Shaping Pharmaceutical Strategy
Recombinant Innovation Management (RIM) – How to Stimulate Breakthrough Innovation within Large R&D Organisations

Catenion

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“The greatest inventor of all time. Accident.”

Mark Twain

“All decisive advances in the history of scientific thought can be described in terms of mental cross-fertilisation between different disciplines.”

Arthur Koestler

“...the fortuitous facts that inspired many critical discoverers were seen a number of times before they were noticed.”

Ernst Mach

Introduction – Pharmaceutical R&D is in a Creativity Crisis

Pharmaceutical R&D is in a state of crisis: productivity is declining both in terms of output per spending as well as total output, while patent expirations threaten many successful product franchises within the next years. In addition, the industry's innovation mix has shifted even more towards 'incrementally modified drugs' and lifecycle management. At the same time companies have poured enormous resources into enabling technologies, often with the promise to 'automate' drug discovery. Propagators of heavy investments often talked of "fuelling the innovation engine". However, several years down the road, the innovation engine is still sputtering. The main issue is that impressive advances in process productivity have not translated into more novel products addressing unmet needs.

In our view, there lies at the root of the much talked-about "R&D productivity crisis" an even bigger creativity crisis. Many companies have delegated creativity to an ever increasing arsenal of enabling technologies and the biotechnology industry. Not surprisingly, in some companies, R&D has been reduced to a statistical numbers game and precise throughput or output targets linked to incentives have been defined for each step in the R&D process. The mantra seems to be "meet the numbers and innovation will follow".

Consequently, more pharmaceutical companies depend on in-licensing potential breakthrough innovation from the biotechnology industry or academia to compensate for the disappointing track record of their own labs. R&D spending per new drug has reached such high levels that many senior executives are beginning to question the sustainability of the fully integrated pharmaceutical business model.

At Catenion we believe the time is ripe for the pharmaceutical industry to rediscover the main value drivers that led to success in the first place: human creativity and breakthrough innovation.

Only true creativity can lead to discontinuous and unexpected 'leaps' in innovation that can shape new markets and open up long-lasting competitive advantage. Too many companies have driven out "unmanageable, serendipitous, chaotic creativity" by fully adopting the 'Managed Research' paradigm with its abhorrence of everything uncontrollable.

In this commentary, we will introduce a systemic approach that has been designed on the basis of epistemological and organisational patterns of breakthrough innovations in various industries: Recombinant Innovation Management (RIM). The promise of RIM is not to make breakthrough innovation predictable, but to increase the likelihood of its occurrence to follow Pasteur's famous quote that "chance favours only the prepared mind". The ultimate goal of RIM is to combine the best of the world of 'Managed Research' and incremental innovation with that of creativity and breakthrough innovation.

Innovation Always Involves the Individual and the Environment

Much of the confusion surrounding innovation management stems from the different perspectives involved, primarily the psychological or epistemological perspective and the real or organisational perspective.

The psychological perspective focuses on the individual and the mental processes of perception and conceptualisation. In the 1960s, the historian Thomas Kuhn introduced the concepts of 'Paradigm', 'Normal science', and 'Scientific

Revolution' into the sociology of science to discuss the mental structures scientists require to produce incremental progress. Kuhn showed how these structures or paradigms all too often turn into unconscious mental barriers that inhibit scientists from creatively dealing with unexpected observations. As early as the 1920s the German physicist and Nobel laureate Werner Heisenberg had famously made the same point by remarking that a new scientific worldview can only fully establish itself once the proponents of the previous view have passed away. One cannot help thinking he must have had Einstein on his mind, who had expressed his opposition to the new quantum mechanics by saying: "God does not throw dice."

While any systematic approach to understanding and furthering innovation necessarily addresses the mental barriers in individual minds, the organisational dimension of innovation should not be underestimated. This deals with the processes of recognising the potential value of new ideas, funding their development and ultimately turning them into products despite their unconventional and high-risk nature. Organisations also set the culture, expectations and reward systems within which individuals work and strive to fulfil their objectives. Innovation dries up when scientists produce great ideas but cannot get funding and vice versa, when funds are available but no creativity is left to produce worthwhile ideas.

The literature on innovation often focuses on one or the other of these perspectives, fully integrated views are rare. In this commentary we will take the fully integrated perspective, since both views are intimately linked with one another.

The Nature of Breakthrough Innovation

In the literature on industrial innovation there are two models that dominate the discussion: the 'invention' and the 'adoption' models. In the invention model there is a well-defined path from problem definition to hypothesis generation, testing, design and launch. In the adoption model the invention is performed by somebody outside the company, therefore the process starts with the decision to internalise the invention (as in pharmaceutical in-licensing).

