic evidence in R&D prioritisation decisions, as well as outcomes research and policy managers who could talk about the use of economic evidence in public reimbursement decisions. Further contacts with industry experts were arranged through personal contacts of the core ASTEC research team.

Both face-to-face and telephone interviews were used. Face-to-face interviews with pharmaceutical industry representatives were all held at the interviewee's offices. One firm provided a written response, complete with copies of relevant public domain literature. In addition, industry experts were given the opportunity to comment on an early draft document, and many produced detailed and helpful comments.

All interviewees were willing to provide general information; most also provided detailed written comments on a first draft of this report. However, none was willing to give detailed firm-specific information, or to release 'grey' literature not in the public domain. The one exception was that experts from large firms were generally willing to share the firm's official responses to NHS consultation documents on the National Institute for Clinical Excellence.

Difficulties were encountered obtaining reliable and verifiable information about firms' current evaluation activities and future plans, since firms are reluctant to publish up-to-date information about the details of their business strategies. So it was hard to verify claims made by some industry representatives that firms are already responding on a voluntary basis to the criticisms summarised in this article.

### 3. Trends in pharmaceutical evaluation

Pharmaceuticals are more comprehensively evaluated than any other commercial or non-commercial health interventions. All new pharmaceuticals go through a costly series of regulated tests and trials during a development phase typically lasting 10–12 years, and culminating in large-scale Phase III clinical trials in human patients.

In the past, pharmaceutical evaluation activity focused almost exclusively on quality, safety and efficacy. During the 1990s, however, the evaluation of a wider range of clinical and economic outcomes—known as 'health technology assessment' (HTA)—expanded dramatically. In particular, clinical trials have been redesigned in three main ways with HTA in mind: (1) evaluation of

patient's quality of life outcomes as well as biomedical outcomes (e.g. cholesterol levels), (2) measurement of economic costs alongside trials, and, in some cases, (3) evaluation of outcomes compared with alternative drug therapies as well as placebo. The inclusion of cost data has generally increased the sample size of Phase III trials, although not the duration. From interviews, it was found that all large multinational drug firms have set up multidisciplinary pharmacoeconomics departments, often boasting several post-graduate qualified staff, to advise on trial design and to perform secondary evaluation of clinical and cost effectiveness from primary trial data.

Most large firms are now redesigning earlier Phase II trials to provide internal information for the 'big money' decision to move to the much larger and more expensive Phase III trials. Evidence on clinical and economic outcomes is being produced and used internally by firms at increasingly early stages of the development process, in order to help predict the price response of customers to new products and hence to inform go/no go decisions. Evidence of a 'good' safety and efficacy profile is no longer sufficient to guarantee market success, and the prospect of marketing failure due to evidence of poor comparative or cost effectiveness can be enough to kill compounds.

Table 1 summarises the different types of outcome that can be evaluated, and gives an indica-

tion of frequency of use at different stages of the product life cycle. This is based on one author's (RC) interpretation of interviews with industry experts, coupled with one author's (JH) experience in performing evaluations for industry as a research contractor, and is presented purely as a focus for discussion.

Safety is by far the most frequently evaluated outcome: it is routinely evaluated at all stages of research and development, and post-marketing surveillance studies are routinely conducted following the introduction of a new drug to test for rare or long-term adverse events that may not be picked up in large-scale Phase III trials.

By contrast, none of the other outcomes listed in the table is routinely evaluated post-launch, despite widely recognised limitations in the usefulness of pre-launch data in assessing these outcomes [6]; see Section 4 for further discussion.

