PHASE III
COMMERCIALIZATION

SUMMER 2007

WHAT IS PHASE III?
The Definition of the Commercialization Phase

ALTERNATIVE ENERGY MOVING INTO THE MAINSTREAM
The New Climate of Opportunity

WHAT'S IT WORTH?
Basic Valuation Approaches for Technology Companies

DAWNBREAKER®
The Commercialization Company

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EDITOR'S NOTE

Phase III is the ultimate goal of small businesses, Federal agencies and service providers participating in the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs. Although Phase III is the common goal, confusion abounds regarding its definition. What exactly is Phase III? Does the definition vary depending upon the Agency with which you work? How do you know if you have achieved Phase III status? How do you get there and how do you measure the impact of assistance programs designed to facilitate Phase III success?

Phase III Commercialization is a new publication dedicated to addressing these questions. Our approach cuts across agencies, industries and disciplines, focusing on three broadly defined content areas—medical, energy and defense—as well as highlighting Phase III issues and financing options. Our goal is to provide insight and information to those who are intent on being successful in transitioning, commercializing or infusing their technology into the marketplace.

Enjoy this publication and feel free to send me suggestions for future articles of interest to you.

Sincerely,

Jenny C. Servo, Ph.D.
President, Dawnbreaker®, Inc.
"The Commercialization Company"

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by Jenny C. Servo

What is Phase III?

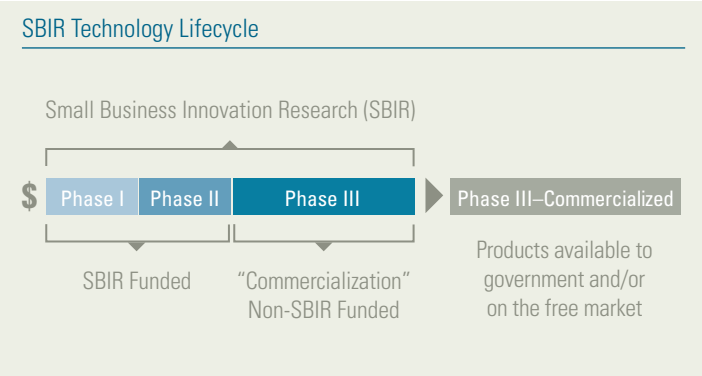
Knowing when commercialization has been achieved.

From the outset, the Small Business Innovation Research (SBIR) program has been conceptualized as a three phase process. Phases I and II are funded by Federal agencies participating in the SBIR program, while Phase III is hallmarked by funding from non-SBIR sources—specifically, the private sector or federal and/or state agencies that purchase goods and/or provide funding subsequent to completion of Phases I or II of an SBIR award.

Many aspects of this initial conceptualization have contributed to the confusion regarding, "What is Phase III?" One would naturally assume that if a program is described as a 3-phase process, that each phase would be funded by funds from that program. However, this is clearly NOT the case. Phase III, by definition, is NOT funded by the SBIR program.

Phase III is also often referred to as the "commercialization phase," making it appear that commercialization is something that you attend to after Phases I and II are complete. However, commercialization should be attended to from the outset. Commercialization should never be an after-thought, but rather pursued from the start.

Further confusion also arises because Phase III can follow Phase I and not just Phase II. It is also curious that most agencies do not consider self-funding, subsequent to the completion of Phases I and/or II, to be Phase III. However, sales are considered Phase III irrespective of the organization that funded further development (the company itself, private sector or the Federal government utilizing non-SBIR funding).



According to the Small Business Association's Directive, a Phase III is funded work that "derives from, extends, or logically concludes" prior SBIR work and is funded with non-SBIR funds. Thus, a Phase III is any funded effort that promotes progress on Phase I and II work along the commercialization continuum. At best, however, funded Phase III work is only one subset of the myriad activities that constitute the "commercialization continuum" and must occur to achieve the end goal of a commercialized product or service. While Phase III customarily refers to funding additional efforts, commercialization of a product may also involve regulatory, procurement, tax, corporate, organizational, patent, licensing, joint venturing, teaming, further technology advancement and other issues and activities.

A Commercialization strategy is a clarification of the series of financing options that a company entertains to move a potential product or service from concept to product introduction.

Table 1: Stages in the Commercialization Process – Robert Cooper

Step 1:	Initial Screening
Step 2:	Preliminary market assessment
Step 3:	Preliminary technical assessment
Step 4:	Detailed market study
Step 5:	Predevelopment business/financial analysis
Step 6:	Product development
Step 7:	In-house product test
Step 8:	Customer test of products
Step 9:	Trial sell
Step 10:	Trial production
Step 11:	Precommercialization business analysis
Step 12:	Production start-up
Step 13:	Market launch

Commercialization as incremental funding

SBIR solicitations describe commercialization as "the process of developing markets and producing and delivering products or services for sale (whether by the originating party or by others) ... commercialization includes both government and non-government markets."

Because commercialization is a process, it happens incrementally. Robert Cooper, in a landmark book entitled *Winning with New Products*, described the stages that successful companies go through between conceptualization and product introduction. His 13 stages are listed in Table 1.

Dawnbreaker expanded upon Cooper's work, stating that a "commercialization strategy" is a clarification of the series of financing options that a company entertains to move a potential product or service from concept to product introduction. The stages in between do not have to be limited to those described by Cooper. In fact, Dawnbreaker recommends that others be added that are pertinent to that industry, technology or market. Examples of pertinent milestones to add include Phase II Clinical Trials and FDA approval for those working with the National Institutes of Health.

