Organic Process Research & Development

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Editorial

In Praise of Emerging Pharmaceutical Companies

One of the attractions of my job as a consultant is to visit—and hopefully provide useful advice—to emerging companies, often classed as "biotech" companies, although this is often a misnomer since they are frequently involved in small-molecule chemistry rather than biotechnological work. So I get to travel to interesting places such as Montreal, Vancouver, San Francisco, San Diego, Boston, Melbourne (Australia), as well as a number of European cities such as Barcelona, Copenhagen, Stockholm, and Helsinki. Although my hard schedule this year (eight trips to the United States/Canada already from the United Kingdom) might not be everyone's "cup of tea", it certainly keeps the airlines in business!

The visits to the emerging companies are always enjoyable, partly because of the sheer enthusiasm of the scientists, the can-do attitude of everyone from the top downwards, the team spirit, and the lack of bureaucracy; this can lead to high productivity as evidenced by the number of new drugs currently in phase III studies, or already on the market, which originated from this sector. This is something that the larger pharma companies have sometimes lost, particularly after a merger/acquisition, where staff morale can be depleted, bureaucracy increases, and productivity suffers.

Where the larger pharma companies excel, in a process R&D context, is in an early evaluation of the scalability of a discovery chemistry synthesis, and the willingness to allocate resources to route scouting and evaluation of potential long-term manufacturing options. Too often, the smaller, emerging pharma companies contract out a discovery chemistry synthesis, which may be acceptable for the first 100 g or possibly even a kilogram of new drug, but they fail to make plans in sufficient time (and most importantly to budget for) an investigation of alternative, convergent, scaleable, manufacturing-friendly and cost-effective syntheses using readily available reagents which are safe and environmentally friendly.

In the long term, scaling up a problematic discovery route, which does not deliver the required amount of drug substance on time and of the desired quality, can be much more expensive than devoting time, and money, on a contract to a reputable company specializing in devising new, cost-effective syntheses (rather than in just grinding out a few kilograms of product).

I get the same view when talking to some of the above-mentioned process R&D companies—too often they are presented with a synthesis on paper and asked to make a few kilograms: "just do it" and "do it quickly" are the usual instructions. The process R&D company can see all the potential problems and could suggest many new routes which would be far better in the long-term, but often is not given the opportunity. Short-term interests seem to take precedence over the long-term benefits to the project. The message in this editorial to all emerging companies is to put into your budget and your timeline an allowance for some new-route evaluation. This is best done—for scientific and cost reasons—as early as possible in the project. And do think about contracting this work out to a company with a good track record of innovative synthesis and with a manufacturing and cost-conscious viewpoint, as an alternative to allocating the task to a talented discovery chemist with an enthusiasm for organic chemistry, but who may have little knowledge about scalability, raw material availability, or costs of manufacture. Using a consultant to advise on alternative chemistry in conjunction with ideas from within, or from a contract company, can achieve fast results.

One of the other attractions of working with the "biotechs" is that the discussions can be wide-ranging, from synthetic organic chemistry, to raw material sourcing and availability, analytical and specifications issues, regulatory issues, particle size and physical properties of the API, salt selection and polymorphism issues (which seem to affect all companies these days), environmental issues, and new technologies. The latter could involve new technologies for formulation of the

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API as well as for its synthesis and scale-up. Often I cannot provide advice on all problems, but with the networks available, I can find a person who is more suitably qualified to give a better perspective on a narrowly focussed issue, particularly in formulation and dosage forms.

But first and foremost, emerging biotechs need someone who is a generalist, who can advise critically on all aspects, see if a potential problem is a show stopper, do a reality check on decisions which have already been taken, or more usually, advise on potential problems that have not been envisaged or issues which have been "swept under the carpet" in an attempt to meet an aggressive timeline.

The issue of "who is the best company to partner with" is one that emerging companies find difficult if they have not been involved in contract work. Too often they accept the lowest quote, rather than go for the company which, even though it is more realistic in its costing and timelines, has a good track record and will eventually deliver what the customer wants—the desired amount of API of an appropriate quality at the right time. The choice of CRO, these days is bewildering with the vast expansion of numbers of high-quality companies from North America, Europe, and Asia, and one or two from Australasia, Africa, and South America.

Emerging companies always need outside help, in the form of CROs and consultants, at the early stages of their work, but slow expansion involving the appointment of experienced professional staff who have "made their mistakes elsewhere" can help to minimize the total dependence on external resources. As long as the expansion does not jeopardise the flexibility, the team spirit, and the can-do attitude and keeps bureaucracy down, these companies should continue to be a joy to work for—and with.

Postscript to the University of Sussex:

Thanks to all of you who responded to my last editorial to save the Chemistry Department at the University of Sussex, UK. The good news is the Department has been saved. A new department of Chemistry and Biochemistry will continue to offer a full range of degrees in Chemistry and provide research facilities for many years to come.

Trevor Laird
Editor

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