The table distinguishes three types of 'economic' data: purchaser budget impact, cost effectiveness and cost utility. Purchaser budget impact refers to the total cost (per time-period) for the purchaser of funding the new drug, in terms of the relevant health care budget(s). By contrast, the other two kinds of data evaluate the 'value for money' of the new drug as compared to an alternative, in terms of an incremental cost per unit of health gain. This is quite different from purchaser budget impact: a new drug may represent good value for money

Table 1  
Evaluation of different types of pharmaceutical outcome

Type of outcome	Frequency of use at this stage of product life cycle					
	Development			Marketing		
	Phase I trials	Phase II trials	Phase III trials	Early	Middle	Generic
Safety	▶▶▶	▶▶▶	▶▶▶	▶▶▶	▶▶▶	▶▶
Efficacy	—	▶▶▶	▶▶▶	—	—	—
Comparative effectiveness	—	—	▶▶	▶▶	▶▶	—
Purchaser budget impact	▶▶	▶▶	▶▶▶	▶▶	▶▶	—
Cost effectiveness	—	▶▶	▶▶▶	▶▶	—	—
Cost utility	—	▶▶	▶▶	▶▶	—	—
Impact on inequalities	—	—	—	—	—	—

Source: Authors' interpretations of interviews with industry representatives and research experience. Key: —, evaluation never or almost never performed at this stage; ▶▶, evaluation sometimes performed at this stage; ▶▶▶, evaluation always or almost always performed at this stage.

even if it has a large total budget impact, and vice versa.

The bulk of the ‘value for money’ data being produced is cost effectiveness data, which measures health gains in terms of context-specific clinical endpoints—e.g. median time to progression for cancer patients, or gains in cognitive functioning from an Alzheimer’s drug. This type of data encompasses a range of economic evaluation methodologies, including those sometimes known as cost-minimisation analysis and cost-consequence analysis [7].

Cost effectiveness data informs purchasers interested in two main questions: (1) will introducing this new drug improve the health of patients with this disease, and (2) will there be any non-pharmaceutical resource use savings (in this or other disease areas, or outside health care) which partially or completely offset the increase in pharmaceutical costs?

However, this does not help purchasers interested in broader social questions about the population health outcomes of shifting money towards this new drug and away from alternative uses (inside or outside the health care sector), such as (1) will introducing this new drug result in improved total population health, and (2) will introducing this new drug result in reduced inequalities in access to care or in lifetime health expectancy between different population sub-groups?

To address these questions of population health, broader evidence is required which enables comparison of health gains and losses between population sub-groups using a generic unit of health which combines length and quality of life into a single measure, such as the ‘quality-adjusted life-year’ (QALY). This kind of data is often called ‘cost-utility’ data [7]. Only about 10% of European pharmacoeconomic studies published in the three years 1995–7 produced cost-utility evidence in terms of generic health outcomes (e.g. QALYs) that allow economic comparisons of treatments in different disease areas [2].

The final type of outcome listed in Table 1 is ‘impact on inequalities’. This could involve, for example, analyses of expected differences in clinical outcomes for patients from advantaged and

disadvantaged groups, or analyses of the effect of not granting public reimbursement on inequalities of access to effective care between such groups, or even evaluation of impacts on inequalities of life expectancy and lifetime health. However, analyses of health inequality impacts are rarely performed and no standard methodologies have yet been developed.

A salient feature of commercial evaluation activity, clearly revealed in Table 1, is that clinical and economic evaluation activity peaks around the time of product launch. This is the inevitable result of the current regulatory environment. Given the pressure to expand sales volumes as rapidly as possible after licensing while the new drug can still command a high price, firms have a strong incentive to prepare economic evidence for purchasers as soon as possible after licensing. Purchasers also want economic evidence as early as possible, since they know that it becomes difficult for regulators and managers to rein in the diffusion of a new clinical technology once doctors and patients have become accustomed to it. Since all the key regulatory and purchasing decisions are focused around the time of product launch, the flow of commercial evaluation evidence naturally tends to be channelled towards the transition from development to marketing.

#### 4. Trends in medical device evaluation

Historically, new medical devices have been evaluated less comprehensively than pharmaceuticals, without using clinical trials, during a much shorter development phase of typically only 1–3 years. According to industry experts, one reason is that safety concerns are often less pronounced, because many devices have less extensive physiological effects than pharmaceuticals, and those that do (e.g. implants) tend to have long-term physiological effects which cannot be assessed in short-term trials. Another reason is less concern over proof of efficacy, as opposed to mechanical performance, because the efficacy of devices is more closely tied to the skill and judgement of the clinician who controls the use of the technology on patients. A final reason is that purchasing organi-

sations are normally less aggressive about cost effectiveness, since new devices usually have less extensive impacts on health care budgets than new pharmaceuticals.

