Innovation and Entrepreneurship

The Risks of Innovation

As most innovators and entrepreneurs know, risks come in all sizes, shapes, colors, and flavors. Commercialization of an idea means dealing with and overcoming many types of risk, including personal risks; those that affect family and friends; legal risks involving patents, lawyers, and law suits; manufacturing risks, such as fabrication of the product, delivery dates, and rejected products; and financial risks. Perhaps financial risks trump all others because they are intertwined with the other types of risk and because an innovative venture requires money. To obtain start-up capital and keep the cash flow coming without losing the company is a task few can accomplish.

The story of an entrepreneur who surmounted these risks and accomplished the almost impossible task of bringing more than 1 product to market can be found in the autobiography of William B Dragan, DDS. His book, provocatively titled *How to Become an Overnight Success in 30 Easy Years*, is a first-person account of a journey through a thicket of risks and the emergence of Centrix, Inc.

The book's title, as well as the bold graphics of the words "become an overnight success" on the book's cover, gets peoples' attention. When I recently was reading this book on an airplane, the person in the adjacent seat couldn't help but glance over at the book's cover. Finally about 10 minutes after departure, the passenger, clearly unable to restrain his curiosity any longer, apologized for reading over my shoulder and asked, "So how does he do it? How do you become an overnight success?" I smiled, showed him the book's cover and pointed out the part of the title that was printed in a smaller font, "in 30 Easy Years." And if that isn't sufficiently eye catching, Bill Dragan adds a touch to the title that reflects on his journey and is a commentary on his sense of humor: the word "Easy" in the title is crossed out with a bold red X.

The story exemplifies hard work and dedication, as one might expect in such a book, but also describes in entertaining detail the risks involved with finding partners during the early years of setting up the company. It details the legal risks—in fact, from the number of pages devoted to his legal issues, the author must have spent at least one half of the 30 years in litigation. His description of the financial risks is educational, explaining what he had to do and, in some cases, not do to raise the capital to get started and maintain the effort. In a tale that could easily be a *Mission Impossible* screenplay, Dr. Dragan tells of a weekend plot to move the company from one location to another. This story, involving interoffice intrigue, locksmiths, clandestine meetings, frantic phone calls, and burly movers, is worth the price of the book. Along the way the author shares what he learned; he provides an excellent description of a patent and provides an insightful commentary on his colleagues in the dental industry. In the final chapter, he shares his concerns about the future of the dental industry.

Of all the risks discussed by Dr. Dragan, money is mentioned many times. For example, early in the story he notes, "As an entrepreneur, you must be willing and able to risk your own money even before risking someone else's."[1] Money is needed for patents, manufacturing, personnel, and, most of all, pursing legal battles. Near the end of the book, Dr. Dragan returns to money with the following: "Expect to spend money if you decide to make and sell your own product. The biggest reason most products fail is lack of money—not only to make the product but, more importantly, to sell it."[1]

Edward F Rossomando, DDS, PhD, MS
Professor and Director
Center for Research and Education in Technology Evaluation
University of Connecticut
School of Dental Medicine
Farmington, Connecticut
erossoma@nso2.uchc.edu

Table—Biotechnology Activities of Respondents Working in Human Health

Applications
DNA-based
Gene probes, DNA markers
Bioinformatics
Genomics, pharmacogenetics
DNA sequencing/synthesis/amplification, genetic engineering
Biochemistry/Immunology
Vaccines/immune stimulants
Drug design and delivery
Diagnostic tests, antibiotics
Synthesis/sequencing of proteins and peptides
Cell receptors/signaling, structural biology
Combinatorial chemistry, 3-D molecular modeling
Biomaterials
Microbiology, virology, microbial ecology
Bioprocessing-based
Culturing/manipulation of cells, tissues, embryos
Extractions, purifications, separations
Fermentation, bioprocessing, biotransformation
Environmental
Bioleaching, biopulping, biobleaching, biodesulfurization
Bioremediation, biofiltration

Money: Where to Find It and How to Get It

To help underwrite the financial risk, the National Institutes of Health (NIH) sets aside a total of 3% of its extramural budget to assist research leading directly to new products or technologies. This set-aside provides funds for 2 programs: the Small Business Innovation Research (SBIR) program, which receives 2.5%, and the Small Business Technology Transfer Research (STTR) program, which receives 0.5%. In 2002, the National Institute of Dental and Craniofacial Research (NIDCR), the NIH component that funds most of the academic dental research in the United States, set aside $6.7 million for these programs, funding 44 proposals for development of new products. These are grants, not loans, meaning the money need not be repaid. In addition, the intellectual property developed with these funds belongs to the company, not the federal government, so the company may patent any new discoveries or products developed during the project period.