However, if one takes a closer look at so-called breakthrough innovations both from the pharmaceutical and other industries, they often follow a different pattern. This pattern can best be described as the recombination of already existing problems or solutions across diverse and seemingly unrelated fields of knowledge or application. Contrary to popular belief, de novo inventions are relatively rare. In many cases, already existing solutions are simply put into a new context (matched to a new problem) or vice versa. Thomas Edison and other 'geniuses' were masters of this Recombinant Innovation process.

One example from the pharmaceutical industry is the serendipitous discovery that a drug's adverse event can be turned into a potential solution for an existing problem. This has been the case with Viagra, whose development for the original cardiovascular indication was not successful, but an 'adverse event' was a solution for the problem of erectile dysfunction. Another example is the advance in the field of gene chips which is based on the recombination of existing solutions in the field of basic chip technology with the problem of fast recognition of molecular patterns.

Most pharmaceutical companies have had experiences with serendipitous (= recombinant) events that ultimately led to the discovery of major drugs: based on a quick review of the literature, serendipity accounts for at least 50 marketed drugs, many of them breakthrough innovations. It is widely assumed that such recombinatorial events are beyond management control and therefore purely left to chance.

Recombinant Innovation is also at work in the most fundamental of all innovation processes, namely evolution. It is well established that in the evolution of proteins, the recombination of entire modules and genes may play a greater role for the success of a phenotype than simple point mutations. This is in perfect analogy to the difference between incremental innovation as the optimisation of existing solutions within an established framework or knowledge field (= evolution through small changes like point mutations) and breakthrough innovation as the recombination of existing solutions (= entire protein modules) with problems in a seemingly unrelated knowledge field (= different protein gene on another chromosome).

Recombinant Innovation is at Odds with the Socialisation of Scientists

Breakthrough innovation presupposes the recognition of hi den connections between seemingly unrelated fields. This is why so many of the early breakthroughs were created by generalist 'geniuses' like Leonardo da Vinci and in later times Thomas Edison. They were able to recombine existing problems and solutions across diverse fields with ease; something that has become progressively difficult due to the enormous explosion of knowledge in many areas of human thought.

We live in an era of specialisation. This paradigm is deeply engrained in our educational system where it allows for the formation of deep insights and knowledge. There exist undisputed advantages to specialisation, but true breakthroughs are hampered by developing psychological barriers. In the literature these barriers are described as "trained incapacity" or "occupational psychosis". Unfortunately, many of these barriers develop after a relatively short period of specialisation, often appearing after little more than three years. In the world of pharmaceutical research everyone is familiar with the barriers presented by the 'not invented here' syndrome, which refers both to organisational and scientific silos.

The Traits of Creativity

In spite of all the barriers, every organisation has a number of highly creative individuals who, based on their personality traits, are more likely to create breakthroughs than 'normal' scientists. So, what sets these individuals apart? Usually they have a threshold level of intelligence coupled with strong intrinsic motivation – they lack conventionality, are risk-takers more obsessed by their hunches than interested in their careers, are experts at activating tacit knowledge, have a preference for complexity and fit the T-Model (to know everything about a little thing and a little thing about everything). Creative individuals tend to think in analogies and patterns, systematically exploring boundaries of different fields through recombination.

The most important factor is that creativity in the applied fields of science crucially depends on working on real problems right at the workbench level. This is one of the reasons why 'Think-Tanks' or 'Synergy Committees' are not helpful – they are too far away from the real problems they attempt to address. For creativity to become productive in dealing with a problem, a scientist must immerse himself in the issues at hand – deeply enough so he can recognise adequate potential solutions from other fields where he possesses expertise, but not too deeply lest he become a victim of the mental constructs into which each problem is embedded.

There is a huge body of literature exploring the fluid boundaries between creativity in the sciences, arts and philosophy as well as the pathological traits of many highly creative individuals. No wonder such individuals do not fit into a highly controlled and managed environment and are often viewed with a degree of suspicion by their more 'normal' peers and superiors.

The Limitations of the 'Center of Excellence' Structure

The true potential of creativity can only be unleashed in the right organisational environment. This is especially true for the large percentage of researchers that do not possess the personality attributes described above to thrive even in a purely process- and productivity-driven environment. To date, many organisations consist of a few 'unmanageable,' highly creative individuals who exist almost outside of the normal organisation and a large percentage of researchers who are tightly bound to the logic of the ruling 'Center of Excellence' structure.