Clinical trials and subsequent economic evaluations are starting to be performed for new devices at the high-risk, high-revenue end of the spectrum. However, this expansion in HTA started later for medical devices than for pharmaceuticals tends to be done by health services after the diffusion of technology, and has made less progress. In addition, more progress has been made in some areas than others—for instance, economic evaluation is currently much less likely to be performed by manufacturers of radiological devices than those in the cardiological field. Moreover, clinical trials are not performed for the vast majority of new devices developed by small-to-medium sized firms with national or European orientation. These firms are concerned that stronger evidence requirements in the future may lead to rationalisation of the European device industry, as smaller firms struggle to cope with the financial and organisational burden of performing HTA evaluations.

Some of the medical device experts interviewed for this study argued that HTA requirements should remain less stringent for devices than drugs due to special difficulties, in particular:

- 1) Shorter product life cycle: Device firms cannot afford to engage in the same lengthy trials as pharmaceutical firms, as devices are more rapidly overtaken by technical advance.
- 2) Lower cost: Devices tend to have lower expected utilisation rates and sales revenues than drugs, so it is more difficult to recruit large sample sizes and to recoup the fixed costs of performing evaluations.
- 3) More confounding factors: Medical devices are generally used as one part of a complex and variable series of health care activities performed by clinicians, whereas pharmaceuticals are generally administered by patients themselves. Hence trials of devices are more vulnerable to confounding factors arising from variations in clinical practice between different places, different clinicians and different patients.

- 4) Greater role of process utilities. The value of some devices (e.g. more convenient bandage application and removal) lies chiefly in the improved process of care ('process utility') rather than improved clinical outcomes.

However, while recognising these difficulties, most HTA experts agree that the European evidence base for medical devices is poor in comparison with pharmaceuticals, and that greater use of clinical trials and other forms of evaluation is essential if purchasers are to make informed decisions about high-cost device products at the time of launch.

## 5. Criticisms of current pharmaceutical and medical device evaluation

There is general consensus that the requirement for routine clinical trials since the 1960s has helped to prevent repetition of large-scale pharmaceutical safety disasters like thalidomide. There is less consensus, however, about whether or not the redesign of trials and the growth of HTA in the 1990s have helped improve health.

Most HTA specialists in industry and academia agree that the scientific validity of HTA evidence available prior to launch has improved markedly over the last 10 years, but that it is still not as rigorous as it could be. In particular, there are concerns that evidence about clinical and especially cost effectiveness is less likely to meet appropriate scientific 'gold standards' than evidence about safety and efficacy. The perception in both pharmaceutical and medical device industries is that large health care payers around the globe have yet to signal a demand for state-of-the-art evidence of clinical and cost effectiveness.

Widely recognised limitations in the pre-launch evaluation of comparative effectiveness include:

- Trials usually make comparisons with placebo and/or with older, long-established therapies, rather than 'head-to-head' comparisons with the leading alternative therapy.
- Patients with multiple illnesses are often excluded from clinical trials, even though these

patients are major users of pharmaceutical products [8].

- Clinical trials are performed under strict research conditions which may give a misleading impression of outcomes in routine practice [9].
- Trial duration is often too short to detect longer term outcomes.

Industry representatives argue that these limitations in the evaluation of comparative effectiveness are due to unavoidable ethical, methodological or commercial difficulties in the design of Phase III trials—for instance, difficulties obtaining informed consent from patients, achieving internal validity (i.e. correct attribution of cause and effect), and meeting registration time frames. While academic specialists accept that genuine difficulties of this kind exist, they argue that nevertheless there is scope for further improving the design of trials in order to facilitate pre-launch evaluation of effectiveness. They also argue that regulations currently give firms a perverse incentive to obtain a product licence by providing narrowly focused evidence of efficacy for one particular indication in one particular patient sub-group—in the hope that clinicians will engage in off-label prescribing which facilitates the expansion of prescribing volumes for wider uses, before the licensed indications are increased.