Table 2: Equity Investment in Parent Company

Milestone	Financing Method
Concept Development–SBIR Phase I	Sweat Equity
Prototype Development–SBIR Phase II	Science for Hire
Product Introduction	Private Placement
Market Penetration	Debt Financing from equity Investors

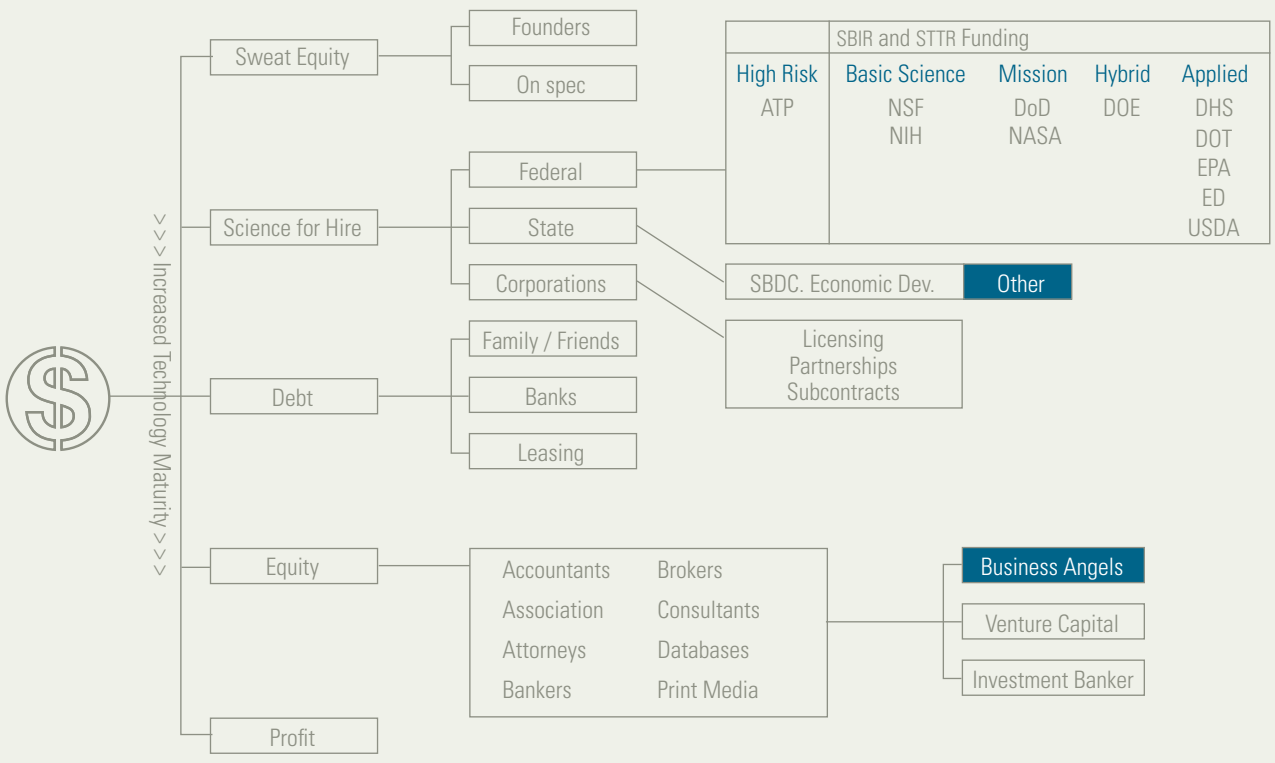
When "commercialization" is operationalized in this fashion, many advantages accrue. First, it becomes apparent that Phase III, the commercialization phase, can be said to have occurred when a company receives additional funding [subsequent to completion of Phases I and or II] from non-SBIR sources to further mature a technology towards the ultimate goal of product introduction. Therefore, when a company receives funding, utilizing non-SBIR dollars, to further mature a previously funded SBIR technology—it is a Phase III. When a company licenses out the SBIR-funded technology to another entity, it is a Phase III. When a company receives an equity investment in a spin-off, built around the SBIR funded technology, it too is a Phase III ... so is a sale, and so is a contract resulting from a congressional "plus-up." These are all examples of Phase III.

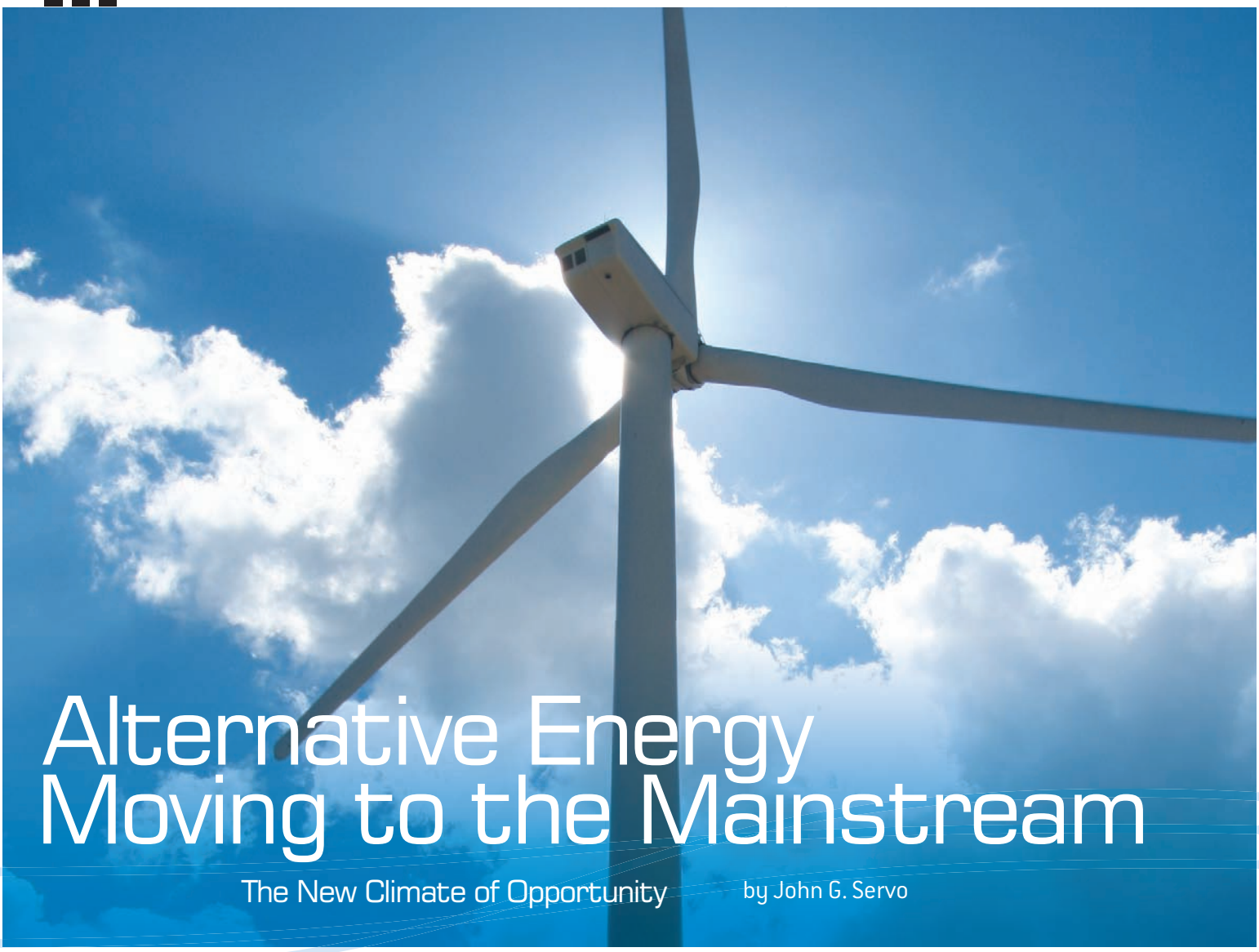
When can you say a technology has been commercialized?

