

Comparing Some of the Issues Facing University and Non-University Biotechnology Start-Up Companies

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Although biomedical research in Alberta, Canada, has attained a very strong international reputation, this strength has not fully translated into commercial success, where commercialization was and is an attractive and feasible option. Case studies have shown that when commercialization has occurred, the coordinated efforts of municipal government, academic institutions and provincial/state government in the creation of incubator facilities has led to the growth of companies, with a resulting positive impact on local economic development.

For many biotechnology start-ups, attaining self-sufficiency is highly dependent on the presence of local facilities at the appropriate time in their development. In addition, these companies have needs that extend beyond physical facilities; knowledge of regulatory, legal, financial and intellectual property issues, as well as general business expertise is critical. Individuals with the appropriate background and experience may be beyond a young company's means.

While many universities have established technology transfer offices to deal with the early phase requirements of biotechnology start-ups, companies soon outgrow their university facilities. Frequently, the problems associated with leaving the university environment prove to be too onerous. A lack of resources (both human and capital) often forces them to either license the underde-

veloped technology to a manufacturer or to enter into inappropriate strategic alliances.

We argue that the culture of the university often deludes researchers into thinking that they can translate their research skills into business/management skills, and thus, be treated as equals by their business counterparts. This says nothing of those companies whose genesis occurs outside of an academic environment. These non-university start-ups face a different array of challenges, only some of which are shared by their university counterparts. They have difficulty accessing local resources because access is often predicated on the assumption that local start-ups will always develop from an academic environment. For the non-university start-up, the local academic center is usually its major source of outside technical assistance. In short, while university start-ups are being moved toward "the door" and into separate facilities, non-university companies are clamoring to get in. Other differences can be seen in the way that various university policies (mostly intellectual property) are applied to non-university versus university start-ups.

The purpose of this paper is to compare and contrast some of the issues facing university and non-university biotechnology start-ups from the perspective of one non-university biotechnology company.

UNIVERSITY START-UP COMPANIES

Before profiling our non-university company, we'll review the challenges faced by university biotechnology start-ups.¹

As its *raison d'être*, the university must be a place where ideas can flourish. As such, it is an institution committed to the pursuit and development of knowledge. The university's role is to enable and encourage teaching, research and, more recently, economically relevant development (applied research and intellectual property protection). In theory, academic freedom ensures both the openness and responsibility of comment and

1. In addition to our own experiences in the university environment, we have relied upon the following sources of information: University of Calgary Policy on Intellectual Property and Guidelines for Company Creation on Campus; and "Issues with respect to commercializing Canadian university research," Project # 98848, prepared for the Expert Panel on Commercialization of University Research of the Advisory Council on Science and Technology, January 28, 1999.

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criticism of all intellectual matters. Scholarship demands not only its own pursuit but also that the results are shared with the community at large. This responsibility sometimes runs counter to commercial and market-oriented interests.

Universities recognize their unique role in the production of knowledge and thus have an obligation to exercise this role in order to produce benefits for society through publicizing research findings and, where appropriate, encouraging the application of research in tangible ways. University intellectual property (IP) policies are vehicles by which the application of research results are encouraged and facilitated. These policies are typically designed to grant a high degree of flexibility to the creator/inventor, the university and society at large while simultaneously encouraging the disposition of IP in ways that will ensure the maximum benefit for all.

In order to encourage the development of ideas, the University's resources are made available to every member of its community. Inventive, scholarly and creative activity is the result of this milieu and IP is the material or communicable product. At Canadian universities, initial IP ownership is vested in either the creator(s)/inventor(s) or the university but, regardless of ownership, the creators share in the net revenues earned from commercializing the property. There is no overall consensus as to whether university-owned or inventor-owned IP is the better policy and neither the industry nor the investment community seems to have a preference. What they desire are clear, unambiguous policies. Those who do favor the former argue that:

- The benefits from publicly-funded research should belong to public institutions;
- Domestic societal benefits are more likely when inventors can't simply sell IP to the highest foreign bidder;
- There is greater incentive to commercialize;

- It's easier to protect both the rights of the inventors and those of the university;

- It minimizes the problem of industry playing one university against another during negotiations;

- It reduces the time and effort required to negotiate deals with industry and investors

- It doesn't preclude universities from subsequent attempts to commercialize after initial failure; and

- It's easier to account for and monitor commercialization activities.

Those who favor the inventor-owned IP model argue that:

- It fosters more entrepreneurial thinking on the part of researchers;

- It tends to encourage more localized company creation; and

- It can work to reduce the bottlenecks that occur when technology transfer offices (TTOs) or university-industry liaison offices (UILOs) are working at maximum capacity.

