2 Wood, C. *et al*. (2004) Patch clamping by numbers. *Drug Discov. Today* 9, 434–441
3 Sigworth, F.J. and Klemic, K.G. (2002) Patch clamp on a chip. *Biophys. J.* 82, 2831–2832
4 Wang, X. and Li, M. (2003) Automated electrophysiology: high-throughput of art. *Assay Drug Dev. Technol.* 5, 695–708
5 Trumbull, J.D. *et al*. (2003) High-throughput electrophysiology using a fully automated, multiplexed recording system. *Receptors Channels* 9, 19–28
6 Venter, J.C. *et al*. (2001) The sequence of the human genome. *Science* 291, 1304–1351

Char-Chang Shieh
Neuroscience Research
Department R4PM, Building AP9A
Global Pharmaceutical Research and Development
Abbott Laboratories
100 Abbott Park Road
Abbott Park, IL 60064-6125, USA
e-mail: char-chang.shieh@abbott.com

Real options are neither complicated nor unrealistic

In a recent issue of *Drug Discovery Today*, Pandey [1] gave a clear overview of the different valuation techniques that are available for pharmaceutical R&D projects. In the framework of strategic capital allocation, proper valuation enhances the quality of the decision-making process. As described by Pandey, companies today have the choice between three techniques – discounted cash flows (DCF), decision trees (also known as scenario analysis) and real options. In our opinion, the article written by Pandey does not adequately explain or use the notion of an option, and consequently falls short of describing the full potential of the real options approach. In this discussion, we would like to address some of the common misunderstandings relating to the real options that are applied to R&D valuations.

What is and is not an option?

Abandonment of a project following negative clinical trial results should not be seen as an option. A compound that yields negative results in a clinical trial phase (i.e. is ineffective or results in severe side-effects) cannot be launched. No company would continue the development of such a compound; such an abandonment is forced and in no way optional. Therefore, the consideration of project termination under these circumstances should not be confused with option valuation.

The largest risk associated with an R&D project is its technical uncertainty, that is to say, whether or not the compound under investigation works in the way that the researchers hope, without causing severe side effects. The clinical development of a compound serves to resolve this uncertainty. However, clinical trial results, which are the manifestation of the technical risk, not only influence the decision concerning whether or not a compound passes a clinical trial phase, they also impact on future sales expectations. The results acquired from the different stages of clinical trials about the efficacy and safety of the compound enable a more precise estimate of future sales than before clinical trials commenced. Thus, even compounds showing positive results in initial clinical trials might be abandoned. The choice of this particular option is driven by the future market potential of the compound. Although the market potential of a compound is determined by pharmacoeconomic parameters, including demographic developments, the regulatory and political framework and competition from other therapeutic agents targeting the same illness or disease, the quality of the drug itself also influences market potential.

The termination of a project because of negative results is not considered to be an option, as is often argued by defenders of the DCF method. However, the voluntary abandonment of a project because of changed conditions and further evidence of the sales potential of a drug is an option.

Decision trees – casting light on real options

Pandey [1] mentioned the incorporation of different scenarios into the valuation process. Unfortunately, the added value of the analysis of these scenarios was somewhat left in the dark. It helps to quantify precisely the real options that are available to a company.

Undoubtedly, the most important option concerning a compound is the option to launch (or the option to abandon despite approval) the product onto the market. The launch of a new product means an enormous marketing expenditure. The company only undertakes this endeavor if the estimated sales revenues exceed the launch costs.

The scenario analysis helps to identify situations where the company could exercise its option to abandon the project.