In such a 'Center of Excellence' a group of specialists, often with similar backgrounds, works in a defined area and is supported by enabling technologies and the latest management tools (project and portfolio management, incentive and reward systems, balanced score cards, etc.). Taken together, this is the world of 'Managed Research' that currently rules pharmaceutical R&D. This model has obvious benefits and has proven extremely successful in producing

small, incremental steps of innovation, thus the increase in 'incrementally modified drugs' over the last ten years. However, the major limitation of the 'Center of Excellence' structure is that it reinforces the epistemological and organisational barriers to Recombinant Innovation. In such an environment, breakthrough innovation often happens 'in spite of' rather than 'because of' the organisation. As the majority of researchers is only fully creative and capable of breakthrough innovation in the right environment, this organisational model leaves large potential untapped.

Existing Efforts of Cross-Fertilisation Often Fall Short

Many companies have realised the limitations of the 'Center of Excellence' model and have engaged in numerous activities to blur the boundaries such as synergy committees, knowledge management, cross-functional project teams, matrix functions, enabling technology groups, etc. Most of these approaches, while well-intended, fall somewhat short of fulfilling the basic epistemological and organisational requirements for Recombinant Innovation.
A few of these requirements would be:

- Creating ideas at the bench and not in a committee
- Activating tacit knowledge
- Recombining problems and solutions freely across fields
- Making untied funding available
- Self-selection to work on topics in a variety of fields
- Organisational flexibility ('budding out' of new units and 'organisational apoptosis', if not successful)

To explore one example in more detail: many researchers who have been part of a drug development team will agree that these teams, while truly cross-functional in structure and intent, often consist of experts who meet frequently but never actually leave their 'Center of Excellence' modus operandi. Sub-optimal project strategies are a typical outcome when experts sit in meetings, but are not willing to engage in truly recombinant discussions.

Recombinant Innovation and Personalised Medicine

A current illustration of the limitations of the dominating organisational paradigm in dealing with breakthrough innovation is the emerging field of Personalised Medicine.

Personalised Medicine resides squarely at the intersection between the pharmaceutical and diagnostics sectors. In spite of initial enthusiasm and early successes like Herceptin, the field is still struggling with technical difficulties and business model issues. The pharmaceutical industry is approaching these with a mixture of reticence and limited appreciation of the statistical difficulties involved. Diagnostics companies often lack the insight to assess the impact of predictive tests on the processes of pharmaceutical development and marketing and struggle with value creation for themselves. They ask: "How can we generate adequate returns by engaging in the development of tests linked to pharmaceutical products with high attrition without participating in the commercial upside of our pharmaceutical partners?"

In our view, a major (and often hidden) factor contributing to the relatively slow adoption of this breakthrough innovation lies in its recombinant nature. Personalised Medicine is about recombining existing 'solutions' or hypotheses from the world of diagnostics with efficacy or safety 'problems' from the pharmaceutical sector. All of the barriers that have been discussed briefly in this commentary such as the 'not invented here' syndrome, 'organisational psychosis', and the limitations of existing 'Centers of Excellence' are seen here in full force. To make matters worse, the pharmaceutical and diagnostics sectors are separated much further in mental, organisational and economics terms than, for example, two therapeutic areas within a pharmaceutical company. Even those healthcare companies that combine diagnostics and pharmaceutical divisions under one roof do not seem to have found a workable organisational solution to take full advantage of the potential of Recombinant Innovation in this emerging field. In our view, Personalised Medicine will only live up to its potential with the development of innovative

organisational approaches and business models that fully capture its recombinant nature.

The R&D Business Model Crisis

One of the recent consequences of the productivity and creativity crisis of pharmaceutical R&D is that several senior executives and industry observers have begun to question the value of a full-blown in-house research effort. The argument of these 'deconstructionists' is that alternative models such as the 'search, develop & market' approach used by Forest Labs could potentially create more value than the fully integrated model.

At Catenion, we have a somewhat different view on this topic. Although many current breakthrough innovations stem from academia or biotechnology companies, we believe that major pharmaceutical companies should be more prone to Recombinant (= Breakthrough) Innovation due to their 'knowledge space coverage' and scope, which in comparison to their much more narrowly focused biotechnology or academia counterparts, is vast. To mine this untapped potential would require that the major companies begin to view 'Economies of Scope' as a complementary competitive advantage to 'Economies of Scale'.

It is Catenion's view that precisely this untapped potential of 'Economies of Scope' within large and diverse R&D organisations could come to the rescue of the fully integrated pharmaceutical business model over the next years. But this will happen only if companies identify better ways to organise for breakthrough innovation.