Although these are the published consensus models, neither can escape scrutiny, and we would argue that none of the criteria listed above provide any particular support for either model. The university-owned model emphasizes IP ownership whereas the clarity of ownership is perhaps more important. If a university or non-university company fails in its initial attempts to commercialize a technology, the university company is likely to have more resources for a second attempt but is no more likely to experience success.

Furthermore, another organization (university or company) could have successfully patented the technology in the interim (e.g., U.S. patent law rewards reduction to practice, not "first to file"). With respect to inventor-owned IP, a current owner is likely to be entrepreneurial, but this fact will not, in and of itself, change the entrepreneurial mindset of the research community at large. In this context, is entrepreneurship being confused with avarice? On the other hand, local owners of IP are probably more likely to set up a company locally,

with or without the assistance of a local TTO or UILO.

Many universities have experience with accommodating the laboratory needs of a number of start-up biotechnology firms. Typically, these involve current faculty members engaged in attempts to commercialize the results of their research. Universities with strong biosciences, medical, forestry and agriculture programs and increasingly facing the question of biotechnology start-up companies on campus. Issues surrounding university start-ups are complex and raise questions that need to be systematically addressed. These include not only such basics as the ability to accommodate the company's needs (is the space available and can the support services be provided without adverse affect on academic programs) but also more sensitive issues such as conflicts of interest and how to manage them. Conflicts of interest are inherent in technology transfer involving both the university and its personnel. It cannot be made to go away (except, of course, by steering clear of technology transfer altogether) but it can be effectively managed if recognized and taken into account early on in the proceedings.

Most universities have policies and procedures as well as suggested guidelines that seek to streamline the process of university start-up company creation and manage, or at least minimize, any conflicts of interest inherent in the process of company creation and ongoing management. Most adhere to a number of principles; first, the technology involved must have resulted from university-based activities and therefore the university has a legitimate interest in seeing it reduced to practice; second, the university must not (and must not be seen to be) using public funds to subsidize commercial activity. In addition, most guidelines require as clear a division as possible between company and university activities, plus full disclosure and ongoing monitoring. Most guidelines also require that any university-company arrangements and approvals are generally

known within the academic unit affected.

Thus, with respect to university biotechnology start-ups, the following types of guideline will generally influence company creation:

1. The activity (technology transfer) must be consistent with the role of the institution (e.g., to move the results of university-produced research to industry, to the benefit of Alberta and Canada).

2. Financial arrangements for the company's operation must be such that the university is not subsidizing the activity with public funds or by the uncompensated use of resources provided by public funds for academic purposes.

3. The arrangement should be time-limited (i.e., for an agreed period of time, after which the company will be expected to move its operations off-campus).

4. The company operation must be based in space that is separate from any other space used by the professor for other research and the activities may not deny students or staff access to equipment or facilities provided for academic activities. In practice, this is very difficult to accomplish, is an added expense and is frequently ignored. Realistically, there will be overlap between corporate and academic work done within the same space, and it is often the first area of disagreement.

5. The involvement of the professor and any other university staff member or student, together with the nature of their involvement (e.g., company employee, executive, share-holder, etc.) is a matter of local record.

6. The details of arrangements must be properly approved, based on full disclosure (typically within the framework of a confidentiality agreement). The general nature of these arrangements must be known within the academic unit and faculty approved.

7. The university must have an interest in the activity pursuant to applicable university policy to justify the arrangement in the first place.

8. The company must have and use an independent corporate

address. Again, in reality this may not be practical, and again, is often ignored.

9. Any request for third-party funds involving the university must fully disclose the arrangements to the potential sponsor, (i.e., the company cannot benefit from, or "trade off", the reputation of the university without disclosure).

10. No special conditions of confidentiality can be imposed upon academic activities involving students or staff as a result of the company's activities. Established university policies apply, except for those matters specifically covered by a confidentiality agreement.

11. The company must comply with all university requirements related to safety and the conduct of certain types of research. University inspectors must be able to enter company space to determine compliance.

12. A monitoring mechanism must be devised to review all arrangements and activities on an ongoing basis; this monitoring should include review of the use of university funds normally and properly available to the professor.

The basis for biotechnology company creation is most often found in the technology itself. At the heart of any technology is the IP. IP and the manner with which it is managed are two other major distinctions between university and non-university biotechnology start-ups. Historically, university TTOs or UILOs have tended to focus on transferring academic innovations to industry through licensing arrangements, however the biotechnology boom has resulted in an emphasis on developing platform technologies where the best route for commercialization is often company creation. This is a challenge faced by many researchers, especially in the health sciences where the intent to commercialize is often with a view to developing human therapeutic agents.