Is it sufficient to say that a product has been commercialized when it receives incremental funding? The answer to this is "No." Many R&D projects do not make it to the marketplace, even though they have garnered additional support, subsequent to completion of a Phase I and/or Phase II SBIR award. Clearly, the goal of the SBIR program is "producing and delivering products or services for sale," but there exists a financial and a business gap between the Phase II R&D award and the ability of a small business to move through all of the stages that Cooper references. A technology will have been commercialized only when it is brought to market in its final form by the SBIR funded firm or others. Funding agencies are most interested in seeing technologies commercialized, transitioned or infused. However, commercialization can be a lengthy process, sometimes bridging many years and requiring incremental Phase III funding. While a commercialized product is the ultimate goal of this process, it may be useful to differentiate between early indicators of potential commercial Phase III funding and ultimate success in the marketplace.

In this publication and in subsequent issues, expanded discussions of potential sources of financing will be highlighted. Figure 1 serves as an organizing tool. In this premier issue we will focus on business angels, as well as state and federal funding initiatives.

Figure 1: Roadmap of Financial Options





Alternative Energy Moving to the Mainstream

The New Climate of Opportunity

by John G. Servo

There are many factors contributing to the new push for alternative energy.

Alternative energy, moving hand in hand with the threat of global warming, has moved to the mainstream, entering the pop culture arena and even prompting an Oscar win for Al Gore's *An Inconvenient Truth*. The discussion around alternative energy has broadened, and the emerging business climate has reduced many typical funding and partnering barriers. On top of the more favorable business climate, both state and federal governments are adding incentives for alternative energy technologies, including wind, ethanol, bio fuels, wave, Municipal Solid Waste (MSW) and Ocean Thermal Energy Conversion (OTEC). Entrepreneurs are encouraged to look to these opportunities as potential sources of Phase III funding for maturing advanced alternative energy technology.

The Bullish Clean Technology Market

The current business and political climates are creating a bull market for those working and investing in alternative energy. The need for alternative fuels has been highlighted in two State of the Union addresses as well as in numerous press briefings, with President Bush stating that America is addicted to oil and that, "It's in our vital interest to diversify America's energy supply—the way forward is through technology. We must continue changing the way America generates electric power, by even greater use of clean coal technology, solar and wind energy, and clean, safe nuclear power." He then called for the setting of a mandatory fuel standard to require 35 billion gallons of renewable and alternative fuels in 2017.

This year, the President presented an FY 2008 budget request of $2.7B for the Advanced Energy Initiative, a 26 percent increase over the 2007 request. According to the U.S. Office of Management and Budget, the DOE's Advanced Energy Initiative is to, among other things, accelerate the diversification of the Nation's sources of energy for homes and businesses by providing additional research monies for alternative energy technologies. The President's budget request included $385M for the Coal Research Initiative, $148M for the Solar America Initiative, $179M for the Biofuels Initiative (for producing ethanol not just from corn, but from wood chips, switchgrass and other organic materials), $81M for More Efficient Vehicles and $309M for the Hydrogen Fuel Initiative.

The government isn't the only sector that has taken notice of the need, and potential impact, of new energy sources. What was recently considered an emerging sector, "clean technology" has been billed by respected venture capitalists and private equity investors as one of the single largest economic opportunities of the 21st century. While the investment category of clean technology covers a range of industry segments, it is the energy component that comprises nearly 70 percent of the in-

vestments in the industry and the initial public offerings (IPOs) of these alternative energy companies have been heating up over the past two years, especially those in solar power.

High fuel prices combined with a high projected price-floor rocked the economy for a few months, with long-lingering consequences. Those high prices, combined with increased instability in both the Middle East and South America, the fuel shortage following Hurricane Katrina, melting ice caps and other climate issues, have caused the mainstream to be driven towards alternative fuel options. This effect has created a burgeoning market.

Now that the market, as well as the government, is getting behind alternative fuels, there is a move by investors towards accepting higher risks in alternative energy. For example, corn has climbed to more than $4 a bushel, up from $2.25 last year, just from the increase in corn-base ethanol. The increased interest has attracted hedge funds and other speculators to jump into this volatile market, driven mainly by the projected demand for biofuels. Having the market, as well as the government, backing alternative energy creates greater access to capital—from incentives, venture capital and from initial public offerings.

"DSIRE"ing to Take the Incentive

When introducing the Energy Tax Incentives Act of 2003, Sen. Chuck Grassley, then the chairman of the Committee on Finance said, "It makes sense to use the tax code to develop alternative energy. Cutting taxes is an effective way to encourage positive, environmentally conscious ways to produce electricity and fuel." These incentives, not only from the federal government, but also from the states, offer a growing opportunity for small energy technology firms and can be easily researched by visiting the DSIRE website. The site, developed by the North Carolina Solar Center and the Interstate Renewable Energy Council (IREC), is updated weekly, with an average of 60 programs being updated or verified per month through contact with program administrators and other stakeholders throughout the United States.

Incentives fall into two broad categories: renewable energy and energy efficiency. The DSIRE site has easily accessible tables that summarize the nature of the incentives provided by each state. Incentives include personal, corporate, sales and property tax incentives; as well as rebates, grants, loan, and production incentives. The rules and regulations effecting both energy efficiency and renewable energy can also be found on this one site. Of the individual states, not surprisingly, California offers the most incentives for renewable energy and energy efficiency, followed closely by Minnesota.

