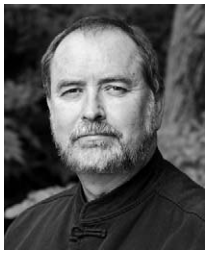
editorial



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Competitive collaboration in the pharmaceutical and biotechnology industry

The title was selected specifically because the phrase 'pre-competitive collaboration' [1,2] (see Supplemental Information) is being bandied about and the potential conflicts require acknowledgement, critique and a way forward that pushes through that conflict, even if resolution is not forthcoming. In fact, the very ambiguity of that term could lead to an inadequate response as industry leaders try to decide what is actually before ('pre') the competitive acquisition of knowledge.

We are advocates for redefining competition and for recognizing that pharma and biotech are not exactly like every other business when it comes to a combative/competitive spirit. In fact, it is possible to be the CEO of a successful pharmaceutical company and still have your life (or your mother's life) saved by the drug launched by a competitor—maybe even one in which they beat you to market just in time for that life to be saved.

The reality is that we need to be sharing information and collaborating in arenas that may be frankly in the middle of the competitive zone. At the same time, we need to reassess what constitutes the points of competition—recognizing that: first, explicit in almost all pharmaceutical company mission statements is the intent to serve mankind's health needs; and, second that it does not seem unreasonable to suggest that such a declaration at least *implies* that it will be done in a way that mankind can afford to access it.

Please do not assume that this is a call for nationalization or socialization of medicines research and delivery. This is not even a call to abandon all points of competition—a healthy free-market process that has, over 10 or 15 decades, produced great strides in technology and great impacts on both the length and quality of life.

The problem is simply that, contained within the adjective 'pre-competitive' is the suggestion that there is a scenario in which the value chain of pharmaceutical innovation has some sort of 'break point,' only after which the knowledge created takes on a competitive advantage. This, of course, is no more true in the pharmaceutical or biotechnology industry than any other endeavor seeking to compete on the basis of intellectual property and knowledge gained in advance of competitors.

In pharmaceutical research and development, the value chain (for most companies) shows as stage 1: 'Target Identification.' That is pretty early. Not a lot is 'pre.' It certainly includes efforts in basic biology. It is well before the publicized 1/10 000 odds of success (which figures into the astronomical total costs of development [3,4] and which references the much later stage of conducting a structure activity relationship around a lead molecular structure.)

While using the same descriptor, many pharma companies are using this phraseology to define their efforts in what they might

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more rigorously call exocompetitive collaboration. That is, collaborating on the research tools, the IT systems, the means rather than the ends. We applaud their efforts [1,5,6] (Supplemental Information). But the risk still exists that too many will consider these knowledge edges just as much a competitive advantage and still not candidates for collaboration. Rather, they will collaborate only where they feel they have little unique to offer for the benefit of other firms. And that is the exact circumstance in which the collaboration would bear the most fruit and produce the greatest gains in research efficiency.

No, the industry needs to collaborate smack dab in the middle of the more frightening 'competitive' zone and say so explicitly. In fact, we wish to go further and say that a new level of, and new modalities of, collaboration may be the very key to the survival of the new medicines industry. Collaboration is a means to lower risks and costs at crucial stages in the value chain and allow sustainability in the face of decreasing margins and even greater competitive pressures from generics, imports, price controls, and so on.

But, we should also allow that, in a great many cases, the failure to share and collaborate is not directly tied to the competitive motives of the corporations. It is, in some cases, a consequence of the present-day scientific system in which research studies are carried out. If you were to read much of the scientific literature, you might be astounded to find that we live in a world where hypotheses are almost invariably confirmed, concepts validated and theories supported.

It is the proclivity of both authors and publishers to focus publications on what works and unfortunately leave buried in notebooks the greater incidences of failure. In the world of pharmaceutical research that means we have lots of data on successful medicines and successful findings *en route*; but where would one learn what NOT to do? What classes of chemicals need NOT be restudied as potential receptor modulators? What delivery adjuvants are too toxic to even bother testing again? What formulation methods are NOT optimal for highly lipophilic drugs?

To be fair, SOME of this gets published, but there is not an *organized* system for documenting failure in the same way that success is documented, and avoidance of failure would be a pretty good efficiency gain in an industry that takes as many expensive scientific risks as the pharmaceutical industry does. Without a path for public recording, it is often inefficient to even invest in going back to evaluate the exact mechanism of why a drug candidate has failed [7].

As deep a change as it may be, we still need a small place to start. What we'd like to see are collaboration tools (or systems) and industry engagement in the following areas:

1. Adverse toxicity findings that have NOT been published.
2. Phase I/II clinical data on abandoned candidates.
3. SAR datasets for abandoned targets.
4. *In vitro* and *in vivo* ADME data for compounds no longer being pursued.

These organized records should all be constructed using tools that allow search by intended pharmacology, physiological response and molecular class—at a minimum. The search capabilities and data organization would bring greater utility even to those elements that could in theory be extracted through freedom of information efforts (a cumbersome and search-unfriendly system). Wherever possible, these records would contain information relevant to cause: a molecule failed, for example, targeting a particular protein X, rather than the generic 'phenotypic description', for example, blood pressure increase.

There are three major costs and barriers to this effort:

1. Platforms need to be created.
2. The data, resident in pharmaceutical companies and to some extent FDA records, need to be input.
3. Ownership for creation and maintenance of these systems needs to be defined.

None of these are even close to insurmountable problems. A great many platforms already exist or could be modified from other applications [8]. But ownership for doing so is ambiguous at best and perhaps there is no ideal answer (we are certainly open to suggestions). Perhaps such an undertaking could be funded by a non-profit foundation, or possibly a government funded NGO could take ownership. It is even possible that if a viable business model could be defined (with appropriate returns) that a traditionally investor funded entity could be created. In any event, the incentives (or rules of engagement) need to insure a system that is of validated quality and completeness.

Of course, some will undoubtedly just see this as the role of the industry itself. Whatever contribution they have to make (and it is substantial), the ownership and costs for this initiative should not be borne by pharmaceutical companies alone. Being fair to all parties with all their agendas, that is probably a non-starter. Industry's argument could be that time spent dragging out old records is time NOT spent developing new medicines. They are right. And any mandate simply by fiat is as likely to hurt the overall health efforts as it is to help them. There should be appropriate incentives for contributing information just as there should be appropriate costs for accessing it.

Common sense should prevail. Competition should continue to exist. Creators should be rewarded for the fruits of their efforts, their ingenuity and their risk-taking. But in the end, we simply ask ourselves, how can the lack of sharing NOT take a significant toll on the speed with which medicines come to market? How can they NOT raise costs, but rather require that two or more separate companies each travel unproductively down the same dead-end research path? It seems very likely that we can drive more data sharing, that we can lower the failure-related costs across the board without the risk of destroying the competition that has so favorably worked to our advantage. In an undertaking as complex as human health, failures will remain—but the pointless failures, the retreaded failures, should be avoidable by all. Such an endeavor should be of widespread personal interest. Whatever our role in life: pharma exec, philanthropist, or government regulator, there are precious few that ever escape the role of patient. Ultimately it is they who pay for research inefficiencies—with their dollars and their lives.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drudis.2009.10.003.

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