mount importance is the requirement to keep public health care at the highest scientific level, based on evidence and medical competence.

CONFLICT OF INTEREST STATEMENT: Professor Max E. Scheulen is an employee of the University of Essen and it can be confirmed that there is no conflict of interest involved in this paper, nor in his participation in this entire event.

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SHOULD REGULATORS BE CONCERNED WITH PHARMACOECONOMIC ISSUES?

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Risk–benefit analysis should be the only basis for approval or registration of a new agent. However in addition to this, in Sweden, for example, there is an obligation to promote cost-effective use of drugs based on written information or workshops that include subscribers. The National Institute of Clinical Excellence (NICE), a special health authority of the British National Health Service, deals with issues of cost and reimbursement. Regulators may think of considering cost effectiveness when they request data to substantiate efficacy of new anticancer agents as long as patients are provided with best possible treatment. If, however, society is not prepared to pay for new products, then they should not be developed.

The goal of regulators is to limit unnecessary queries because they needlessly increase the price of new drugs. A tradeoff exists between quality of data and cost and data quality cannot be lowered below some point. Industry dislikes segmented pricing, but, particularly in the case of drug combinations, costs are prohibitive for many countries. Differential pricing, based on the region where a drug is being marketed, is one way to maximise income. Regulatory authorities should take this factor into account as they consider registering or licensing new anticancer therapies.

Oncology involves a very special group of drugs. Is a new drug development model for oncology drugs required to get them to the market more quickly? Is conditional or accelerated approval the best means to do so? In theory, conditional approval should work although it is a relatively new process. Linking conditional approval to conditional reimbursement, however, needs to be very carefully evaluated as it should be possible to reassess the cost–benefit of a conditionally approved therapy and take it off the market if the cost–benefit analysis is not favourable (although it would be a very difficult situation).

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THE ETHICS OF PHARMACOECONOMICS FROM THE PATIENT'S PERSPECTIVE

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This discussion on pharmacoeconomics involves not only industry and academia, but also real people who have cancer. Some people are treated and cured, but many have to live with the disease. Results of a keypad voting survey[1] regarding the patient access to anticancer therapy of 104 cancer advocates in May 2005 are shown in Table 1.

Interestingly, 100% of respondents from France indicated they knew of no one who had been refused access to a cancer treatment because of cost, whereas 100% of those from Poland responded that they did. Clearly, cost is a factor, and the ability to access new anticancer therapies varies greatly across Europe. Patients do not think like consumers, though, because they do not care about price; they just want the best treatment.

Therefore the question is that if a significant number of people in Europe are not able to access technologies, what is the point of developing or testing them? To ensure that real people can benefit from new drugs means eliminating barriers to access, which include the high price tag of the drugs and the time it takes for registration or licensure. Clinical trials, regulatory agency review and health technology assessments (HTAs) all take time, but patients with life-threatening disease often do not have that luxury.

The goals of new-drug development should be to provide patients everywhere with timely access to safe and effective therapies and to ensure that patients are not put at undue risk by taking innovative medicines. Thanks to the informed consent process, patients understand risk and many are willing to accept it by participating in clinical trials, even if they might not benefit directly. Nevertheless, placebo-controlled trials present challenges because patients generally desire the opportunity to take a potentially effective drug. Patients are likely to benefit from the regular monitoring provided during clinical trials, but their

Table 1 – Results of a keypad voting survey of cancer advocates, 2005

Survey item	Response (%)
Are you aware of any cancer drugs that are not available in your country but are available in others?	
Yes	54
No	46
If yes, why is the drug not available?	
The drug(s) are not licensed in my country	39
The public health authority will not reimburse the drug(s)	56
Physicians will not prescribe the drug	0
Do not know	5
Do you know of anyone who has been refused access to a cancer treatment, because it was considered too expensive?	
Yes	51
No	49

ability to access these trials usually depends on their clinician's involvement. Obtaining information about trials is often very challenging for patients. The main issue is time, which cancer patients lack.

