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Delivering nanomedicines to patients: A practical guide

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Abstract

This is a perspective on the current state of development of nanomedicines in Europe. The view is expressed that a much higher translational success rate could be achieved, with rewards for all stakeholders, if researchers understood the industrial decision points required for new drugs. Getting a drug through the clinic will not help patients unless it is developable by industry. This article is written in the hope that it will help researchers and SMEs to decide where they are in the established process, whether they are making progress and to determine what to do next. It attempts to map the early stages from ideation to first (time) in man (FIM).

Key words: Translation; Development; Commercialize; TRL; Milestones

Stakeholders, such as funders, clinicians and especially patients are anticipating exciting nanomedicine products. Some really innovative nanomedicines are indeed moving steadily through the standard approval process and have attracted commercial interest and significant funding; some of course have already been delivered and are on the market (around 45)[1,2] and twice as many are now in clinical trials, inching closer to the market. However, basic science research has created many concepts, which whilst clinically interesting, are impossible to develop commercially and will never get to the market.

The failure of these concepts lies in part with the researcher who lacks sufficient knowledge of the translational steps required beyond basic research, or even sometimes a willingness to acquire the understanding. Transferring this knowledge has been a *raison d'être* of the European Technology Platform for Nanomedicine (ETPN) over many years, but unfortunately without significantly changing the mindsets of researchers. Whilst this problem has been commented on in the past,[3-5] the aim here is to provide a wider framework on which to map and audit project progression. Ignorance of the regulatory and industrial requirements for development of healthcare products has led to a poor return on investment for investors and research funders for applied healthcare research and nanomedicines. The conduit between academics and the SME based supply chain required for open innovation is absent and will not provide what is needed without substantial changes.[6] The blame partly lies with research funders, who for the most part use advisers without appropriate drug development experience. Funders are also often driven by political pressures and disease specific lobbyists, rather than applying new technology in its best industrial setting for exploitation.

The supply chain

No single action will overhaul the supply chain of nanomedicines, but there are a number of very practical steps discussed here that should assist approaching that goal. Firstly it is essential that researchers working on drug development are familiar with the decision points for industrial development. These can be acquired *via* sabbaticals or using industrial contacts and advisers to the full. It is rare for departments not to have these people, who would be delighted to be asked, not just for current information, but for informed views as to what the future

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will hold. One of the most productive activities is to invite industrial participation onto panels evaluating early research ideas. This is a powerful teaching tool and if possible spectators should be permitted to these meetings. Most students will leave academia and join large companies and SMEs and an early and positive interaction with the industrial culture is extremely valuable. It is unlikely that industrial scientists will give a lot of time to bridge the gap, so it is vital that any such interaction is efficient and valued. It should not be a one-sided conversation, if anything; it should be biased to extracting views and information from visitors. There is a need to find out industrial priorities and there are few ways for outsiders to glean this knowledge; although there are a number of industry-facing Web sites (e.g. www.firstwordpharma.com) which provide up to the minute commentaries on who is doing what.

The pharmaceutical industry is very flexible on choosing new drugs and if they do not achieve proof of concept in a few years, that field is abandoned and new targets will be considered. Academic groups tend to explore a technology and indeed this may be a fruitful approach, however all ideas are not equal in healthcare and it may be more prudent to consider exploring an alternative technology or a different application.

Many healthcare projects are complex and require a range of different skills, which are rare to find in one R & D group, and necessitate teamwork. Some clinical groups work in teams very well as this is part of their skill-set; however some academic groups may require encouragement and training in these skills.

Funders – the key gatekeepers for translation

A few funders are on the right path, such as Innovate UK; here the level of industrial oversight is probably above the European average, whilst measured risk taking is encouraged. In addition, the ETPN is on the verge of establishing in 2015 the first European Translational Advisory Board; a pool of experts with translational expertise dedicated to helping research projects and SMEs in the field of nanomedicine.[7]

The single most important lever for translation is to use industrial criteria, both when proposing healthcare proposals and then when peer reviewing them. Whilst the former may seem an insurmountable obstacle to academics and start-ups at first; experience shows that researchers soon master and manipulate these new funding metrics. The importance of acquiring this new mindset cannot be underestimated. It provides academics with the same language and thinking as industry and points potential innovators in a fruitful direction, which they can control and master in their own time. These industrial criteria include competitive edge, business plan and future market size just for example. The second most important lever for research funders is to use advisers with appropriate hands on experience of drug development. Funders should avoid being driven by political pressures and disease-specific lobbyists, but consider new technologies in their best industrial and disease setting for exploitation. Disease specific calls reduce the diversity of the regional portfolio and thus, perhaps perversely, reduce the chances of success. Diversity increases the probability of translation as only a very few drugs can be viable in any one market – the winner takes all. This is radically different from the academic culture where there is no limit on the number of competitors.

Some will say it is hard to predict what is developable and what is not. However, the rules of acceptance for drug development are well established in industry and should assist decision making, whilst also presenting fresh challenges. Sadly, the fact that development often is never considered at the outset of research or during implementation leads to many projects ending up in the wrong place, because of a lack of commercial interest. For patients commercial interest is as important as getting to the clinic; a focus only on the clinic will lead to frustration. Blue sky and innovative research must be supported, especially with open innovation in mind, but for applied research not to be capable of eventual application, even factoring in the risks, is not ethical.[8] Society has created the drug approval processes to protect patients and nanomedicines must pass the same regulations. It has been said that industry is conservative in adopting new technologies, some perhaps were and still are, but the real problem is that academics and many SMEs are taking the easy way out by not addressing the prescribed regulatory and commercial framework. Accepting the additional development challenges will, perhaps surprisingly, stimulate a more creative and blue-sky approach to healthcare challenges and expose unexplored research space. The potential supply chain either needs to embrace open innovation or become redundant in the face of global competition. To adapt requires changes in the educational process to ensure students and lecturers are trained also in development skills and not only in research. The benefits will be greater challenges, career development and although such involvement is anathema to some non-profit organisations – a big increase in research monies.

There are some really good innovative projects in Europe that have accommodated the regulatory framework. Industry is interested in these, although they still present some challenges. It was said recently at a nanomedicine panel session at BIOEurope 2013, “Five years from now every pharma will have a dedicated nanomedicine programme”.[9]

Communication of results

Publishers and meeting organisers should accept a responsibility to ensure that what is projected as applied research, is indeed capable of application in the near future or advances the technology towards commercialisation. To meet this objective nanomedicine should *inter alia* be evaluated by its probable impact on patients or on its real likelihood of moving the cutting edge closer to exploitation. Nanomedicine publishers should have a peer review requirement to discuss whether this research can be applied and what the issues are (the author should also discuss this). It remains the case that the majority of applied papers and talks have no prospect of development.

Decision points

The “industry” decision pathway is outlined below which details the type of information required at each decision point.