Nothing Ventured, Nothing Gained

As Governor Schwarzenegger keeps California moving towards energy independence with the use of incentives, venture capital firms are jumping on board the alternative energy boom like never before. January reports from Ernst & Young indicate that venture capital investments in alternative energy companies reached $1.8B in 2006 and, according to a recent survey by the National Venture Capital Association, 2007 is likely to be another boom year.

With the expectation that Congress will be placing the development of renewable energy sources as a high priority for 2007 together with the rising popularity of alternative energy technologies and additional state and federal legislative incentives, venture capitalists have a definite interest in increasing their involvement in this sector. This view is reinforced by the Cleantech Venture Capital Report on North American Venture Capital Investing which suggests that by 2009, 10 percent of VC investment activity will be in the clean technology sector, up from the current 6 percent.

Some prominent VC firms involved in the clean technology sector include EnerTech Capital, which has been in the energy technology business since 1996 and now manages $290 million in two funds, 80% of which is in clean energy and DFJ Element Ventures with $292 million in clean technology investments. Kleiner Perkins Caufield and Byers (KPCB), the VC juggernaut that saw the potential of Google and Amazon, is also in the clean technology sector and has been since 1999.

DSIRE website:
www.dsireusa.org

Take AIM

As the clean technology market matures with the help of VC firms, Wall Street is starting to take notice with a growing commitment to the sector. Some investment banks have already acquired alternative energy assets and many have been taking clean technology companies public. But Wall Street is not the only option for taking a clean technology company public.

Another route to take is London's Alternative Investment Market (AIM). Opened in 1995, AIM benefits from tax breaks offered to investors, as well as reduced regulatory requirements, making it the market of choice for growth companies from around the world. The rising cost of being listed in the U.S., due to Sarbanes-Oxley, and the risk of being a director of a U.S. Securities and Exchange Commission (SEC) registered company, has caused many small companies to look for an alternative.

AIM makes it easier and less expensive for companies to make an IPO, comply with regulatory requirements and make acquisitions in the future, all of which makes the cost of capital cheaper. The AIM provides an alternative path to an IPO for U.S. based companies, but there are risks and possible hidden costs. All options should be carefully researched.

Rehab for Oil Addicts

The push towards alternative energy will intensify as concerns about peak oil supply, national security and high fuel prices grow. And while there is no quick "12 step program" to break America's addiction to fossil fuels, the government, small businesses, large corporations, VC firms and Wall Street are truly beginning to work together towards that common goal.

The next edition of *Phase III Commercialization* will cover the typical barriers small companies face when incorporating advanced technology into alternative energy projects and provide ideas on how to overcome them.

It's in our vital interest to diversify America's energy supply—the way forward is through technology.

What's It Worth?

Basic Valuation Approaches for Technology Companies

by Terry M. McMahon

A question that weighs heavy for many small companies is how to determine the value of their company and/or technology. Looking into the subject of valuation, there are several approaches that can provide small businesses a framework to use when deciding on an appropriate valuation method for their particular situation. This article establishes a perspective on the topic, to help small businesses sort through the issues to consider when valuing an asset or negotiating with a potential buyer.

There are three basic approaches for valuation:

1) The Market Approach: uses comparables for like-type transactions based on actual market data.
2) The Income Approach: uses discounted cash flow techniques to calculate the intrinsic value.
3) The Asset Approach: uses the adjusted book value or liquidation value.

Within each of these approaches there can be various refinements to the valuation.

Market approach

A good example of the Market Approach is the process used to purchase a house. Houses are a commodity item, meaning there are lots of transactions that take place for similar or comparable types of property. When an appraiser is asked to value a home, the approach generally used is to look up the selling price of similar properties sold in the area over the past 12 months to establish a price range and average selling price. They then price the property being appraised at an amount that is close to the average selling point.

This approach can also apply to businesses that can be viewed as a commodity item—particularly in the retail area. A good example of this would be a convenience store. These are found everywhere and, like houses, many selling transactions of similar types occur during the course of a year. With enough similar transactions in a 12 month period, it is possible to obtain a baseline of selling prices and earnings to reasonably assess the value of the business.

The issue that then needs to be addressed is how to compensate for different sales volumes or earnings. Again, the preferred approach is to use comparables. In addition to the business sales price, an appraiser would look at various ratios associated with the companies sold. The appraiser would then compute a range of ratios as well as an average ratio. Common-type ratios that are examined are selling price to net earnings, selling price to net sales, selling price to book value and market value to book value (book value being the net asset value of a company, calculated by total assets minus intangible assets and liabilities). Companies with an actively traded stock would want to at least look at the market value/book value, as market value is determined by multiplying the stock price by the number of outstanding shares.

Of course, with technology companies, the short-coming of this approach is the difficulty in finding truly comparable companies. The selection of comparable companies is often considered to be as much an art as it is a science. Often, there are large swings in the ratios between individual companies. There is also a danger that mature companies will be compared with emerging companies. Since the market approach generally uses the most recent year financial results as the basis of valuation, it doesn't distinguish between companies that have sharply different growth rates. For these reasons, it generally is not the best method of valuation for an early-stage technology company.

