**HTAi Policy Forum 2014**

**Case Studies Exercise: Explanation, Options, Proposed Process and FAQ**

The 2014 HTAi Policy Forum Meeting will focus on “adaptive approaches” to licensing, HTA and the use of technology within health systems. This topic stems from a continuing theme in past Policy Forum discussions on the subject of “progressive decision making” where decisions are revisited after initial adoption decisions. A similar theme has emerged among regulatory bodies of medical devices and drugs resulting in proposals for “adaptive licensing”.

Discussions in the literature and other fora have identified a range of possible advantages, disadvantages and challenges of adaptive approaches. While it possible to discuss these in theoretical terms, the Policy Forum Committee believes that discussion at the Forum meeting needs to be informed by consideration in some detail of how an adaptive approach might have been applied to some specific drugs and devices that have gone through existing routes for licensing, HTA and coverage, and the possible benefits, problems and challenges that might have been associated with a more adaptive approach.

The agenda for the meeting (attached) therefore includes a session on the Monday morning where break-out groups will work through case studies in this way, so that the discussion that follows in the remainder of the meeting is grounded in that learning. This approach is consistent with others working in this field, in particular the influential work of NEWDIGS.[[1]](#footnote-1) It is important for Policy Forum members to keep in mind that the intent of this exercise, therefore, is to evaluate the impact of different decision-making approaches, and not the relative impact of different technologies.

**What will a case study look like? -** Individualcases will be presented as a structured abstract of publicly available information. Individual cases will be summarized in 2-3 pages. These will aim to be factual and accurate descriptions of events and will avoid interpretations of or judgements on these. The proposed structure of each descriptive case is as follows:

*Case Study Structure*

* The name and purpose (licensed indication(s)) of the technology, and its producer/licensee(s))
* Relevant aspects of the technology’s pre-market development
  + Pre-market studies description
    - Population, design, outcomes, comparisons and purpose
  + Timeframe of pre-market studies
* Relevant aspects of technology regulatory approval process in US/Europe
  + Timeframe including date(s) of initial application and approval
  + Final decisions and recommendations including changes from initial application
  + Agreed Phase 4 plans at launch
  + Any concerns raised publicly by regulators or producers, at or after launch
  + Any subsequent revisions to regulatory approval and/or ongoing monitoring
* Relevant aspects of HTA and payer approval processes
  + Timeframe(s) including date(s) of initial submission to some key HTA-based payer/coverage bodies, and dates of recommendations / decisions (as below)
  + Main characteristics of the HTA process that lead to approval/rejection (e.g. level of stakeholder involvement-who, type of assessment done etc...)
  + Recommendations and decisions including price (where applicable) and changes in use from initial application, including any requirements for “managed entry” (ME) or “coverage with evidence development” (CED)
  + Concerns raised publicly at initial approval/rejection by payers/HTA bodies or producers
  + Any subsequent revisions to approval and/or price (whether ad hoc or as part of an established ME or CED process)
* Any publicly available information on positions adopted by patient groups and industry in respect to either licensing or HTA/coverage (e.g., material on patient group websites, public submissions to regulatory/HTA/coverage bodies, newspaper articles etc.)
* Relevant aspects of its real-world use
  + Utilization (in approved indication)
  + Market share
  + Competitor introduction and timeframe
  + Label expansion
  + Initial pricing and changes
  + New information regarding safety or effectiveness
* A summary of the issues that the case was seen to present, as shown by information in the public record
* A suggestion as to which of the goals of adaptive approaches (as defined by Eichler et al.[[2]](#footnote-2)) might have been most likely to be achieved had a more adaptive approach been applied to this case

**What is the process for discussing case studies?** - Case studies will be discussed by break-out groups, each of which will have a mix of industry and HTA/coverage Forum members, together with regulator and other invited guests. Each break-out group will discuss one case study. It is proposed that there will be 6 break out groups (each with 12 or so members) and three case studies, and that each case study is therefore discussed in parallel by two break out groups.

Each break-out group will be co-chaired by a Forum member from industry and a Forum member from an HTA/coverage body. The co-chairs will introduce the case and summarise the key facts in it, but will not be expected to have any deeper personal knowledge of it. The Forum Scientific Secretary (who prepared the cases) will move between groups and be on hand to answer any key factual questions that may arise – in so far as that is possible and relevant to the task (see below).

After their introduction, the co-chairs will invite a **brief** discussion of the facts of the case as presented and invite anyone with direct knowledge of the technology to add to these.