What the Pharmaceutical Industry Can Learn from Other Industries

In our conversations with scientists and executives in pharmaceutical companies we have continually met with scepticism when suggesting that pharmaceutical R&D could actually learn from other industries with respect to organisational approaches and innovation management. The prevailing view seems to be that the pharmaceutical sector is the most research-intense of all industries and is already applying – if not pioneering – most of the best practices from the domain of 'Managed Research'. We find this view very revealing and see it as yet another illustration of the 'not invented here' syndrome.

There are research-intense companies in the high-tech engineering and computer industries that are very good at Recombinant Innovation. The design engineering company IDEO is just one example. IDEO, located in Palo Alto, works for clients in over 40 different industries and often recombines existing problems and solutions to solve specific design engineering tasks. The company has frequently been charted on various lists of the 'most innovative' companies in the world. Some of the principles that IDEO employs are:

- Recruiting T-shaped people
- Witnessing of customer needs directly
- Experimenting and prototyping rapidly
- Exploring boundaries, recombining existing problems and solutions
- Using intuition of engineers as a 'management tool'

Interestingly, engineers tend to have less of a problem with the 'not invented here' syndrome and fully functional cross-collaboration than researchers from the pharmaceutical sector. A major challenge for the pharmaceutical industry is to get biologists, biochemists, pharmacologists, chemists, physicians and others to collaborate freely. Very often, prejudice and a subtle form of educational arrogance inhibit the effective collaboration of the different disciplines.

As another example, the strategy consulting industry depends on the successful application of Recombinant Innovation. Strategy consultants make a living by recombining solutions they see in one industry or company with problems they observe in another industry or enterprise. All this takes place in truly cross-functional teams with various backgrounds, often co-located for months in one small room. The model, unfortunately, all too often fails when an in-depth understanding of all relevant aspects of a client's problem is substituted for intellectual brilliance and occasional arrogance. Successful consulting firms know that knowledge management is much more than an IT and database question, it is about culture, incentives and creating ways to share tacit knowledge within the consulting team, and more importantly, to tap into the tacit knowledge of the client organisation.

RIM – The Next Source of Competitive Advantage for Large R&D Organisations

Based on our experience in pharmaceutical R&D and experience gained in many other sectors, including our own, we have over the last ten years developed Recombinant Innovation Management (RIM). RIM is a systemic organisational approach that aims at increasing the likelihood of breakthrough innovation in large and diversified R&D organisations.

RIM's intent is not to put functional organisations at risk by overhauling entire structures or by jeopardising undisputed advantages of the 'Center of Excellence' model, but rather to leverage these structures to reach beyond their formal boundaries.

RIM touches on the major elements of the pharmaceutical R&D business model – values, beliefs & goals, strategy, structure, processes, people & rewards, governance, and culture. Since RIM ultimately impacts peoples' way of working, behaviour, and mind-set, implementation must be accompanied by a persistent change management effort.

RIM Puts People First

At the core of Recombinant Innovation Management are the people that can make innovation happen. In adapting the existing organisation and designing new elements, it is crucial to recognise the heterogeneity of personality types and their different potential contributions to the overall process of innovation.

Schematically speaking, RIM distinguishes between three groups of employees:

Firstly, all the 'normal' scientists and technicians whose day-to-day contribution to incremental innovation provides the basis for all major breakthroughs – they form the large majority of any R&D organisation.

On the other end of the continuum is the second group – those highly creative individuals who are driven by their obsession to pursue what they think is right, even if told otherwise.

There is a very important third group in-between: those scientists and technicians with a higher than average creativity potential and the desire to apply this in their work, but who lack the personality attributes to resist the sometimes counter-productive impact of objectives and incentives provided by 'Managed Research'.

RIM provides a framework and the organisational approaches and building blocks to create a working environment in which all three groups can fully reach their creativity, productivity and innovation potential.

Catenion Value Proposition

RIM is a systemic approach that has been designed to help large R&D organisations reach their full innovation potential – both incremental and breakthrough.

Given the subject matter, the complexities inherent in R&D, and the sophistication of the people engaged in its pursuit, at Catenion we do not believe in 'cookie cutter', 'one size fits all' approaches to implementing Recombinant Innovation Management.

What we can offer is a well thought-out conceptual framework and process with diverse organisational approaches and building blocks such as Unit X, Internal Scouting or Technology Brokering.

Our in-depth understanding of the complexities of pharmaceutical R&D and organisational development expertise enable us to assist clients in tailoring our framework to the specific culture, history, structure and requirements of their organisation.

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