Table 1: Market Approach: Valuation-Comparable ratio analysis

Recent comparable transactions

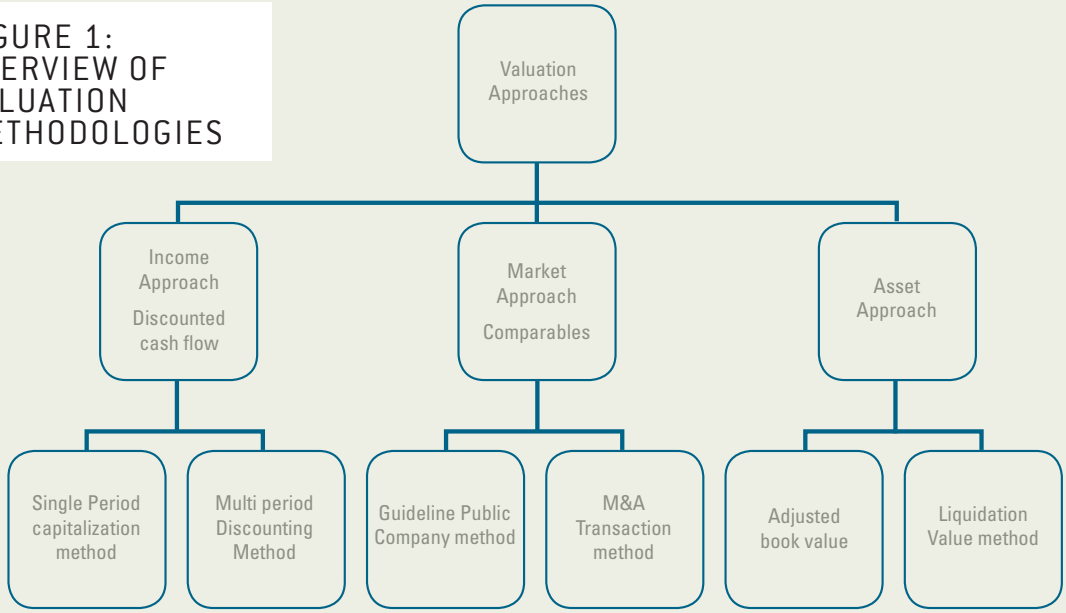
Company	X	Y	Z	AVG	Company X	Implied value
Price/Earnings	7	5.2	6.3	6.2	2,000,000 (earnings)	12,400,000
Market Value/ Book Value	3.8	2.8	1.6	2.7	5,000,000 (book value)	13,500,000

When technology companies talk with venture capitalists or business angels in the seed stage or later rounds of the financing stage, it is often common for these investors to use comparables and apply them to a pro forma sales and earnings forecast to determine the percentage of ownership needed to yield the required return.

The Income Approach

The income approach relies on the method of multi-period discounting of free cash flow to calculate the intrinsic value of a company. When using this method, pro forma sales and earnings forecasts for the business are very important as they be-

FIGURE 1:
OVERVIEW OF
VALUATION
METHODOLOGIES



The discounted cash-flow valuation models are better suited for high-growth situations and most suitable for high-tech firms.

come the basis of valuation. This approach can handle multiple growth rates as well as address risk. It can also handle different perspectives and the valuation of alternatives.

Key perspectives to consider and evaluate when selling or acquiring a business are the view point of the seller and the viewpoint of an acquirer, because they are important in negotiating the valuation of the company.

If the acquirer is another company, the acquiring company will develop a forecast scenario of the company being acquired, for revenue and earnings as if it would remain a standalone company. This is the value that would then be offered to the company being acquired.

The acquiring company will then identify the synergies, which is often the reason why they are interested in the company to begin with. Synergies have a value and can come in the form of sales growth (the acquiring company can do more with the technology than the acquired company can do by itself), cost savings (eliminating duplication of resources or leveraging better purchasing power) and financial synergy (lower cost of capital, taxes and/or debt capacity).

There is a natural tension between a buyer and a seller. The seller wants to receive from the buyer what he feels it is worth, including all of the synergies, and the buyer wants to pay for what the business or technology would be worth if it continued as a standalone business.

The company being acquired needs to make its own assessment of its baseline value and synergies. The key to understanding synergies is knowing how important the acquired company's product/technology is in obtaining these synergies. If no alternatives exist and the company to be acquired has the technology or distribution channel that is the basis for most of the synergies, then they are in a stronger position to negotiate a value that takes into account a portion of the synergies. The result would thereby increase the valuation above the baseline value. If the acquired company only plays a small part in realizing the synergies, then they have a weaker negotiating position.

When a company can be purchased at a price less than the full valuation of the combined baseline and synergies, it has created shareholder value for the acquiring company. The discounted cash-flow valuation models are better suited for high-growth situations and most suitable for high-tech firms.

Asset Approach

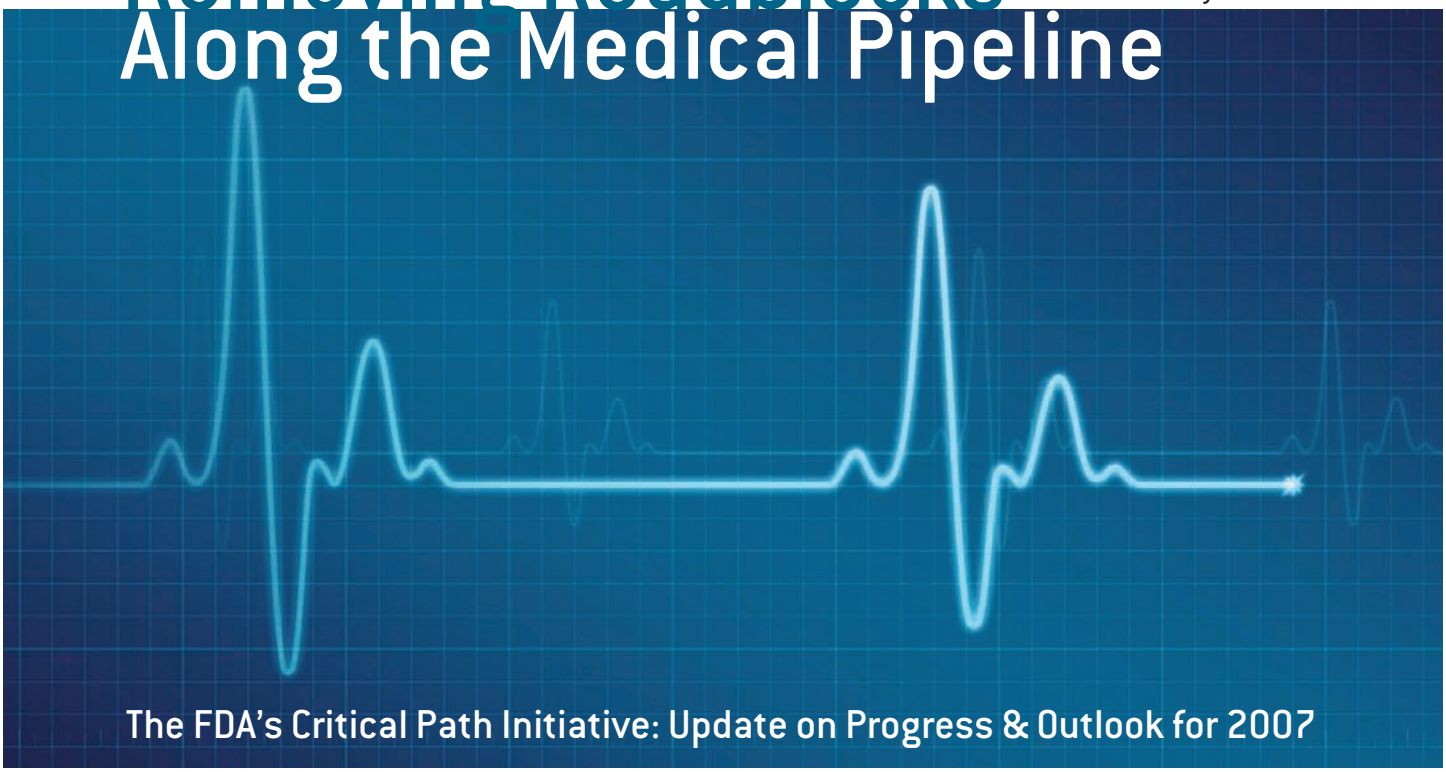
The asset approach is often used when the selling company has low or negative earnings, but the company owns a significant amount of tangible assets. A company in this situation would create little value from its operations, so an income valuation approach, based on positive cash-flow, would not yield meaningful results. An example of this type of company might be a railroad company or airline, which is operating at a loss but owns much land and equipment. In this model it is important to obtain an accurate appraisal of assets that could be sold. The company would be valued at the liquidation value of the assets. This is not an approach that is suitable for technology companies.

