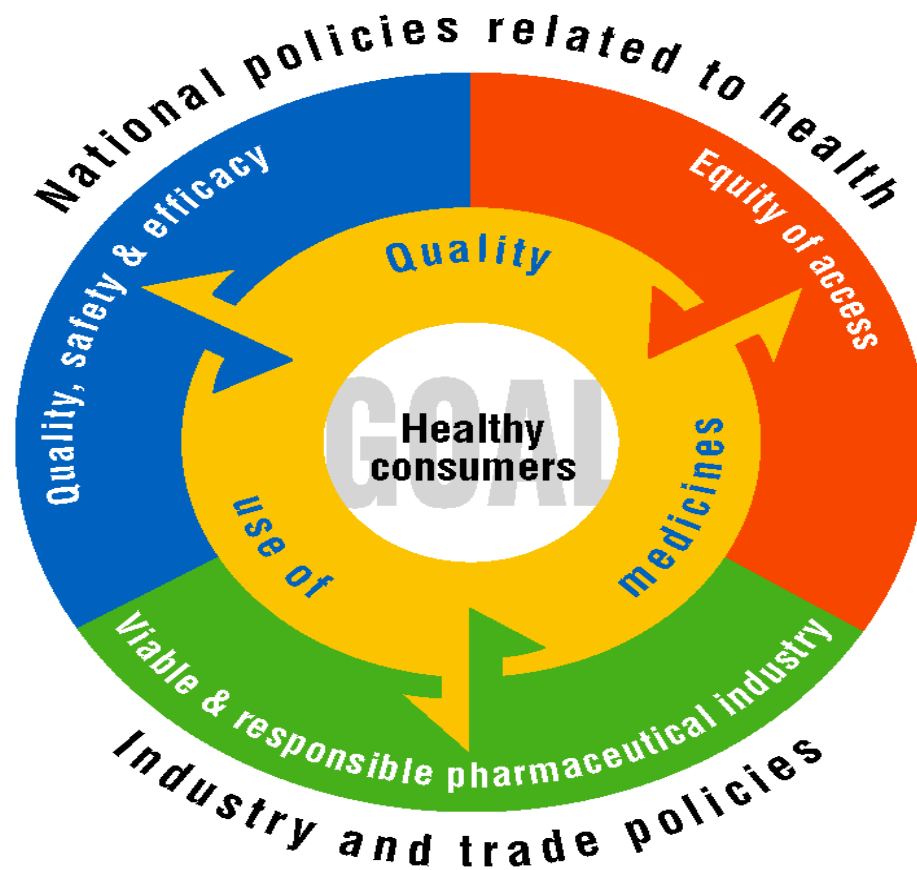


Interaction between Regulators and Payers

Professor Lloyd Sansom AO
Chair, PBAC
Australia

QUM and the National Medicines Policy



HEALTH TECHNOLOGY ASSESSMENT (HTA)

- HTA involves the medical/scientific, social, ethical and economic implications of the development, diffusion and use of a health technology. HTA has been positioned as a ‘bridge between scientific evidence and the needs of policymakers’

HEALTH TECHNOLOGY ASSESSMENT

- The major aim of health technology assessment for registration is to provide consumers with safe and effective drugs
- The major aim of assessment for subsidy is to ensure that the cost effectiveness of a drug represents “value for money” taking into account opportunity costs

REGISTRATION v's SUBSIDY

- The assessment for registration and subsidy ask different questions and the requirements are different
- The assessment for subsidy may be dictated by the registration decision eg registered for second line therapy where other agents have failed

Reason v's Excuse

- ‘The over-riding reason for these areas not being addressed to the satisfaction of the PBAC in the original submission is due to the paucity of clinical data for..... against any active comparator’

Submission to PABC 2007

Registration versus Subsidy

- “...so there is an increasing obligation for the developers of new treatments to provide evidence on a broader range of questions and outcomes in addition to the efficacy and safety data required by licensing authorities”

*Freemantle et al Pharmacoeconomics
2005;23(8);747-754*

Registration vs Subsidy

- **subsidy considered on the basis of effectiveness and cost, including comparison with other treatments which may be non-drug (eg standard medical care)**
- **comparative efficacy/toxicity, cost or cost effectiveness are often not considered by regulatory agencies**

THE WALL STREET JOURNAL

March 7, 2008

- “If the FDA has been given the power to make decisions that have such huge ramifications, it must be accountable for the cost-benefit ratio of these decisions. In this case, a study showed there was no survival benefit yet the costs will be billions of dollars per year. Is there any wonder why our health care expenditures are expected to double to over \$4 trillion within 10 years”

McCabe et al Int J Tech Assess Health Care 24,140-145 (2008)

- “Pharmaceutical regulators and healthcare reimbursement authorities operate in different intellectual paradigms and adopt very different decision rules. As a result, drugs that have been licensed are often not available to all patients who could benefit because reimbursement authorities judge that the cost of therapies is greater than the health produced”

McCabe et al Int J Tech Assess
Health Care 24,140-145 (2008)

- “This finding creates uncertainty for pharmaceutical companies planning their research and development investment, as licensing is no longer a guarantee of market access”

CONTEXT OF THE ASSESSMENT FOR THE CONSUMER

- A therapeutic option decision might be very much influenced by the comparison of studies using placebo as comparator relative to those using an active comparator which may be a treatment option. The comparative risk/benefit/cost options may be different in the two scenarios.