Advanced decision trees – real options

R&D investments occur over several stages and, thus, there are various points at which decisions must be made, not only immediately before the launch of a new product. Each phase of the process generates new information about the product. Perhaps the product did not meet the goals of the clinical trials – in this case the project must be abandoned. Perhaps the product only partially met the goals of the clinical trials, or a competitor launched a similar product. In these cases, an abandonment of the project should be considered because the revised estimate of the future sales must be lowered. To handle these options, the decision tree must be expanded slightly. In decision-tree construction, the sales potential of the product could assume several different states only at the time of launch (i.e. several scenarios are investigated at product launch). However, as the company acquires more information from clinical trials, it can be assumed that the sales potential of the product

  PII: S1359-6446(04)03110-1

could increase or decrease each year. This expanded analysis yields the same states at product launch, but it is now also possible to plan the decision situations during R&D. The expanded decision tree is equivalent to the binomial trees that are used to simulate market fluctuations in financial theory [2].

The solution of the decision tree is just a slightly more-complex scenario analysis. At each node, the potential (probability adjusted) revenue is compared with the capital already invested. If the capital invested is greater than the potential revenue, then the project is abandoned. With this type of decision tree analysis, all the options to abandon the project during the development of a compound can be considered. Real options valuation is nothing more than solving this decision tree [3].

Advantages versus disadvantages

Frequently raised arguments against the use of real options are that real options are difficult to understand, that this approach relies heavily on hypothesis and that sales revenues are not volatile enough to justify a real options valuation. Although real options are not trivial, we have shown that real option valuation is not much more than reiterated scenario analysis. The argument that the real options approach is reliant on hypothesis is aimed primarily at the modeling of market uncertainty. Scenario analysis and Monte Carlo simulations deal with the same problems. DCF assumes the cash flows to be of a predetermined size, which is a hypothesis as strong as assuming a particular probability distribution. Considering the issue of sales revenues, examination of the sales returns of medical compounds on the market illustrates the stability of sales revenues; the healthcare market is rather predictable. However, it must be kept in mind that until the product is on the market the efficacy of the product and client acceptance are unknown parameters. The clinical development phase helps to remove this uncertainty. During R&D, the uncertainty concerning the potential sales revenues is much higher because the levels of efficacy and safety of the product are only partially known. Real options valuation is the only method that assumes that the management will react to changes in the factors that influence the revenue (value drivers) of a project.

Biotechnology puts the techniques that are necessary to address specific diseases and syndromes into the hands of researchers. Typically, the targeted patient group is smaller than the patient group of symptom-fighting pharmaceutical compounds. The requirement for managerial flexibility is particularly high for focused medications that have a relatively small target group. The expected sales revenues are not significantly larger than developmental costs and a negative turn in the market could easily result in sales revenues falling below developmental costs. The case study by Borissiouk and Peli (O. Borissiouk and J. Peli, MSc thesis, University of Lausanne, 2002) came to the same conclusion – for projects with moderate potential, real option valuation is the most suitable approach.

Conclusion

The hypotheses underlying real option valuation are not as unrealistic as some would like them to be. Moreover, the complexity of this approach is not an impassable obstacle. Real options provide a valuable insight into the scenarios that could arise during a project. This is particularly important for highly specific products that stem from biotechnological discoveries.

References

1 Pandey, M. (2003) Investment decisions in pharmaceutical R&D projects. *Drug Discov. Today* 8, 968–971
2 Wilmott, P. (1998) *Derivatives – The Theory and Practice of Financial Engineering*, John Wiley & Sons
3 Villiger, R. and Bogdan, B. (2004) How to conquer a lady, an introduction to real options in pharma and biotech. *Wilmott Magazine* May, 54–62

Ralph Villiger* *and* **Boris Bogdan***
RiVal
Risk Valuations
Im Kirschgarten
CH-4102, Binningen, Switzerland
**e-mail: ralphvilliger@bluewin.ch*

Neurodegenerative disease research in the 21st Century

Kelly R. Bales, Neuroscience Discovery Research, Eli Lilly & Company, Indianapolis, IN 46285, USA; e-mail: bales_kelly_r@lilly.com

The *Screentech World Summit* meeting, which was organized by IBC Life Sciences (http://www.ibc-lifesci.com) and sponsored by Southern Research Discovery (http://www.southernresearch.com), was held in San Diego, CA, USA on 21–25 April 2004. The conference comprised four concurrent sessions that covered neurodegenerative diseases, protein