Figure 1 above recaps the valuation approaches and highlights some variations for each approach.

This should give small companies a better perspective on the various valuation approaches and the knowledge of when they are best applied. As has been said, there are many options to consider and much research to be done. For a technology company looking to be acquired or to sell a product line, the income approach is generally the most appropriate. It would still be wise to compare this intrinsic value approach with market comparables, just to measure the gap.

Removing Roadblocks Along the Medical Pipeline

by Carol B. VanBuren



The FDA's Critical Path Initiative: Update on Progress & Outlook for 2007

Since its 2004 inception with the publication of its "Innovation or Stagnation" report, the Food & Drug Administration's (FDA) Critical Path Initiative (CPI) has been focused on redesigning the process for taking new drugs and medical devices to market. Coined as the "medical pipeline problem," the main issue facing CPI was that the pace of pharmaceutical R&D spending had simply outstripped the ability of industry to continue to generate new medicines, particularly as many established blockbuster drugs have come off patent.

Among the issues caused by the medical pipeline problem are abysmally high failure rates for new medicines and new medical devices. New compounds going into Phase I clinical trial today have a mere eight percent chance of reaching the market successfully, down from 14 percent just 15 years ago. Alarmingly, the Phase III clinical trial failure rate is 50 percent versus 20 percent a decade ago.

To guide the new process for taking new drugs and devices to market, the CPI uses the three dimensions of safety, efficacy and manufacturing quality. Combined, these are intended to drive innovation costs lower and speed the availability of new medical treatment options that are safer, of higher quality and greater clinical efficacy.

Ultimately, CPI offers the promise of personalized medicine—an approach to tailoring preventative measures or medical therapies to an individual's specific genotype, thus maximizing the ROI of each health care dollar and saving more lives. While no one is discounting that there is a long road ahead, an impressive amount of progress has been realized since CPI's inception.

> **The pace of pharmaceutical R&D spending had simply outstripped the ability of industry to continue to generate new medicines, particularly as many established blockbuster drugs have come off patent.**

It is important to note that changes in an industry such as this often gives rise to new markets and new opportunities for small businesses. The FDA's CPI shows every sign of doing just that. The remainder of this article provides information on recent progress and some key challenges ahead.

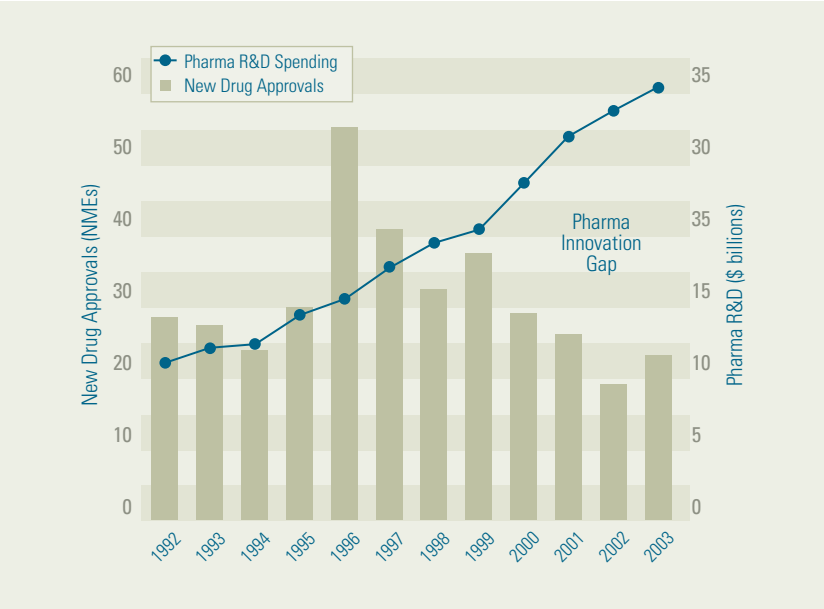
Gaining Momentum in 2006

Collaboration has been pivotal to CPI's progress. Leading the charge has been the Critical Path Institute (C-Path), an independent non-profit institute founded in 2005, that serves as a "trusted third party" enabling scientists from the FDA, academia and industry to work together for the public good.

With over $10M in both private and public seed funding, a key focus of the C-Path has been in leading collaborative biomarker initiatives. This has led to public-private partnerships including the Biomarkers Consortium, Predictive Safety Testing Consortium, Cardiovascular Drug Safety and Biomarker Research Program, and the Oncology Biomarkers Quality Initiative.

Other CPI activities last year included the FDA's publication of the *Opportunities List* in March followed by the *Opportunities Report* in October (www.fda.gov/oc/initiatives/criticalpath/reports/opp-report.pdf). The *Opportunities Report* mapped the 76 opportunity areas into six priority topics:

- Better Evaluation Tools—Biomarkers and Disease Models
- Streamlining Clinical Trials
- Harnessing Bioinformatics
- Moving Manufacturing into the 21st Century
- Products to Address Urgent Public Health Needs
- At-Risk Populations



Since 1999 the actual number of new drug approvals has been inversely proportional to the R&D spent. On average, it takes 12–15 years and about $1 billion to develop each new drug entity (NDE) and an additional $1 billion to take it to market.

