

# Nine steps to heaven

The response of pharmaceutical companies to increasing economic and competitive pressures has been to 'try harder'. This has been manifest in the adoption of approaches to increase throughput and reduce cycle times through implementing automated systems, better IT systems, optimizing outsourcing arrangements etc. But these are operational issues.

Jim and David Matheson, founding director and principal, respectively, of Strategic Decisions Group (SDG), argue that the key to successful R&D management lies in achieving excellence in both operational management and strategic management. Furthermore, it is essential for any organization to grasp that these represent completely different functions. The father and son team have advised

some of the world's largest companies on their strategic management. A case study of their work in directing processes for making resource-allocation decisions for SmithKline Beecham's portfolio management was recently published in the *Harvard Business Review* [Sharpe, P. and Keelin, T. (1988) March–April issue, pp. 3–10]. Further examples of practice with companies such as Monsanto, 3M, Procter & Gamble and Merck are illustrated in their book: *The Smart Organization; Creating Value through Strategic R&D*, published earlier this year.

## Operational versus strategic management

The Mathesons argue that a fundamental lack of understanding of these issues explains why several of the companies

identified as exemplary for their operational management by Peters, T. and Waterman, R. in the seminal business management work *In Search of Excellence: Lessons from America's Best Run Companies* (published in 1982 by Harper & Row) have since experienced a decline in fortunes. Many companies are operationally sound, but strategically weak. For example, biotech companies are not always clear what their exact role is in terms of therapeutic focus, technology status, whether they are a discovery company, pharmaceutical company or technology partner. If the role of the company is not clearly defined, benchmarking becomes impossible. Jim Matheson cites Syntex as the classic case of a company being organizationally effective but strategically deficient. 'Syntex was braindead,' says Matheson, 'What was the consequence? Roche harvested the organs, like productive assets and talented people'.

The Mathesons argue that smart R&D is about making quality decisions – those that create the best prospects for creating value. Strategy is all about providing shareholder value, but that should be interpreted flexibly, not simply in terms of stock value or shareholder dividend.

## Problems for the project advocate

One problem that is entrenched, even enshrined, within many corporate structures is the role of the product champion or project advocate. The Mathesons argue that there are two fundamental flaws with this system:

- Projects can be pushed by the individual advocate long after their strategic sell by date has passed. For example, a competitor may gain an unassailable lead, at which point a project should be stopped.
- The most articulate and vocal advocates achieve greater success for their individual project in-house. But it may not be the best strategic choice.

A more teamwork-based strategy is therefore likely to be much more effective. And teamwork should be promoted

### Box 1. Nine key principles of strategic R&D

- Have a value creation culture – everyone in the company knows who the customers of the organization are and how the organization captures value by serving them.
- Understand that good decision-making requires hard thinking that creates alternatives – there is ample evidence of a wide range of good options that are carefully considered and rejected in favour of better ones.
- Continually learn what customers want and deliver it with efficiency – change is viewed as positive and productive, even if painful at the time. Changes are generally motivated by opportunity.
- Embrace uncertainty – plans focus on major decisions and sources of uncertainty. Commitments are made based on achievable goals and people are held accountable for things they can control, based on an explicit understanding of risk and uncertainty.
- Have an outside-in strategic perspective – executives and managers have a broad view of external forces shaping the industry and customers, the positions and strategies of the competition and the implications of shifts in the outside world that will affect the organization.
- Employ systems thinking – when making strategic decisions, many factors are considered, then narrowed down to a list of the most important factors that drive value creation. They develop and use sensitivity analysis and systems models to develop depth insights.
- Encourage open information flow – managers get the organization's best information quickly. There are few secrets. Informal channels and internal networks are fostered and encouraged.
- Align and empower management – there are clear, aligned strategies at all levels that provide guidance for decision-making. Decisions require few approvals.
- Have disciplined decision-making processes – there is a formal decision-making process understood by all. Management and staff can explain the processes that lead to decisions.

in terms of the vertical corporate strata as well as the horizontal. This enables rational selection of projects to progress. Importantly, it also means that funding and budget decisions can be made on the basis of dialogue between different levels of management. So often, the relationship is one of parent-child. The consequence is a 'liar's game' decision spiral: project proposers know that management will cut any project budget as proposed, so inflate their figures accordingly; management expect proposers to submit inflated figures, so cutting the budget becomes a reflex. The Mathesons argue that this is best resolved by looking at projects in terms of the predicted value consequences of three 'what if' project alternatives versus the current plan:

- Buy-down plan. 'What if the project's costs had to be reduced?
- Buy-up plan. What if more money were available?
- Salvage plan. Abandon the plan, conserving as much value earned as possible.