Widely recognised limitations in pre-launch evaluation of cost effectiveness include, in addition:

- Trials do not always collect a full range of economic data on either the cost side (e.g. purported cost offsets) or the benefit side (e.g. generic utility measures of health gain).
- Cost effectiveness comparisons between disease areas and between regions are seriously hampered by wide variation in economic evaluation methodologies [10].
- Economic evaluations do not adjust cost effectiveness or budget impact predictions to take account of patient or provider behaviours such as inappropriate prescribing.

Both industry specialists and academics agree that there is substantial scope for improvement in

economic evaluation, including greater use of modelling to address the more unavoidable limitations in trial design from an economic point of view. They also argue that the key obstacle to further improvement in economic evaluation is the lack of demand for better quality data from large purchasers.

A second major source of concern is that evaluation efforts fall rapidly after product launch, and there has been limited use of ‘naturalistic’ data gathered post-launch about comparative and cost effectiveness in routine use [11]. Naturalistic studies include ‘pragmatic trials’ under life-like conditions as well as observational studies based on post-marketing surveillance. This is unfortunate, because naturalistic studies are the best way to assess comparative and cost effectiveness in routine use [12,13].

Industry experts say that some naturalistic studies are funded by industry, as ‘seeding’ studies to familiarise prescribers with a new product, or to obtain marketing advantage for a new entrant into an existing class of drugs (as, for example, with the new SSRI drugs for depression competing with the market leader, Prozac). There are concerns that industry funding of such studies through provision of free drugs may bias results by influencing prescribing behaviour. In principle, however, it should be possible to devise reimbursement mechanisms to overcome this difficulty. Alternatively, naturalistic studies could be directly funded and organised by health authorities, although at present they rarely seem to consider the effort and expenditure worthwhile.

Finally, many critics argue that too little progress has been made in improving processes of transparency and peer review scrutiny in the reporting of evidence. There are signs that industries are responding to calls for greater transparency [14], but only in terms of publishing trial protocols, not results [15,16]. Firms argue that enforced publication of trial results would harm the position of research-based firms by giving less innovative firms a competitive advantage; critics argue that transparency of trial results would enhance the competitive position of truly innovative firms by allowing more widespread scientific scrutiny of marketing claims made about products

[17]. Critics also argue that voluntary regulation by the journal peer review process is currently inadequate to identify potential biases in economic modelling work. Even the best medical journals are unwilling to devote enough peer review time and resource to rework all the calculations and detect serious forms of error and bias [18].

## 6. Five challenges for European policy-makers

The most important challenge is for national purchasers to become more transparent and accountable in the way they themselves use evidence in pricing and utilisation decisions. Until this is done, purchasers will remain open to three serious and long-standing criticisms: (1) that evidence is used to address narrow medical concerns, rather than broader social concerns about public health and inequities in health; (2) that evidence is used to address narrow accounting concerns about pharmaceutical and equipment budgets, rather than wider economic concerns about social efficiency; and (3) that evidence requirements fluctuate according to short-term financial and political pressures, creating business uncertainty and distorting long-term R&D incentives for developing cost effective new technologies [19].

Addressing these criticisms will require routine publication, in a structured format suitable for making comparisons between products and between reimbursement decisions, of full details of the evidence used in decisions, and of the evidence requirements that were communicated to firms in advance of the decision. Since non-specialists find it hard to understand economic evidence, it will also require greater efforts to translate findings into ordinary language coupled with more widespread training of health professionals in basic economics concepts.

A second challenge is to redesign European licensing regulations to improve the scientific validity of HTA available at product launch. This is a particular challenge for high budget impact devices, which in many cases are still evaluated on the basis of mechanical performance in laboratory tests rather than clinical trials capable of measuring the outcomes that matter

to patients. It is also a challenge in relation to clinical trials of pharmaceuticals, which can be criticised for providing the wrong sorts of HTA data on both clinical effectiveness grounds (for example, failing to perform ‘head-to-head’ comparisons between the new drug and the leading alternative therapy) and cost effectiveness grounds (for example, failing to use generic quality of life measures suitable for comparing health gains between disease areas).