The lead priority topic, Better Evaluation Tools, included many of the biomarker opportunities which translated to a number of 2006 initiatives. Rated as the second highest priority, Streamlining Clinical Trial Design has several initiatives focused on standardization and harmonization efforts, such as the Clinical Data Harmonization Initiative and the Clinical Data Integrated Standards Consortium. The area of Adaptive Trial Design continues to evolve, with efforts including the global perspective of the World Health Organization.

In parallel activity, the Center for Medical Progress at the Manhattan Institute convened 25 experts from industry, government and the scientific community in a Task Force on the 21st Century FDA. In its June 2006 white paper, "Prescription for Progress: The Critical Path to Drug Development," written by Robert Goldberg, Ph.D., Co-Founder of the Center for Medicine in the Public Interest and Peter Pitts, Director of the Center for Medicine in the Public Interest, the group came to many of the same conclusions as the CPI—including the notion that collaboration between the FDA, researchers and pharmaceutical companies can lead to, among other things, an improvement in clinical trials by creating one standard for collecting and using data from electronic medical records.

Key to the Critical Path are the three dimensions of:

Safety: how to predict and assess the risks of a potential product?

Medical Utility: how to predict and demonstrate that a potential product will have a medical benefit?

Industrialization: how to manufacture a product at a commercial scale with consistently good quality?

Picking Up Speed in 2007

Evident in 2007 is the redefinition, or repurposing, of the Critical Path Initiative to the "Critical Path to Personalized Medicine." Hints of this were underway in the FDA's 2006 year-end budget proposal, as well as in a lead chapter of the 21st Century Task Force's white paper, mentioned above. The FDA's 2007 budget now includes $5.94M allocated to the "Critical Path to Personalized Medicine Initiative." It is the first dedicated federal funding specific to CPI.

The budget places emphasis on biomarker development and improved clinical trial design in its funding mandates. Importantly, the language used in budget justification moves beyond the biomarkers, to the 'end-vision' of personalized medicine—"Without clinically proven biomarkers and innovative trial design, we cannot modernize medical product development and realize the promise of personalized medicine."

Other new initiatives within the FDA's 2007 CPI budget include a Medical Imaging Initiative, Improving Cardiac Drug Eluding Stent, the ECG Warehouse Project, and a draft guidance for industry on the safety and efficacy of biomarkers.

In complement to the direct FDA-funded activity, C-Path Funded Initiatives for 2007 include:

Fast Path 1: Accelerating drug development for rare disease
Safe Path 1: Toxicogenomic cross-validation consortium development
Safe Path 2: Community Pharmacy Safety Network—creation of an early alert surveillance system for the detection of toxicities post release

Manufacturing is on the Map

While much of CPI's work has focused on the role of new science, more recent dialog has begun to engage the manufacturing sector in its role in modernizing the drug and medical device production processes.

In January, Dr. Janet Woodcock, M.D., Deputy Director and Chief Medical Officer of the FDA, began her keynote to a meeting of the International Foundation of Process Analytical Chemistry (IFPAC) by suggesting that "the basic thesis behind FDA's CPI, which really resonates across manufacturing, is that investment and progress in basic medical science has far surpassed investment and progress in the medical development process." She went on to discuss how both the CPI and the FDA's new Process Analytical Technology (PAT) Initiative were important in shaping the necessary improvements of the overall drug development and manufacturing process.

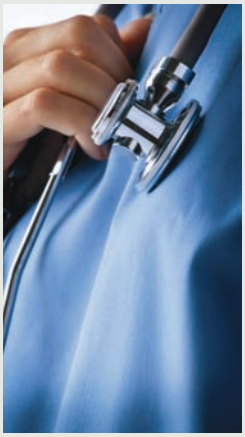
The Road Ahead

Ultimately, all roads seem to lead to personalized medicine. In Woodcock's February 2007 paper on the prospects for personalized medicine in drug development and drug therapy, the controversy over its exact definition—how, when and whether it will be brought about, and what means could be used to measure its attainment—are reviewed. She states that, "the concept of personalized medicine is a sort of shorthand used to represent the logical next steps in the progression of medical science toward greater mechanistic understanding of health, disease and treatment. This shorthand is attractive to the public community because it glosses over the very real scientific and implementation challenges."

The FDA's Critical Path Initiative is just one of the programs that federal agencies in the health care arena are using to promote innovation within their mandates. These agencies are working together and with others in the health care sector, in a variety of ways to create an environment that encourages the development of innovative technologies. The next edition of *Phase III Commercialization* will examine work being done by the National Institutes of Health to promote the transformation of the nation's medical research enterprise and to help move new discoveries into clinical testing.

Moving Medicine into the 21st Century

Several government agencies, both individually and in collaborative efforts, are playing roles in advancing health care for 21st century. Three of these agencies and a brief synopsis of their individual missions are listed in the table below.