Clinical Trial Data-some questions relevant to Regulators and Payers

Generally the uncertainty in cost-effectiveness results from the uncertainty in clinical effectiveness

Clinical Trial Data-some questions relevant to Regulators and Payers

- Is the difference between a medicine and its comparator statistically or clinically significant?
- Is there head to head trials versus a relevant comparator?
- Are there applicability issues relating to patient selection and the population in whom subsidy is proposed?
- Were the dose ranging studies appropriate- do we really know the ‘true dose’
- Were the trials conducted with fixed or variable dosing?

Clinical Trial Data-some questions relevant to Regulators and Payers

- Was the duration of the trial(s) adequate?
- Was the drug terminated at some stage eg on disease progression
- Use of un-validated surrogate outcomes invariably adds uncertainty
- Was the outcome a composite endpoint?
- Was there early crossover?
- Is there consistency in the methods used by agencies to evaluate the data eg in the evaluation of indirect comparisons is relative risk or odds ratios used?
- Were quality of life measurements taken during the trial?

Clinical Trial Data-some questions relevant to Regulators and Payers

- Was post-marketing data collection required as part of the registration- if so-,what how,when ?
- Hybrid technologies-eg evaluation of tests associated with a drug's use eg molecular targets false negatives,false positive-is it really a treatment effect modifier-what's the evidence?
- Factors which may impact on quality use of medicines eg packaging and labelling-were these considered?

Data translation from registration to subsidy

- The results of the trial may need to be applied, extrapolated and transformed into a decision analysis
- *The participants in the trial might not be the same as the intended population for subsidy (**application**)-eg sub-group analysis*
- *The duration of the trial might be less than expected (**extrapolation**)*
- *The outcomes measured may not be patient-relevant (**transformation**)*

Surrogate outcomes

<i>Proposed SURROGATE MEASURE</i>	A biomarker or clinical outcome intended to substitute for a TCO	Target clinical outcome(TCO)	Final Outcome
Biomarker	Clinical outcome		
eg LDL	eg chest pain	AMI,death due to CV disease,overall survival	QALYs gained
imperceptible	perceptible	Perceptible and important to patients	
Disease centred measure		Patient –centred outcome	

Post Marketing Surveillance

- Is it risk management only ie identification of adverse outcomes

OR

- Data collection for assessment of adverse events AND benefit in clinical use

Post Marketing Surveillance and Coverage with Evidence Development

- The regulatory authorities are becoming more interested in post marketing surveillance as a means of managing clinical uncertainty
- The sponsors want earlier funded access under a coverage with evidence framework
- Are PMS and CED the same ?-if not how do they differ
- Does this whole area need to be considered as a continuum under a common framework-since uncertainty in efficacy and/or safety has a direct impact on uncertainty in cost effectiveness

Post Marketing Surveillance

- Both regulators and payers are being challenged in regard to a greater utilization of post marketing observational data to enable earlier registration and subsidy ie as a means of managing uncertainty.-but are we simply adding uncertainty on uncertainty?

Post Marketing Surveillance

- The two agencies have a common interest and there must have a common purpose in this matter
- How can we enhance the debate about the benefits of the linkage of data sets while at the same time protect the privacy concerns of consumers?. This is a challenge which must undertake.

HEALTH TECHNOLOGY ASSESSMENT

The processes must be seen as the start of a continuum from evaluation of risks/benefits and cost effectiveness to optimal health outcomes. While the results from registration and subsidy considerations can have a significant impact, there are many other factors which can and do have a significant influence and to which greater attention must be paid including in the evaluation processes

What data is needed?

- The questions are significant, but we have a responsibility to contribute to an international debate about these issues
- A reduction in data requirements increases risk

BUT

- A greater demand for data also presents a risk for reduction in availability of new agents due to lack of research and/or increased cost and subsequent access
- **HOW CAN WE BE SMARTER?**

Streamlined Process

- Simultaneous submissions to PBAC and TGA-pilot study commenced
- Need for close arrangements between the 2 evaluation groups
- The 2 processes ask different questions and often evaluate different data sets because of the comparative requirements of payers

Conclusions

- These important issues can only be tackled in a cooperative way by HTA agencies-for regulation and subsidy
- While they have different responsibilities they have a common purpose
- Greater interaction must occur