Drug discoverers – you need us! – Reply ▲

Initial letter: Federsel, H-J. (2001) *Drug Discov. Today* 6, 397–398

A consistent message

A letter expressing personal views on the process R&D–drug discovery interface published earlier this year[1] in this section has so far received replies from three senior people in the pharmaceutical industry[2–4]. My initial letter strongly advocates a high degree of involvement and integration of process R&D with the medicinal chemistry part of drug discovery based on several well-documented facts. In the 6–12 months preceding the candidate drug (CD) nomination, close links need to be established to allow process R&D to assume the role of an interactive player during this decisive phase; this will hopefully emanate in the appointment of a high quality CD with good future prospects. As a particularly important driving force in this context, inputs on scalability, future manufacturing options for the active pharmaceutical ingredient (API), SHE (safety–health–environment) aspects, raw material supply, and cost of goods were highlighted. A total or partial neglect of these parameters at the start could eventually cause large amounts of money and resources to be wasted in the further development of a new CD that, from the beginning, would have had little chance to survive if these factors had been taken into consideration. In essence, what we can learn from this is the need for a mutual understanding of what contributions can be expected and are needed from the different competency areas, teamwork, and close collaboration between disciplines!

The encouraging and sympathetic words by King[2] (Medicinal Chemistry, GlaxoSmithKline, Harlow, UK) mention the overall 'status of Process R&D as a state-of-the-art technology' provider and its 'greater involvement in the drug candidate selection process' as two particularly interesting points. With respect to candidate selection he connects the AstraZeneca model[1] to their own in-house developability concept that has the ultimate goal to reduce failure rates and improve the probability of success. This is nicely summed up by saying that the candidate to be chosen must not necessarily the be one with the highest potency or *in vivo* activity, but more importantly 'the one with the best overall profile for rapid and successful development'. A statement that cannot be but applauded by anyone in process R&D!

In a thorough and rather detailed account by Meanwell[3] (Dept of Chemistry, Bristol-Myers Squibb, Wallingford, CT, USA) several new considerations are brought into the discussion, which, together, provide further strength and enhance the previous arguments. Thus, a key element that has to be acknowledged when looking for drivers that effect the interplay between process R&D and other functions is the need for educational inputs addressing 'challenges faced in producing bulk drug substance'. Efforts that enable or facilitate this have to be prioritized by ensuring a geographical closeness, participation in cross-functional project teams, and even secondments of, for example, discovery chemists into various process R&D disciplines, and all with a clear target to 'influence strategic thinking' in people. There is no doubt, as Meanwell concludes, that these types of initiatives should not remain on a strictly chemist-to-chemist level, but rather should be directed towards a much broader audience involved in the development of new drugs to cultivate them to become more sympathetic. Particularly the final conclusion gets my full support: we need to be out there to talk and make noise about our science.

Beginning by drawing a, somewhat amusing, parallel between drug discovery and oil exploration (expressing risks as 'attrition rates' and 'dry holes', respectively) Shultis[4] (Albany Molecular Research, Albany, NY, USA) puts forward a set of well-founded arguments as to why process development is essential, especially now when new compounds intended for clinical evaluation display an ever increasing structural complexity. It is indeed true that process development, more than ever before, might become a bottleneck in the entire drug project. This enables Shultis to introduce the term 'telescoping' to specify the backward integration of process R&D into drug discovery, which at the end of the day will have saved valuable time and, ultimately, will have speeded up time-to-market: a key criterion for success. Superficially, if a project fails then that particular development work can be regarded as lost. However, there are so many well-documented examples from industry where the experience and know-how gathered in one case can be directly applied in another. (Screening a few issues of *Organic Process Research and Development*, for example, will clearly confirm this to be the case.) Hence, Shultis' standpoint that 'process expertise is a precious resource' is too true to be ignored.

Now that so many well-founded arguments from industry professionals talk the same language what remains to be done? Well, those that are new to this mode of operation should go from theory to practice, whereas others should try to develop this integrative process further and share their experiences and best practices with the pharma industry community as a whole!

References

1 Federsel, H-J. (2001) Drug discoverers – you need us! *Drug Discov. Today* 6, 397–398
2 King, F. (2001) Drug discoverers – you need us – Reply. *Drug Discov. Today* 6, 455
3 Meanwell, N.A. (2001) Drug discoverers – you need us – Reply. *Drug Discov. Today* 6, 664–665
4 Shultis, K. (2001) Process chemistry is not just for manufacturers. *Drug Discov. Today* 6, 716

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