The co-chairs will then invite discussion of:

* Which of the various goals proposed for adaptive approaches appear most relevant to the technology in question (i.e., reduce uncertainty around an endpoint, broaden treatment-eligible population, reduce statistical uncertainty, enable new-new combination development, reduce uncertainty around study design, ensure “real world” effectiveness, address rare adverse events)
* The form that a more adaptive approach to licensing and HTA/coverage might have taken to try to achieve this/these goals
* The possible benefits for patients, health systems and industry, and problems that might have been associated with a more adaptive approach
* The barriers and challenges to taking a more adaptive approach and what would be needed to address these

**What specific outcomes should be discussed?** – The groups will compare the hypothetical adaptive process against what happened in the case study with an aim to “bring to light” the possible outcomes of an adaptive process in the following areas:

* Timeframe – what would be the impact on the timing of pre-market studies, new license applications, and applications to HTA/payers
* Populations – what would be the impact on access to technology for licensed and expanded license populations
* Data Requirements – what changes to data requirements / studies / design would be needed?
  + What data is feasible / infeasible to gather?
* Outcomes –
  + Would an adaptive approach have led to better or worse overall patient outcomes?
  + Has it helped/caused problems for the work of HTA and coverage/pricing decisions?
  + How might an adaptive approach affect short and long term revenue from sales?
* Processes –
  + What interaction would be required between regulators, payers and producers to deliver potential benefits and address possible challenges?
  + Has it helped/caused problems for the organization of health care?
  + Are multi-national arrangements possible?

**What should not be discussed? –** The actual merits or drawbacks of the technology and its handling by industry, regulators, HTA/coverage bodies, health systems, clinicians and patients are NOT the focus of discussion. Policy Forum members are NOT being asked to judge the various impacts of a technology such as whether it is safe, effective or cost-effective. They are also NOT being asked to judge whether regulatory, payer or producer decisions regarding its development and use were good ones. Past decisions and impact are taken as given – the break-out groups are asked to consider whether patients and the processes used to manage technology introduction would potentially have been helped or hindered by a different (adaptive) approach, and what would have been needed to ensure that any potential benefits were actually delivered.

**What are the overall learning objectives? –** Case studies are intended to facilitate the following learning objectives for the Policy Forum and for Policy Forum members:

1. Identifying overall opportunities and barriers to implementing adaptive approaches for new technology
2. Identifying specific areas where adaptive approaches could be applied and articulating potential shortcomings and strengths to these.
3. Understanding how regulators, payers/HTA bodies and producers and health care systems might be impacted by adaptive approaches and where there will be a need for enhanced interaction and common requirements across these groups
4. Developing a preliminary understanding of possible principles and standards required before considering implementing these approaches
5. Understanding whether there are other revealed goals for adaptive approaches beyond those proposed

**What cases are being proposed? -** Some of the goals proposed for using an adaptive approach (Eichler et al.- see above) will align more directly with the goals of some stakeholders than others. For example signals re: rare adverse events may be more relevant to the role of regulators; reducing uncertainty about real world outcomes may be more relevant for payers; and more immediate access with intent to broaden populations may be most relevant to patients and manufacturers. The goal of the Forum is to promote the exchange of views and discussion between industry and HTA/coverage bodies. Case studies should therefore be selected that cover goals or relevance to both industry and HTA/coverage bodies.

Some technologies would not be appropriate for case studies at the Forum meeting because of the relationship they have to the remit of Forum members and/or invited experts. It would be inappropriate for the Forum to discuss drugs currently under regulatory or HTA/coverage consideration in Policy Forum member jurisdictions, for example. It may also prove difficult within the timelines available to develop case descriptions of technologies that are proprietary products of Policy Forum Member companies. For such technologies, the Forum member would naturally wish to be involved in the development of the case study. While this would potentially be helpful, it could also present challenges around what is presented, and how, timing of preparation of cases, and who is ultimately responsible for deciding the content of the case study. Policy Forum Members may also not feel completely free to explore issues surrounding these technologies.

For these reasons, the Policy Forum Committee recommends that the two drug case studies focus on drugs that are not products of Forum member companies and using only descriptive public information. As noted above, the cases have been selected to reflect diverging goals as a means of highlighting different stakeholder interests and issues. Two key goals have been selected: providing access and to generate data to consider access for potentially broadening populations; and, reducing uncertainty re: effectiveness outcomes.

**Brentuximab** (Adcetris; Takeda/Millenium Pharma (EUR) - Seattle Genetics, Inc (US))

* For HL patients after failure of ASCT or after failure of at least two prior therapies in patients who are not ASCT candidates
* Approval based on non-randomized, non-comparative phase II study in very high need population
* Potential goal of providing early access and broadening populations

**Lanthanum Carbonate Hydrate** (Fosrenol – Shire)

* In adult patients with chronic renal failure on dialysis with high serum calcium levels
* High degree of clinical and cost-effectiveness uncertainty, despite potential unmet need
* Potential goal of reducing payer uncertainty or identifying key subgroups

**Transcatheter aortic valve implantation (TAVI)** (Various producers)

* Clinical and cost-effectiveness uncertainty
* Obvious potential benefits but requires additional resources and specific training and regulated access
* Potential goal of reducing payer uncertainty or identifying key subgroups

1. See, for example, Baird LG et al. Comparison of Stakeholder Metrics for Traditional and Adaptive Development and Licensing Approaches to Drug Development. Ther Innov Reg Sci 2013;47(4):474-483 [↑](#footnote-ref-1)
2. H-G Eichler et al., “Adaptive Licensing: Taking the next Step in the Evolution of Drug Approval,” *Clinical Pharmacology and Therapeutics* 91, no. 3 (March 2012) [↑](#footnote-ref-2)