Development of Biological Products

Approaches in Pharmaceutical- and "Red" Biotech Companies

Sometimes product development is being regarded as trivial. As a result it tends to be neglected as a necessary evil. In this short article we would like to present our view of some – in our eyes special – issues.

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Development

Many smaller pharmaceutical- and red biotech companies posses an excellent research department. In spite of this, an unrealistic approach is often adopted, when aiming at putting a product on the market in a very short development time and with a relatively limited budget. Reality proves, that this cannot be conducted as optimistically as desired. The reason for this misconception often lies in the fact, that the scientific thinking of the research people cannot be fruitfully transformed into the development process. In this article, we would like to investigate this question. The enlargement of scientific thinking by function is the most important part of the development thinking. The development thinking uses this approach as a base, in order to obtain a product, which will pass the regulatory hurdles. The scientific thinking however should stay in second place, since development is not research driven. Another way of thinking should therefore be the bottom line in the development process.

Development in the first instance is rather process-oriented. The registration of the remedy lies at the end of this process. This registration must be primarily oriented towards the fulfillment of guidelines given by the regulatory bodies. In spite of the fact, that nowadays one can have a well-founded exchange of thoughts with „DRA-people" in governmental offices, which often leads to usable suggestions, one has to follow the given guidelines rather strictly without any deviance. However, these guidelines are mostly not composed from the standpoint of a researcher (therefore not primarily driven by scientific thinking) and accordingly reflect foremost the interest of the regulatory bodies, i.e. to reach satisfactory product safety. Thus the authorities protect themselves from liability law suits, since – as far as foreseeable – only safe and efficacious products will be approved.

Safety

Recently, the safety orientation of regulatory authorities has increased continuously and they tend to act more and more cautiously, which naturally does not speed up the regulatory process. A quite well-established safety orientation of the authorities finally leads to dramatically longer development timelines as well as higher development costs. Generally speaking, concerns of the regulatory bodies are based on negative experiences in the regulatory process and are in general well-founded. As an example for the increasing caution of the regulatory bodies we perceive the withdrawal of Merck & Co's pain drug Vioxx, Biogen Idec`s temporary withdrawal of the MS medication Tysabri or Pfizers unvoluntary withdrawal of its pain drug Bextra, a COX-2 inhibitor like Vioxx, or the not too recent phase I study of TeGenero, resulting in necessary changes of the guidelines. On the other side it still are the agencies, having the greatest experience with different biological products as overall there are relatively few recombinant or other biological products on the markets.

The Development Process

In the development process there is – as very often in every day's industrial life – the evaluation of risk and benefit. As an example in the early development phase (or rather still in research) the risk factor

of the timing of filing a patent should be mentioned, as should later on the risk/benefit evaluation in toxicology as well as the selection of the right CRO in pre-clinical and clinical development. Further disputed areas are which dose of the drug the clinical stage should be commenced with, how many toxicological-studies are really needed or what is a meaningful procedure in case you develop a monoclonal antibody? What has to be done at which point in time and at what stage does it no longer make sense, to continue the product development? It is very difficult, to change the formulation or the production scale during a running registration. This means, that in contrast to chemical drugs a rather well established production process has to be fixed early on in development, as it hardly can be changed during the course of the clinical development (increasing GMP gradient). Otherwise toxicology or initial safety/dose-finding studies have to be redone, before starting expensive phase III studies and this easily can become a nightmare. And nightmares can get expensive! The key word to be mentioned here is „bridging" (research towards development production).

Avoiding Mistakes

At the end of the day it is not only important, to do the right things, but to do things right. Naturally the question upraises, how young biotech- or small pharmaceutical companies can undertake this process? The easiest and most cost-neutral way is, having experienced developers in the board or at least in the supervisory board. But even here attention has to be paid to the fact, that the board – or supervisory board member – in spite of often coming from the R&D department of a larger firm – should preferably be development-biased. The research-biased guys should better sit in a scientific advisory board, where developers, who always have an eye on the market, will be extremely helpful, too.

So, how can other mistakes be avoided? In the first place by the suitable and solid planning of an experienced developer and the incorporation of a professional project management system. Here, a clearly structured procedure, backed by the full support of the upper management, is the key to success. Depending on the size of the firm, the project management should always work according to documented rules and not simply as a co-ordination function doing things as good as they can be done. Sometimes it might be helpful, to hire an external consultant, to monitor the established system, in order to identify possible weaknesses and to optimize processes. The utility of an external (project management)-advisor may lie in a professional time- and risk management along with risk mitigation, involvement of external partners (CMOs, CROs) or regulatory specialists as well as in establishing contact to capable advisors (in registration, production, clinical opinion leaders, CRO management).

Quality, a Critical Factor

Routinely, costs and time will be regarded as critical factors for the successful running of a development project. The internal controlling of the process should be regarded at least as important since that way the quality of the registration process might be optimized. And it is the quality of the dossier, which ultimately determines the ease of the registration approval of the remedy. Consequently it is the quality, determining finally time and thus the invested money too (especially, if the registration is turned down). Quality control should always be involved in strategic planning. Unfortunately, in real life we often find an approach, one can classify as „quick and dirty", which seldom pays off in the end. In case a project is planned well and done with the best possible quality assurance, the chance of a successful registration increases dramatically and in the end the company saves time and money, by doing things just once (the right way).

The Personal Aspect

As with all projects, the human side of the development process cannot be neglected. Here it is important to always motivate the co-workers running the projects, assuring them they do, what has to be done for the process. Different cultures in multinational companies or even different goals and company philosophies of co-operating firms drive the results. It may sound very ordinary, but often personal interests diverge from the interest of the company (this however will never be admitted, as the own internal career often depends on the smooth running of the product). As a possible consequence results might be reported overoptimistically and this way painted in a rosy picture. For that reason permanent motivation and conflict solving is a special task for (project) management.

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