

Request for Information: Building a 21st Century Bioeconomy

This response to the RFI posted in the Federal Register Vol. 76, no. 196, Tuesday Oct 11, 2011 will focus on three areas: moving life science breakthroughs from lab to market, workforce development and public-private partnerships.

The views and suggested approaches expressed below represent my own personal views and do not necessarily represent the views held by the Partners Healthcare organization. I am submitting this document as a private citizen.

Moving life science breakthroughs from lab to market:

There are a number of challenges affecting the translation of biological discoveries into products. These start at the level of the investigators who traditionally have no training in development, nor really any interest in doing this type of work. This is not surprising as not only do they not have this training, they are also not rewarded in their career development for performing translational research that may or may not lead to publications or research grants. Thus, institutional policies for promotion need to recognize this effort as important and as a criterion for career advancement in order to begin to change this culture. Funding for these types of activities is also a challenge. Historically, institutions looked to private sector funding to support these activities. While some federal funding has been available through specific programs such as the SBIR/STTR programs and now potentially through specific initiatives catalyzed by the NIH's National Center for Advancing Translational Sciences (NCATS), federal funding, at least in the life sciences, has been devoted primarily to funding hypothesis-driven research. In addition, mechanisms for review and granting of federal funds tend to have a very long timeline and tend to focus on strength of science rather than commercial potential. Further, funding from the private sector including companies and private investors has been markedly reduced since 2008 given the inherent risks and uncertainties in the commercialization of discoveries from the life science sector. Concerns around conflict of interest or perceptions of conflict still surround academic and government institutions, particularly when investigators continue to be involved in technology development through a startup venture or other mechanism that creates a potential financial incentive for the investigator.

Suggested approaches:

1. Changing the academic/governmental institutional culture regarding translational research/R&D: Firstly, this type of activity must be recognized as important to the institution as demonstrated by vocal support from senior administrative officials. This could go as far as incorporating some aspect of the activity (translational research, innovation advancement) into the mission statement of the institution. Secondly, promotion criteria must reflect and take this type of activity, as well as activities which support innovation, into account. For example, promotion criteria could include patents issued, technology licensed, products developed as well as accounting for time spent in these and mentoring activities, such as advising less experienced investigator/entrepreneurs. Lastly, it is not enough to partner basic scientists with clinicians and expect that the result will be translational research/technology advancement. In industry, technology development is a rigorous process based on achieving well defined milestones responsive to market needs. Academic scientists do not work this way, however, it is possible to partner academic/clinical researchers with scientists/engineers trained in this

process (usually coming from industry) to capture the best of both worlds – cutting edge research and technology advancement (see section on Public-private partnerships).

2. Funding: In this current economic climate, there is no question that funding is an issue. Industry, particularly the pharmaceutical industry, is looking at significant losses in revenue and meager pipelines. At the same time, many companies have down-sized by laying off R&D personnel, further compromising the ability to replenish pipelines. Academic institutions need to play a larger role in advancing technologies in the life sciences/healthcare sector to help feed pipelines and decrease technology risk. The question is how to fund these activities, as the traditional private sources (companies, venture capital) have dried up and non-profit (federal sources) have not historically supported this type of work.

One exception is the SBIR/STTR programs which have played a role in supporting the activity. Both programs are set up to require industrial collaboration with a small company that is not institutionally controlled. This requirement is often met by setting up a shell company – which was not the intent of the provision to begin with – the intent being the demonstration of market/industry interest and economic impact. In addition, the creation of a startup company to advance technology can create downstream conflict of interest complications with respect to investigator financial interests. One possible modification of the SBIR/STTR program is to allow funding to come directly to the institution providing that the institution can create a compelling business case and demonstrate market need and/or interest. This would allow advancement of different types of technologies, not just platform technologies that could support a startup, but also improvements which could be licensed to existing companies to supplement their business interests.