### Movie microcosm

Common themes can be found in many industries, says Jim Matheson, 'take the movie industry – on the face of it, it is very different. If you look closely, the parallels with pharmaceutical portfolio management are striking, thousands of candidate scripts are screened, cycle times have been radically reduced, there are a few major players with a large number of satellites, each major player has an annual target for product launches, and will expect, say, one blockbuster in twenty, and it is imperative to squeeze the maximum value from each project.'

### Core principles and benchmarking

David Matheson has defined nine principles that form the cornerstone of the SDG philosophy (Box 1). These principles form the basis for a 'IQ test' benchmarking exercise. The test can be re-evaluated over time to provide a measure of change, hopefully improvement, in performance.

According to Leigh Thompson, formerly Chief Scientific Officer at Eli Lilly 'the fundamental principles they outline were the basis for re-engineering of drug discovery and development at Eli Lilly and Company'. *The Smart Organization; Creating Value through Strategic R&D* is available in hardback for \$29.95 from Harvard Business School Press (Web: <http://www.hbsp.harvard.edu>).

David Hughes

## BAF and neonatal brain damage

Inhibitors of the caspase group of enzymes can protect newborn rats from further brain damage following an interruption to the blood supply, according to research published recently by a US team. The discovery could act as a model for establishing the viability of the compounds as potential drugs for minimizing the often devastating effects on the infant brain during or before birth.

The hydrolyzing cysteine caspase protease enzymes have been associated with programmed cell death (apoptosis); they are used by the body to control cell turnover, but are also involved in unwanted tissue degradation in some diseases. Numerous biotechnology companies have identified the potential of blocking these enzymes. For instance, following a stroke or other blockage to brain tissue, the damage induced by anoxia is often associated with the apoptotic effects of these enzymes.

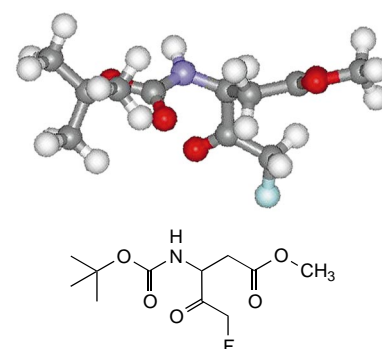
### Effective caspase inhibitor

David Holtzman and former postdoctoral worker Yu Cheng and their colleagues at

the Washington University School of Medicine in St Louis, MO, USA have shown that one caspase inhibitor, known as BAF – boc-aspartyl(*O*-methyl)-fluoromethylketone (see Figure) – protects newborn rats from damage [Cheng, Y. *et al.* (1998) *J. Clin. Invest.* 101, 1992–1998]. 'To our knowledge, this is the first demonstration that delayed treatment with a caspase inhibitor, even when given systemically, can be neuroprotective in a brain-injury model', says Holtzman. He adds that if the inhibitors prove to be non-toxic and pass through clinical trials successfully, then they could provide a useful window of at least several hours when one could administer them.

An interruption to the blood supply to the brain *in utero* or during or after birth is the largest contributor to brain degeneration in children. The range of consequences includes mental retardation, seizures, cerebral palsy and learning difficulties.

Holtzman's rat model mimics the condition by interrupting the blood supply



*BAF [boc-aspartyl(*O*-methyl)-fluoromethylketone] is a caspase inhibitor that has been shown to inhibit apoptosis. It may have potential as a neuroprotective agent for neonatal brain damage.*

to one side of a newborn rat's brain and briefly lowering the oxygen partial pressure of its air supply. This procedure kills neurones, resulting in loss of brain tissue. Holtzman and his colleagues have found