The SBIR/STTR programs are designed to assist innovators and entrepreneurs in a small company. Small companies are defined as those with fewer than 500 employees. Because many dental companies are in this category, these programs are ideal for such companies seeking funds to underwrite the development of a new product. These programs are also ideal for those dentists/innovators with an idea who seek start-up capital. An award from these programs not only provides funds but also, because these awards are made only after a rigorous peer review process, acknowledges that the potential product has merit and is likely to succeed. The funds, as well as the recognition that comes with the award, can be used to leverage additional funds, especially from the private sector, because the award indicates that the federal government shares the financial risk.

Risks for Dental Companies Developing Biotechnology Products

Dental practice has remained somewhat static through most of the 20th and into the 21st centuries. In 2001, the human genome was sequenced, an event that will have an impact on dental practice similar in magnitude to the impact of the flight of the Wright brothers on aviation. Just as the Wrights' accomplishment ushered in a new era in transportation, so sequencing the human genome ushers in the potential for a new era in dental medicine. This will be an era where laboratory-grown teeth and bone will replace those lost from disease, where saliva will replace blood and urine as the body fluid of choice for evaluating our health status, and where vaccines for dental decay and periodontal disease will be as commonplace as vaccines for diphtheria and polio. Whereas biotechnology has produced the first generation of products, the dental profession has been slow to adopt such products.

Considering the slow adoption by the profession of the biotechnology-based products already on the market, the introduction of the second generation of such products represents an even greater financial risk for dental companies. But these products will eventually be adopted. Thus, it is critical for the survival of these companies, especially the small to mid-size companies, that they remain current on these emerging biotechnologies and innovations and seek opportunities for investment and perhaps acquisition. To illustrate this

point, think about the timeline for adoption of computer-based technologies in dental practice. Computers were introduced to the market in the mid-1970s. Now, about 30 years later, we are seeing computer-based products enter the dental office in the form of digital radiographs and orthodontic tooth movement. In fact, some dental schools, including the University of Connecticut, are shifting completely to digital radiography while the University of Illinois at Chicago Dental School has introduced certification in computer-based orthodontic tooth movement into its curriculum. Clearly, other dental schools will follow these early adopters. Experience shows that what dental students learn to use in school they stay with for most of their professional career.

It takes about 30 years for a discovery to mature, attract entrepreneurs, and enter commercial development. Human hereditary material was identified as DNA in the early 1940s and its structure revealed in the early 1950s. In 2004, more than 60 years later, sufficient time has elapsed for these discoveries to emerge from the pipeline as products. Already, evidence for commercialization is evident in medicine, especially in the pharmaceutical area.

Dental medicine is not far behind. Before I provide some examples, let me provide a list from the Department of Commerce of what areas the biotechnology industry is pursuing. The Table on page XXX is a list taken from a 2003 survey of 1,031 biotechnology companies by the US Department of Commerce[2] and presented here in response to requests that I have received from dental companies to understand the scope of the biotechnology industry in the United States. Although the report did not identify which companies are engaged in the dental-device biotechnology areas, a cursory glance of the Table might suggest that the dental field is not represented. However, such a conclusion would be incorrect; biotechnology product development is very much alive in the dental field.

Several dental companies, mostly start-ups and incubators, are pursuing biotechnology products. These products include the engineering and regeneration of teeth, as well as growing mandibular condyles and human mandibles. A brief review of the work in these areas is provided below.

Engineering and Regeneration of Teeth

To reinforce the conclusion that regeneration of teeth is a technology soon to enter the marketplace, the following is quoted from a feature in *Business Week*.[3] The column titled "SciTech Developments to Watch" begins, "Genetic researcher Paul Sharpe at King's College London has successfully grown natural teeth in a mouse's mouth in a matter of weeks. He starts with a cluster of stem cells that are inserted into the gums. The new tooth grows into the jawbone and hooks itself up to the local blood and nerve supply. Sharpe's company, Odontis Ltd, is reported to have obtained $900,000 in public and private financing to test the technique on more mice before turning their hand to human mouths, possibly in about two years."[3]

Two other reports in the *Journal of Dental Research* also suggest that research is moving rapidly from the research laboratory toward clinical testing in humans. In one study, titled "Bioengineered Teeth from Cultured Rat Tooth Bud Cells," builds on the earlier work by a team from the Forsyth Institute in Boston, Massachusetts. This particular study shows how tooth bud cells can produce bioengineered tooth tissues when seeded onto bioscaffolds.[4] In another study from Guy's Hospital London, titled "Stem-cell-based Tissue Engineering of Murine Teeth," the authors showed that stem cells not derived from dental tissues were responsive to signals from oral epithelium. In addition, transfer of these tissue recombinations resulted in the development of tooth structures.[5] In his review of these 2 studies, the editor of the *Journal of Dental Research* noted that there are "significant opportunities to exploit this knowledge for the development of novel regenerative therapies which seek to restore partial tooth tissue loss."[6]