Given the extended timeframe involved in bring a drug from discovery to regulatory approval for marketing (10-12 years), the TTO is often inclined to identify an industrial licensee and realize a more

immediate revenue stream for the researcher and the university (and themselves in the case of a "for-profit" technology transfer or industry liaison). Many researchers, who are passionate about their technology, adamantly push for company creation sometimes against the better judgement of their TTO. Sometimes a compromise is reached, but we are beginning to see an increasing number of researchers attempting to commercialize their research by circumventing university policies without the involvement of the TTO — and more often than not, it is with a view to company creation rather than licensing-to-industry. This circumvention is as likely to include technology that should be licensed out as it is to include technology that warrants company creation.

In our opening remarks, we alluded to the cooperative and coordinated efforts of municipal, provincial and federal government agencies alongside universities and their researchers as contributing to the success of commercialization efforts. However, we detect a developing trend whereby it is the inability of the university and local government (in the form of its economic development branch) to work together that ensures the failure of technology commercialization from the university. Specifically, we see the not-for-profit public agency mandate of company and industry creation increasingly at odds with the for-profit university TTO mandate that typically favors licensing over company creation. This often escalates into "turf wars" over who should be involved in the process and at what stage. Local government accuses the TTO of "gatekeeping," devoting its resources only to bigger pay-off technologies and controlling the flow of technologies into the wider public domain. Adding to an already fragmented situation are the activities of private venture capital companies, which are forced to deal with both parties.

There are, admittedly, many advantages to biotechnology company creation from within a univer-

sity environment. Foremost is proximity to much of the required infrastructure. However, it is perhaps because of a university's mandate to engage in scholarly activities (teaching and research) combined with a more recent mandate to contribute to local/national economic development through increased technology commercialization activities, that some problems can arise. Most obvious is the view that even where technology commercialization is institutionally encouraged, the results of such commercialization are not rewarded or recognized to the extent that teaching and research excellence are.

From the perspective of the researcher, there is the dichotomy of publishing research results while protecting the IP and the commercial opportunity. In addition, company related activities take up scarce research time, and the researcher may still have other academic obligations, for example, teaching. This might be a disincentive for those individuals who want to maintain their academic career together with their commercialization activities. Very few researchers are willing to relinquish their academic security (financial and otherwise) and immerse themselves 100 percent into their business — at least not early on in the process. In all probability, tenured faculty members are less likely to jeopardize their academic appointment than are junior faculty whose funding is generally less secure. A failure to take a decisive step from the academic to the business camp could prove fatal in the long run. In other words, their aversion to risk may compromise the successful commercialization of the technology. To our knowledge, universities are experimenting with policies designed to help a researcher make this choice effectively.

In addition, without a long-standing culture of commercialization — with clearly articulated goals — within the university, unintentional yet serious barriers exist. The drafting of advisories and guidelines and the efforts to administer and enforce university

policies are attempts to quell the sometimes-conflicting constituent parts of the university mandate. However, universities are complex multi-disciplinary organizations where policy implementation and program delivery are most often the responsibility of individual faculties and/or departments. Based upon our personal experiences and observations, university-wide policies and objectives are often not reflected in the practices and objectives of individual departments or faculties. It often appears that the technology-based faculties (e.g., medicine and engineering) are more entrepreneurial but feel stifled by policies that are designed for the university as a whole.

The last issue that we'll discuss is that of accessing or obtaining competent human resources. Biotechnology start-ups are driven by entrepreneurs and require expert management from a very early stage. First-rate, internationally-acclaimed researchers may be deluded into believing that they are first-rate entrepreneurs and managers, when they may, in fact, be neither. Successful commercialization is as dependent on excellent management as it is on exploitation of the technology. In the university environment, TTOs or UILOs may not have the resources or skills to provide this critical component. As we mentioned in our introduction, we would argue that in many cases, the university culture often deludes researchers into thinking that they are the key to success, and that their skill as researchers is immediately transferable or mutable into the business/management world. It is against this generic university scenario that we now describe the activities undertaken, and issues faced, by a non-university start-up biotechnology company.