A third challenge is to harmonise economic evaluation methodologies and reporting formats to improve comparability between disease areas and between geographical regions, using a ‘reference case’ approach [20]. Progress has been slow on this, and the many voluntary methodological guidelines that have emerged have had no demonstrable impact on evaluation practice. In particular, economic evaluation methodologies and reporting formats currently vary so much that cost effectiveness comparisons between disease areas (‘cost per QALY’ comparisons) are often rendered meaningless [21]. Harmonisation of instruments for valuing ‘quality of life’ is an area of ongoing controversy, with different specialists advocating different instruments, and some even arguing that the use of QALY data should be abandoned altogether [22]. However, methodological harmonisation of QALY measurement methodologies is essential if HTA is explicitly to address concerns about population health outcomes and inequalities in health, as well as narrow medical outcomes.

A fourth challenge is to develop and apply new HTA methodologies for the evaluation of inequalities of access and outcome. Prototype methodologies for evaluating equity concerns already exist, for instance the Williams method [23] for evaluating concerns to reduce inequalities in lifetime health outcome. So far, however, the public sector has invested little in developing such methodologies, and has not tried to encourage firms to develop them or to collect suitable data for applying them. These methodologies will become increasingly relevant, however, as European countries increasingly engage in explicit debate about ethical criteria for the ‘rationing’ of health care, and start to realign health policy towards explicit



equity goals such as reducing the health gap between rich and poor.

A final challenge is to find ways of using ‘naturalistic’ HTA evidence gathered from pragmatic trials and observational studies after initial product launch. Pharmaceutical firms are keen to address this issue since they argue that ‘one-off’ evaluation at product launch may kill off many potentially cost effective therapies used in ways unforeseeable at launch, citing examples such as combination therapy for AIDS, the components of which were not initially cost effective as monotherapies. Purchasers are reluctant to accept this argument, of course, since it increases the risk that public money will be wasted on drugs which do not prove cost effective in the long run. One option for purchasers to consider, therefore, would be performance-related reimbursement deals linking future prices with performance in post-launch cost effectiveness studies of how well the drug performs in routine practice.

## 7. The scope for concerted EU action

With the responsibility for health care financing and provision in Europe remaining firmly at the national level, the evolution of a pan-European approach to the problems of economic evaluation of health technologies may be slow. Nevertheless, the increasing convergence in health care practices will create a basis for EU-wide action to facilitate methodological harmonisation and the sharing of economic information between Member States [24].

In relation to the medical device industry, the EU could begin the process of methodological harmonisation by extending EU licensing law to require clinical trials for all high-budget impact new devices. Without this, the production of reliable estimates of effectiveness and cost-effectiveness prior to launch is almost impossible. Any such requirement might provoke opposition from smaller device firms, however: a requirement for trials would increase firms’ fixed costs, perhaps leading to rationalisation of the medical device industry.

In relation to the pharmaceutical industry, where clinical trials are already mandated at EU level, the key harmonisation issues relate to the methods of economic evaluation used alongside those trials. Many experts argue that action is needed at EU level, as well as national level, given the increasingly global nature of HTA production in the pharmaceutical industry and in particular the growing use of international multi-centre trials. However, a difficulty is that voluntary guidelines on methodology have had little impact on economic evaluation practice in the past. The failure of voluntary guidelines may in part be due to the incentives faced by local producers of evidence—for example, academic incentives to product differentiate (i.e. to promote the methodologies they have helped to develop, or have learned to use), and manufacturer incentives to select methodologies on an ad hoc basis which are most likely to cast a particular product in a good light. In the face of such incentives, methodological harmonisation may require a degree of enforcement—which for the time being may prove easier to achieve at national level rather than EU level.