The SBIR/STTR program would be much more effective if the timeline for seed/phase 1 grants could be shortened. In this day and age, technology development moves at a fast pace – in fact all research has essentially “speeded up” given access to automation and new platform technologies. The NIH granting process, has not however, kept up with this pace. This problem is more acute in the translational area as funding from the private sector is typically contingent upon the successful conduct of key proof of principle experiments (funded by SBIR/STTR programs). The hiatus between grant submission and release of funds can result in loss of private funding and/or loss of key personnel.

Funding directed to translational research or technology development could also facilitate access to company technologies and expertise that could be used to understand pathways/targets so as to develop more effective therapies. There is a significant amount of knowhow and expertise in pharmaceutical, device and diagnostics companies that is currently not shared. Companies have approached academia with a willingness to share information and work together to develop new therapeutics, diagnostics and devices. However, in many cases, the only resource the company can offer is expertise/knowhow. Funding is extremely tight and without funding, the academics and clinicians are not able to work in partnership to conduct this important research. A mechanism by which federal funding could be accessed through an expanded SBIR/STTR mechanism or other mechanism could serve to catalyze these types of partnerships.

3. Conflict of Interest: While this is a serious matter affecting public trust, our current climate is very strict with respect to involvement of entrepreneur/investigators in the downstream

advancement of their technology. Our current guidelines/policies essentially prohibit any involvement of the investigator in clinical research if the investigator has a financial interest in the technology. Thus for an investigator to remain involved in development of his/her technology, s/he must eschew any financial interest which includes stock/stock options (in startup companies), cash payments above a de minimus level –and now there is discussion regarding royalty payments received by the institution (and shared with the inventor by law) from licensing of the invention. While the logic behind this approach is understandable, it does not serve technology development well as it creates difficult choices for an investigator and situations that are not optimal for development of early stage technology. While we all agree that our conflict of interest policies serve an important and necessary role, we need to continue to find ways for academic researchers to appropriately work with industry. Guidelines offering approaches to “manage” such conflicts in appropriate ways would go a long way to alleviating this situation.

4. Technology Transfer: Technology transfer offices have traditionally worked on a service and income generating model, with services by and large having the greatest emphasis. There is good reason for this as income generation is largely a happenstance situation that the technology transfer office ultimately does not control (control being in the hands of a licensee/partner company). As a result these offices have been historically funded quite leanly and have limited access to expertise relating to markets, clinical need, technology requirements for competitiveness, regulatory issues and reimbursement issues. However, some offices, due to success, volume of inventions and/or institutional focus, have developed quite specific areas of expertise which could be shared with other offices. However, a model which incentivizes offices to share expertise has not been developed. The Kauffman Foundation explored this issue and concluded that investigators should be allowed to work with whatever office best suits their needs and the needs of the instant technology. While there are a number of problems with this simplistic approach, the concept of accessing technology transfer offices with specific expertise deserves some consideration. As these technology transfer centers of excellence do exist in different fields, the federal government could fund an initiative to identify these centers and then support a limited effort to explore mechanism of expertise sharing and/or consulting on development of specific technologies identified as having superior clinical potential.

Workforce development

We are facing a crisis with respect to trainees in the sciences. American institutions awarded 25,836 doctorates in the sciences in 2009. The majority of these students will not find positions in academia due to decreasing budgets. While a PhD program is an excellent way to prepare one for a career in research and academia, most programs do a poor job of providing students with the skills to pursue other careers, and in many cases don't provide any information regarding jobs outside of academia. Often these individuals drift away from their scientific roots into unrelated careers. These highly trained individuals are a significant resource that could impact US productivity, inventiveness and competitiveness if provided with the right training.