HTAs sometimes present barriers to patient access. Different countries take different approaches to HTAs and sometimes arrive at different conclusions about a given treatment. The process delays patient access. If a product is approved, is its use guaranteed or merely a recommendation? If it is not approved, the regulatory agency needs to be transparent about the reason. Benefits include more than just survival endpoints; quality of life and symptom control are also very important. Extending life, if only by a few months, can be critical to some patients. Having a life-threatening disease also affects the degree to which patients are willing to take risks. Therefore, measuring cost effectiveness is complex, and priorities might be very different near the end of a patient's life.

CONFLICT OF INTEREST STATEMENT: The Roy Castle Lung Cancer Foundation is a registered UK Charity which has received multiple project grants from a number of pharmaceutical companies, strictly within our Policy for working with Commercial Organisations. Dr Fox has been invited to present at a number of meetings, at the invitation of pharmaceutical organizers, but Dr Fox has no personal financial interests with the pharmaceutical industry.

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Case stories

PHARMACOECONOMIC (REIMBURSEMENT) CHALLENGES WITH ANTICANCER VACCINES

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In principle, reimbursement for oncology therapeutics is extremely good, especially in the United States. Medicare is required to pay for indicated and compendia-listed off-label uses regardless of price. There is currently no system in place to measure cost–benefit and impact of a new therapy. The trend in pricing of new therapies has been steadily upward with cost in the range of US $55,000 to $100,000 currently being obtained. Oncology drug pricing has recently come under scrutiny, and if prices go too high, the legislature would probably consider instituting some limits. Co-payments are becoming a concern, however; Medicare patients have to pay 20% out of their own pockets – a significant sum considering the annual cost of some treatments. Nevertheless, secondary coverage is available, and many drug companies have programs to help patients.

In the United States, payers and oncologists consider cost to be of lower priority than clinical measures (Fig. 1). Sixteen payer plans do not consider the cost of cancer treatment in their coverage decisions at all, largely because they follow Medicare coverage which is required to pay for approved oncology therapeutics. However, oncologists' treatment choices can be affected by their perception of patients' ability to pay.[1]

Favrille is the manufacturer of a personalised active immunotherapy product for B-cell non-Hodgkin's lymphoma known as mitumprotimut-T (FavId®, Id-KLH, Idiotype vaccine) which is given together with granulocyte-macrophage colony-stimulating factor (Leukine®, sargramostim, GM-CSF). It is custom-prepared from individual patients' tumour cells. Currently in phase III trials, this immunotherapy appears to meet the criteria of what the Centres for Medicare and Medicaid Services (CMS) would consider an oncology therapeutic.

There are four main issues of concern for the reimbursement of active immunotherapies in the United States: (1) Coverage under Medicare Part B (physician administered) for a non-intravenously administered (i.e sub-cutaneous or intra-Muscular) product will require justification for the treatment to not be considered self-administered (2) Co-administration of GM-CSF (Leukine®, sargramostim) will require coverage for use with the active immunotherapy (3) 3rd party payer misconceptions that this treatment should be covered in the same manner as prophylactic vaccines, which are generally sub-optimal in the US, and needs to be pro-actively addressed. (4) Coverage of a processing fee could be problematic as this is usually associated with diagnostic procedures not therapeutics.

In the European Union, drug costs continue to be an issue despite strict protocols for the use of expensive oncology products. Centralised procedures exist for the assessment of new products and their cost-effectiveness, the most well known being NICE in the United Kingdom. Furthermore, the majority of cancer care in Europe is delivered through specialised, tertiary care centres or hospitals. These centres for the most part have fixed annual budgets and treatment decisions are guided by set protocols. An expensive new oncology therapeutic, such as an active immunotherapy, must have sufficient supportive clinical and pharmacoeconomic evidence to change these protocols and compete for the limited financial resources of the institution. Gleevec® is an example of an expensive, novel, oncology therapeutic that has achieved success in Europe despite these hurdles – sales in Europe as a percentage of global sales exceed those of the US.

In summary, reimbursement is not a significant concern if the following criteria are met:

- Significant improvements in meaningful clinical endpoints are demonstrated (e.g. time to disease progression, overall survival in randomised studies).
- Payment and reimbursement should be on a final per-product-vial basis; avoid processing charges, which can complicate the reimbursement process.