NON-UNIVERSITY START-UP COMPANIES

We feel very strongly that what really differentiates a university start-up from a non-university start-up are the notions of credibility and an awareness of what

constitutes reality. As an extension of credibility and being aware of the "real" world, we see non-university start-ups distinguishing their operations from their university counterparts by (1) being more market-focused early on in the commercialization pathway, and (2) being much more cost-conscious and cost-containment oriented. This latter point has resulted in the founders of the exemplar company (two of the co-authors) assuming the guise of a "virtual" corporation. In short, the formation of the non-university start-up only truly begins when the founders fully relinquish their hold on the kind of supportive environment offered by a university — cold reality must be allowed to enter.

To use the language of Teknekron², many universities tend to subscribe to the "design-build-sell model," whereas successful non-university start-ups will favor a "sell-design-build model." It is the latter scenario that the authors have chosen to pursue. Rather than attempting to sell the technology that was invented, the focus is on resolving a scientific problem where commercial success is tied to resolving this problem rather than focusing on the specifics of any compounds arising from the technology. Thus, there is a conscious effort to bridge the gap between science-oriented and market-oriented objectives. Industry and the investment community often find themselves at odds with universities that approach them with excellent ideas but with absolutely no market potential. We would argue that the university environment fosters a "technology push" approach to commercialization because not every piece of technology is, by definition, commercializable.

Exploiting excellent science for good commercial results is the obvious challenge for any biotechnology start-up company and

2. Teknekron Corporation has more than 25 years in the role of creating commercial value from R&D-derived technology using the "Teknekron," a commercialization technique that combines the best elements of venture capital partnerships, business incubators and intrapreneurship programs of large firms.

implies a process whereby certain ideas and technologies drive the engine of marketable products and services. The parallel process, whereby the scientific direction of the company at a very grassroots technical level is shaped by a vision of what excellent commercial success should and could look like, is less obvious. One can have equally brilliant and entrepreneurially-oriented scientists launching companies, but we argue that the individual operating outside of the university will tend to see the world through a different lens and be more inclined to incorporate the market into his or her thinking.

This is perhaps because for the non-university start-up, reality dawns much sooner! Essentially, its starting point is one of having little, if any, credibility. By virtue of an academic appointment and a history of publishing, a university researcher will have a level of credibility that he or she hopes will mean something to industry and the investment community. However, the non-university start-up can focus on developing the technology with an eye to the market and not worry about credibility. It is this market-driven science, coupled with a low overhead, "virtual" business model that can differentiate a successful non-university start-up from its academic counterpart.

In our experience, investors are much happier dealing with a company having university-trained personnel, but whose last university affiliation was some time in the past. This makes for much cleaner negotiations because there is generally no ambiguity about IP ownership and fewer university policies with which to contend. By virtue of having to satisfy the needs of multiple constituents and having a much broader agenda, the university is a larger, slower-moving, more bureaucratic organization in which start-up companies are not going to be able to operate in quite the manner that their principals might have hoped for. The founders of the exemplar biotechnology firm use a military analogy to describe their non-university

start-up — it is a highly mobile, rapid deployment force, lightly but expertly equipped, taking advantage of all available terrain and resources in its operational area.

Non-university start-ups simply don't have the luxury of immediate access to facilities and infrastructure. They tend to keep more emphasis on outsourcing and contract work in order to keep costs down and use what capital is available more efficiently. Contracting out provides some excellent illustrations of the differences between university and non-university startups. Both types of company will outsource key professional services like legal and accounting, although a given university-based company may not have as much flexibility in choosing the specific firm. For example, a university TTO or UILO may dictate the choice of patent attorney, who may or may not be appropriate to a given technology.

Perhaps the most striking difference is how each entity contracts with academic institutions. The outside company can take advantage of the most appropriate, cost-effective or, simply put, the best university-based researchers available regardless of their location or academic affiliation. The only limitation is the negotiation of an acceptable contract. In theory, the university-based company has the same option and the usual channels for research collaboration should make the process even easier. In practice, collaborations for commercial purposes may appear to be too lopsided in comparison to standard research collaborations, and the university-based company is still encumbered by all of the administrative and political considerations that attach themselves to intra- and inter-university collaborations. For example, if the researcher has to negotiate IP rights with the host TTO, it is not difficult to imagine the problems that could arise when a sister university is brought into the picture. On a more mundane level, the university-based company is probably under some obligation (actual or perceived) to use in-house facilities

and equipment. Different stakeholder interests will influence this decision. University start-ups will often receive subsidies in terms of leasing space and equipment as well as reduced overhead charges, but this will be balanced by claims to an increased revenue share or equity position on the part of the university or its TTO.