Viewing the issue from a different perspective, even those select few PhDs or MDs who find positions in academia, have little or no training in entrepreneurship and technology commercialization. The NIH itself has identified as a priority the need to “develop teams of

investigators from various fields of research who can take scientific discoveries and turn them into treatments and strategies for patients in the clinic". In order for this to become a reality, investigator teams must not only understand the basic science/disease physiology, clinical need and clinical trial design but also understand how all these factors impact marketability and technology feasibility. In other words, in order to have a real impact on patient care, investigators should understand the entire development path and critical pressures both financial and regulatory, that will determine whether a particular treatment is feasible. Understanding the complete pathway will not only help in early stage research but will also inform as to what resources and specific knowledge will be critical in assembling the optimal research and development team.

Suggested approach:

1. Postdoctoral fellowship in technology commercialization: The goal of this program would be to provide training to biomedical investigators (MD or PhD) in technology development including instruction and hands-on experience in areas relating to technology evaluation, business assessment, intellectual property protection, and product development including regulatory, reimbursement and market issues.

While there are a number of aspects of this concept that are already available, there is no single program that provides course-based instruction as well as hands on experience in translational research labs, intellectual property firms and startup companies and/or venture capital. The program would also encompass some career counseling which would allow an amount of "tailoring" of the program to individual interests. In other words, if the candidate were interested in pursuing an academic career, the program would include experience in a laboratory performing translational research as well as shorter rotations in a law firm and/or company. Conversely if the interest were more in the area of intellectual property, the time frame for different rotations would be adjusted appropriately.

I have conducted a limited amount of marketing research with current PhD students in my institution and in others and they have responded with an overwhelming level of interest. As outlined the program would require cooperation and collaboration with different public and private entities including academic centers, law firms, companies and investment groups. Again limited marketing on my part indicates that there is interest and enthusiasm from the private sector. As envisioned this program sits at the intersection of science and medicine,, law and business. Technology transfer offices also sit at this same intersection and many offices including the Partners Healthcare office have provided informal training through internship programs. This fellowship in technology commercialization could have as its administrative home, one or a number of the technology transfers centers of excellence identified through NIH resources in #4, Moving Life Sciences Breakthroughs (above). Funding for such a program is envisioned as a combination of public/private support.

Public-private partnerships

Public-private partnerships are key to advancing technologies and treatments for healthcare as it is becoming increasingly evident that neither the academy nor the private companies have all the expertise and resources needed to achieve effective translation of basic research into safe and effective clinical applications. To date, models of interaction have focused on different ways to bring the relevant

expertise from entities in either camp together in the hopes that proximity will catalyze effective translation. However, academic scientists and industry scientists/engineers work in fundamentally different ways and in many cases appear to speak different languages. There has been little focus on models to bridge this gap, in other words, on effective handoff from one entity to the other. It has been my experience, especially with early stage technologies, that problems in handoff often lead to failure of promising technologies.

Suggested approaches:

1. Technology translators: One approach that is being piloted at a number of academic institutions is to hire personnel with the appropriate background (engineers, chemists etc) and industry experience to work side-by-side with academic scientists. These personnel are experienced in project management and focus on advancing promising concepts through the early phases of R&D. This approach has a number of advantages:
 - a. It protects the academic scientist leaving them free to continue to innovate and to pursue more academic approaches and career advancement.
 - b. It provides for close coordination with ongoing research allowing the development function to feed back into the basic science efforts to stimulate fresh ideas. This has been termed by some as the “virtuous cycle” – translation stimulating further innovation.
 - c. It provides for greater success in raising private funding or in licensing of technologies because it effectively “de-risks” the technology.
 - d. It has the potential to accelerate time to market as the technology advancement is conducted by personnel experienced in project management and technology development. The goal would be that the company would not have to repeat any of the development activities as these would have been conducted according to industry standards. Further the development personnel would also function to transfer the technology to company personnel at the appropriate time.

The federal government could play a major role in this effort by helping to bring together the relevant parties. Important in this effort is coordination with the disease foundations as not only do they have access to patients, they also have broad internal expertise and a knowledge of world-wide research and development programs relevant to their disease indication. Coordination of the disease foundations with academia (and academic medical centers) and industry should not only help address the financial constraints but should allow leveraging of all relevant expertise for translation into effective health care.