Growing Mandibular Condyles

Stem cells also are used to grow mandibular condyles. Work in this area of biotechnology is under the direction of Jeremy Mao, PhD, DDS, professor at the University of Illinois School of Dentistry.[7] In a recent paper, Mao and colleagues showed that stem cells placed inside a mold made from a biocompatible polymer and shaped as a human mandibular condyle would form exact replicas of human mandibular condyles. In the abstract, Dr. Mao

notes that therapeutic applications of the current approach are being explored.[7]

Growing Human Mandibles

In perhaps one of the most dramatic demonstrations to date, a group of investigators grew and successfully transplanted a bone graft in a human.[8] Reporting in *The Lancet*, Warnke and colleagues repaired a mandibular defect using a titanium mesh cage constructed exactly to fill the defect. This was the equivalent of the dental wax-up. However, instead of burning out the wax and replacing it with a nonbiologic material such as acrylic or an alloy, the bio-mold or bio-cage was filled with bone morphogenetic protein and the patient's bone marrow. For "curing," the cage was implanted into the patient's back muscle (the latissimus dorsi) and after only 7 weeks, the cage was harvested and transplanted, repairing the mandibular defect.[9] As when dentures were made using vulcanization and then moved to acrylic, the results of this study indicate that we are moving to a new era—an era of biodontics, the emerging dental specialty that uses biological materials instead of nonbiological materials for construction of prostheses.

Biotechnology and Risk

Considering these examples, operative dentistry and prosthetics will undergo major changes in the future. The dental companies that make traditional products for operative and prosthetic dentistry, such as handpieces and burs, and those that make waxes, acrylic polymers, composites, and implants, need to consider their future and whether it is time to invest in these bio-based product lines. Some element of risk remains, but the level of risk is less today than even 10 years ago and decreases every day.

Sometimes taking a risk can lead to a more interesting journey. As Robert Frost wrote, "Two roads diverged in a wood, and I...I took the one less traveled by, and that has made all the difference."[9]

References

1. Dragan WB. *How to Become an Overnight Success in 30 Easy Years: Centrix, the odyssey of a dentist entrepreneur*. Shelton, CT: Dragan Publishing; 2004.
2. US Department of Commerce, Technology Administration, Bureau of Industry and Security. *A Survey of the Use of Biotechnology in US Industry*. Washington, DC; US Department of Commerce; 2003. Available at: http://www.technology.gov/reports/Biotechnology/CD120_a0310.pdf. Accessed October 29, 2004.
3. Arnst C (editor). Sci Tech Developments to Watch. *Business Week*. May 17, 2004: 66.
4. Duailibi MT, Duailibi SE, Young CS, et al. Bioengineered teeth from cultured rat tooth bud cells. *J Dent Res*. 2004;83:523-528.
5. Ohazama A, Modino SA, Miletich I, Sharpe PT. Stem-cell-based tissue engineering of murine teeth. *J Dent Res*. 2004;83:518-522.
6. Smith AJ. Tooth tissue engineering and regeneration—a translational vision! *J Dent Res*. 2004;83:517.
7. Alhadlaq A, Mao JJ. Tissue-engineered neogenesis of human-shaped mandibular condyle from rat mesenchymal stem cells. *J Dent Res*. 2003;82:951-956.
8. Warnke PH, Springer IN, Wiltfang J, et al. Growth and transplantation of a custom vascularised bone graft in a man. *Lancet*. 2004;364:766-770.
9. Frost R. *A Collection of Poems*. Boston, MA: Thomson/Wadsworth; 2004. The Wadsworth Casebook Series for Reading, Research, and Writing.

In my column in the September 2004 issue of the Compendium, *I noted that 46% of the dental faculty departed their faculty positions in 2002/2003 to enter private practice. In response to my column and this comment in particular, David P Rossiter III, DDS, PhD, a diplomate in endodontics from Northhampton, Massachusetts, wrote the following in a letter dated September 27, 2004: "If the 46% of faculty departures who entered private practice were told that their salaries would be increased by some significant amount; that full-time would be 4 days per week; and that research would not be a requirement of the job, there would be a line at the door."*

I wish to thank Dr. Rossiter for his thoughtful comments, and I am pleased to let him know that alterations in dental school organizations have changed and are continuing to change. For example, income can be increased by faculty practice within the dental school setting, and research is no longer a requirement for successful advancement in many of the 56 US dental schools. In addition, the distinction between part-time and full-time has become blurred, and many more options are available compared with past years.

I plan to follow up on Dr. Rossiter's suggestion and survey the 921 faculty departures in 2002/2003 to determine why they decided to leave academic dentistry. I will be delighted to share the results of this survey with you and the readers of this column. I appreciate Dr. Rossiter's taking the time to write and encourage others with comments and suggestions to send them to me.