If the examples given above and throughout this report are generally applicable, and we have both practical experience and anecdotal reports from others that suggest they are, there would appear to be little medium- or long-term advantage to setting up a company within the environs of a university. While some of the authors, admitting their bias, tend to support this opinion, it is not to say that non-university startups have things entirely their own way. The non-university company is on a very tight schedule to prove the technology's worth and establish some wider credibility before the start-up funds run out. This pits cost-containment against the development schedule and, for example, it may be wiser to use a very high-priced contractor to complete a project in 30 days than to use a cheaper source with delivery in 90 days. The university-based company can typically absorb delays a lot better than its outside counterparts, especially if most overhead expenses are spread across a number of funding sources.

For example, the university-based technician is directed to perform more university and less company work until a company delay is resolved. In contrast, the non-university company is always in search of a reasonably priced contractor, who will settle for a small overall commitment in terms of both contract term and value, and who can meet short delivery dates. Generally speaking, this type of contractor is a university-based researcher, and consequently, the non-university company has to successfully enter the very organization from which it seeks to distinguish itself. If this critical relationship is handled poorly, it can cost the non-university company

dearly. Most notably, since the outside entrepreneur almost certainly has significant academic experience (graduate and postdoctoral training, for example), it may be its turn to be deluded into thinking that it enjoys a closer relationship with its academic colleagues than actually exists. Anecdotal evidence supports the view that in some cases, former colleagues may not be current friends and supporters because in some respects, universities can be more like religious communities than businesses — once you're out, you're out. That also pertains to university startups. Once you decide to set up a business, some colleagues will consider that you have committed "heresy," and they may want you out or may be unwilling to collaborate.

The following example illustrates a common arrangement that can lead to problems for the non-university company. It is not atypical for the outside company to use university space and equipment pursuant to an informal, unwritten agreement with a friend or former colleague. The company may become so dependent on these arrangements that there is a serious impact when the university "finds out" and moves to formalize or terminate the relationship. Quite understandably, the university may claim IP ownership and protection for work carried out in its facilities under informal agreements. A reasonably astute company can avoid these problems by ensuring that all work performed by or for it within a university facility is properly negotiated and subject to a signed contract. If the outside company is unwilling to enter into a frank discussion with the university then it may end up paying far more than necessary for its contract, which would be ironic, since many universities offer incentives (e.g., reduced overheads) to startup companies in their catchment area.

In our experience, problems can arise when the outsider approaches the university with a detailed list of requirements based on too much "insider" knowledge. Most universities have a number of different contract scenarios including straight "fee-for-service" as well as various forms of "contract" and "collaborative" research agreements — each has its own requirements, objectives and pricing structure. For example, if Company A arrives at the university with a predetermined plan to use a particular piece of equipment ("... been idle since I left here two years ago ...") with very clearly defined objectives in mind ("... just need to run 10 samples through it a week ...") then, if successful, they are likely to get a straightforward space and equipment rental type contract, which typically carries the highest overhead rate. Had Company A reminded the university (through its Research Office or similar outlet) that a particular capability (equipment and know-how) was available, it may have negotiated a contract with a "per sample" price structure. Even better, it may have negotiated a flat fee for a collaboration with no transfer of IP, which typically carries the lowest overhead rate.

When it comes to university-industry alliances in biotechnology, the position adopted by the major pharmaceutical companies bears some analysis. A small startup is unlikely to engender the same respect as a multinational pharmaceutical company when it arrives at a university, but this should not overly influence its negotiating position. In short, both the large and small companies need to understand the main functions and objectives of the university, and they need to enter the organization at the appropriate level (i.e., through the director of research, not

through a friend or former colleague). The small company should emphasize its embryonic status because it can afford the university an opportunity to offer a pricing structure designed for local startups. This is a potential "win-win" situation because it saves the company money and meets the university's obligation (handed down from local or national government) to help in the formation of the local biotechnology sector. In a final example, the small company (like its "Big Pharma" counterpart) should be imaginative when it comes to paying for the contract. To be more specific, the same amount of money can go to a simple fee-for-service contract — "what you pay for is what you get" — for example, or to pay for the results the company needs by way of funding a graduate studentship or an equipment purchase. Both examples provide more enduring benefit to the university community and, by way of goodwill, the company.

This paper has drawn heavily upon the authors' experiences both in a non-university biotech company and in a newly created office in the faculty of medicine, designed to facilitate technology commercialization. We hope that this paper has shed some light on the difficulties that both university and non-university companies face during the start-up phase but, more importantly, we hope that it is a modest contribution to resolving some of these difficulties. The long-term goal for any community contemplating growing a biotechnology industry should be a combination of university and non-university companies collaborating and sharing resources in the interest of the local community — much like the biotechnology clusters seen in and around Boston, San Francisco, San Diego and Cambridge.