GAMES WITHOUT FRONTIERS

In the current climate of worry surrounding drug discovery and development, now might be the time to think beyond the conventional systems in place throughout the pipeline.

If you ever travel through the streets of Friesland, a district in the north of the Netherlands, you will receive an object lesson in the value of reassessing traditional ideas and systems. Although the roads seem to carry a familiar steady stream of traffic and pedestrians, there is a palpable sense that something is amiss. Closer inspection reveals why: the road network is devoid of signs, road markings and traffic lights. No divisions exist between the roads and pavements.

What sounds like a recipe for anarchy in fact produces the opposite effect. People drive more carefully, and slow down for pedestrians crossing roads. Average speeds have dropped. Perhaps most importantly, no fatal accidents have occurred, despite some areas, such as the city of Drachten, catering for as many as 20,000 drivers a day. Why such a system works is simple to explain, according to Hans Monderman, the traffic engineer who designed the revolutionary system. Organizing and defining the behaviour of drivers through the use of traffic lights, signs and lane lines subconsciously tell drivers that nothing will happen as long as they behave according to the rules of the system. If drivers have to use their own initiative when driving and start looking at other drivers and pedestrians, they focus more on what is important, and driving becomes safer.

Of course, such a system won't change the behaviour of the small proportion of drivers who will abuse the system irrespective of the rules. But the fact is that the counterintuitive removal of rules and restrictions can, in the correct environment, foster better results than with conventional systems, and variations on this so-called 'shared system' are now being tried in other countries in Europe.

The parallels between the Friesland road system and the pipeline image that symbolizes the drug discovery and development process are too irresistible to ignore. In fact, *Nature Reviews Drug Discovery* was founded on the idea that the greatest hurdle to success in drug discovery and development is a lack of communication between the many different areas of specialization within the pipeline. The journal has encouraged readers to step outside of the conventional barriers and checkpoints of their own specific area of expertise to facilitate the successful development of new drugs.

As many articles published during the lifetime of the journal have shown, there is already a huge desire to think beyond the conventional barriers in order to improve the system. With recent controversies, such as the safety risks of antidepressants, COX2 inhibitors and, more recently, the monoclonal antibody natalizumab (Tysabri) for multiple sclerosis, providing a wake-up call for the industry, now seems an appropriate time to reiterate the message. However, this time the barriers are not just restricted to areas of specialization — they include those that surround the whole drug development process itself.

A great deal has been written in the pages of this journal about the bottlenecks in the pipeline and how to benchmark the process, but what all solutions highlight is that the difference between success and failure in drug discovery and development lies in the quality of the underlying science. In this regard, perhaps there should be a greater focus on comparing the extent to which current progress is helping to create more and better medicines — for example, how informative are current approaches such as the mass screening of reductionist systems to drug discovery and development?

So now might be a good time for pharmaceutical scientists to remove as many barriers as possible from the current process and focus even more on the underlying science to ensure a greater degree of success. Increasing productivity does not just mean identifying more targets and creating more compounds; it also means decreasing attrition rates through smart selection of targets and compounds. As our current series of articles on animal models shows, although they are undoubtedly informative, each has limitations and the closer we can get to the target system, the better. A full biological understanding of targets can identify candidates that are more likely to succeed, and, as illustrated with the COX2 inhibitors, can help to predict potential adverse effects that can be investigated earlier in development. Breaking down as many divisions as possible might seem like a radical departure from the norm, but right now it could be one of the best chances of ensuring that innovation runs more smoothly and successfully through the pipeline.

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