One option to enforce EU-wide methodological harmonisation would of course be for the European Medicines Evaluation Agency (EMA) to incorporate cost effectiveness requirements (or at least economic data gathering requirements) into its licensing decisions. A major difficulty with any such proposal for a pan-European ‘fourth hurdle’, however, is that cost effectiveness and efficiency can vary substantially between countries, due to differences in resource utilisation patterns, costs and national policy goals. In the absence of a pan-European health care system, there can be no such thing as pan-European cost effectiveness. In the face of this difficulty, pressure might arise to adopt ‘lowest common denominator’ standards: i.e. to grant a licence as long as the cost effectiveness standards of any one country are satisfied. Instead of being used to weed out inefficient therapies and to encourage efficient ones, the danger would be that EMA-approved economic evaluations could become a pan-European lobbying mechanism to extract funds for new pharmaceuticals from reluctant national reimbursement authorities.

## 8. Conclusion

The continually evolving shift towards tighter national and international regulation of economic evaluation activity sets the health care industry apart from almost all other sectors of European industry. While evaluation of safety is often heavily regulated in other industries, evaluation of cost effectiveness is typically left as a matter for self-regulation, and organised on the basis of voluntary market transactions between buyers, sellers and intermediaries such as consumer or trade associations.

It can be argued that this difference in regulatory behaviour is the undesirable result of various ‘government failures’ in European health care. In particular, because European governments act both as purchasers and regulators of health care, they may be tempted to use regulation as an instrument for controlling health care expenditures. If so, the regulation of economic evaluation may be cost control in disguise. Regulation may also be used inefficiently to shift the administrative costs of evaluation towards manufacturers and away from public health care budgets. According to this argument, it may be more efficient for purchasers to fund and perform evaluations themselves, rather than forcing manufacturers to do them under strictly regulated conditions.

On the other hand, it can be argued that the regulation of health economic evaluation activity is a desirable response to market failure. As Enthoven has written, in commenting on the UK internal market reforms of the 1990s: ‘Perhaps the most significant overestimate of what the market can do was in the field of information which is, for the most part, a public good that markets under-produce because of the problem of “free-riders” and because many providers consider it against their interest to report data in a uniform format that can be compared with others’ [25]. In blunt terms, as one US commentator recently put it, ‘to rely on the drug companies for unbiased evaluations of their products makes about as much sense as relying on beer companies to teach us about alcoholism’ [26].

Clearly, both government failures and market failures are present in relation to the production

and use of health economic evaluation evidence. The regulation of health economic evaluation needs to be redesigned and strengthened to overcome both kinds of failure: both to improve transparency and accountability in how public purchasers use economic data, and to improve the validity and relevance of economic data provided by manufacturers.

Managing the continued growth in commercial HTA activity in Europe will require action primarily by national governments in developing and refining national ‘fourth hurdle’ systems for the systematic use of cost effectiveness evidence in decisions. The role of the EU is likely to be more limited, since there can be no meaningful measure of ‘pan-European cost effectiveness’ in the absence of a pan-European health care system with standardised clinical practices, financial systems and unit costs. EU can, however, play a role in encouraging co-ordination between national efforts, and ensuring that national authorities have staff with the expertise to interpret correctly the submitted and published evidence on clinical and cost effectiveness. In the longer run, it may also have a useful role to play in the quality control of economic evidence.

Industry can be expected to resist any tightening of evidence regulations, since it increases the uncertainty for firms seeking to guarantee revenue from products in the pipeline. Industry representatives cite the potential threats to competition and innovation (and the jobs, exports and tax revenues that go with it) if ‘fourth hurdle’ regulations are too onerous. However, the point of regulating the market for information is to enhance R&D competition, by facilitating product comparisons and allowing purchasers to make informed choices about which new products offer the best value for money. So long as there is transparency and accountability in the use of cost effectiveness evidence by purchasers, those firms capable of producing cost effective new health care products will flourish, benefiting patients, taxpayers and shareholders alike.

The impact of a strict application of cost effectiveness criteria by purchasers on industry practice and profits would be considerable and unpredictable, as most large companies currently

have a portfolio of products of varying cost effectiveness. Of course, designing an effective regulatory system for the health care industry involves considerations of health, industrial, science and economic policy, going well beyond the regulation of the use of economic data in health care. However, more efficient and transparent production of economic data will enable clearer choices to be made. Those who wish to continue to purchase or produce medical technologies that have not been demonstrated cost effective will find justification for those decisions much harder.

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