	Agency Area of Focus	Making Changes for the 21st Century	Priorities Moving Forward	
FDA–Critical Path Initiative	The Food and Drug Administration (FDA) is charged with ensuring the safety and efficacy of pharmaceuticals, biological products, and medical devices and the safety of foods and cosmetics. They set the scientific standards for safety and efficacy that new medical products must meet and the standards for product manufacturing quality.	The Critical Path Initiative (http://www.fda.gov/oc/initiatives/criticalpath/) was launched in 2004 in an effort to stimulate and facilitate a national effort to modernize the scientific process through which a potential human drug, biological product, or medical device is transformed from a discovery or "proof of concept" into a medical product.	The three dimensions driving Critical Path priorities are: Assessing Safety—ensuring the product is adequately safe for each development stage, with early stage elimination of those with safety issues; Demonstrating Medical Utility—showing that the product is appropriately designed to effectively benefit people; Industrialization—taking the product from a prototype to a manufacturable, high-quality product.	
NIH–Roadmap	National Institutes of Health (NIH) is the Federal focal point for health research. Composed of 27 Institutes and Centers, the NIH provides leadership and financial support to researchers in every state and throughout the world. The agency leads the way toward important medical discoveries, investigating ways to prevent disease as well as the causes, treatments, and even cures.	The NIH Roadmap initiative (http://nihroadmap.nih.gov/) aims to transform the nation's medical research enterprise and help move new discoveries into clinical testing. The Roadmap provides a framework for the priorities NIH must address to optimize its entire research portfolio, laying out a vision of a more efficient and productive system of medical research.	Priorities are grouped into three areas: New Pathways to Discovery—addresses the need to better understand of the complexity of biological systems; Research Teams of the Future—explores new organizational models for team science; and Re-engineering the Clinical Research Enterprise—promotes integration of clinical research networks, the development of technologies for assessing clinical outcomes and improved regulatory processes.	
CMS–Council on Innovative Tech.	The Centers for Medicare & Medicaid Services (CMS) administers the Medicare and Medicaid programs, providing healthcare to about one in every four Americans. CMS (http://www.cms.hhs.gov/) evaluates Medicare coverage for new technology based on whether the item or service is reasonable and necessary for the diagnosis or treatment of illness or injury.	To help speed access to these new technologies, CMS is working on novel ways to better coordinate coverage, payment and coding decisions for a more timely reimbursement process. To address some of these needs, CMS established the Council on Technology and Innovation in 2004 to coordinate activities aimed at speeding beneficiaries' timely access to new medical technologies.	The Council is comprised of two groups. The Effective Innovation Working Group focuses on making agency processes more transparent and improving the efficiency of the coverage, coding and payment processes. The Better Evidence Working Group is to improve the data for medical decision making by implementing strategies for improving clinical evidence for decision-making relating to coverage, coding and payment.	

The Business of Angels

Removing the mystery of finding the right business angel

by Steve C. Orth

Business angels, also known as angel investors or just "angels," may be one of the most important, yet most misunderstood, pieces of the American job and wealth creation puzzle.

Entrepreneurs who start and grow new businesses are responsible for creating most new jobs in the U.S. and the business angel community is the largest source of early stage seed financing that many new businesses will need to succeed. For rapidly growing, high potential ventures, a business angel is a potential source of Phase III funding. But, what is an angel? How do you find one? What do they expect and how can an angel help you? In an interview with Dawnbreaker, Richard Sun, founder and owner of Sun & Co., an investment, management and advisory company based in Virginia, discusses the ins and outs of finding the right angel and creating a successful business partnership.

Often, angels have years of hands-on business experience and problem solving skills in areas young companies face, including raising money, managing growing enterprises and enabling growth of a thriving young business.

What is a business angel?

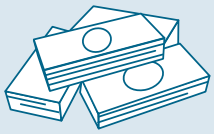
Business angels, also known as angel investors or just "angels," may be one of the most important, yet most misunderstood, pieces of the American job and wealth creation puzzle and can be the saving grace for many technology entrepreneurs. Essentially, a business angel is anybody with a big enough checkbook to invest in an early stage company and the desire to do so. With that in mind, it is important to note that not all angels are created equal and it will serve the entrepreneur well to know as much as possible about angels and their potential role(s) in business.

Most angels are equity investors and operate characteristically in the pre-venture capital arena. Some angels like to start out with companies at the earliest stage. Others don't get involved until there is some substance to the company. This usually means that several hundred thousand dollars have already been invested, a prototype exists and there may or may not be customers and revenue. Angels can even be wealthy individuals with no particular knowledge or affinity for the risk of the business. Those are usually the fellows to utilize only when they are being led by people who are serial

Funding Options for Small Companies

Venture Capital

Venture Capital – Once the product is proven market-ready, funding of upwards of $5M is provided by a venture capitalist or venture capital firm.



Angel Investment

Angel Investment – As the business grows, funding in the range of several hundred thousand dollars to $5 million is provided by an angel investor or group of angels.

Sweat Equity

Sweat Equity – As the business is starting out, funding in the range of $1 to several hundred thousand dollars is provided mostly by the small business owner, family and friends.

As they are frequently cashed out entrepreneurs with the capital and desire to help small businesses, angels bring intangible resources to small businesses that go way beyond capital.

entrepreneurs or venture capitalists (VC) working with earlier stage companies outside of the larger institutional VC business.

"When it comes right down to it," Sun says, "The most defining service an angel performs is to fill the gap between the several hundred thousand dollars financed by the entrepreneur's family, friends, personal credit and SBIR funding and the venture capital industry, which usually picks up somewhere north of $5M." But the business angel can provide not only much needed funding, but also invaluable advice and knowledge for helping a business to grow and thrive.

As they are frequently cashed out entrepreneurs with the capital and desire to help small businesses, angels bring intangible resources to small businesses that go way beyond capital. "Often, angels have years of hands-on business experience and problem solving skills in areas young companies face, including raising money, managing growing enterprises and enabling growth of a thriving young business. They also have one of the most valuable business tools—an established network of key contacts," says Sun.

Historically, angel investors have worked independently. Though over the past 5 to 10 years, groups of business angels have formed to operate as, in effect, investment clubs. Several trends have come out of this investment club approach, including a more standardized method of operation for angels as a whole, and the creation of the Angel Capital Association, an umbrella organization that is an excellent source of information and contacts for entrepreneurs and angels alike. "One of the angel groups I work with has about 60 people," says Sun. "That's a tremendous network of knowledge that can be tapped into. Typically, the group will only invest in an area where at least one of us has professional, hands-on experience and where at least one of us likes the investment enough to put their own money in. Often, there are at least two or three people that fit that mold for each investment and they take the leadership role in due diligence, structuring and post-investment monitoring."

Most angels are equity investors and operate characteristically in the pre-venture capital arena.

What an entrepreneur should look for

According to Sun, "An entrepreneur must be pleasantly, cautiously, professionally skeptical about a potential angel investor, in the same way that an angel investor will be cautiously enthusiastic, yet skeptical about the entrepreneur, his ideas and vision for the future." He suggests that entrepreneurs should explore the following when considering a potential angel investor:

- **Does the angel have experience in something similar to the entrepreneur's business?** That's a tremendous advantage. After the investment, you are going to have to work with the angel and all of your investors. Plans change and you need an investor that can go with the flow.

- **Has the investor gone through several cycles of angel investments?** It is important to have an angel who can work through the tough times, not someone who will break off the relationship if a business has hit a rough patch that is survivable.

- **Is this an investor who will take a pragmatic approach to participating, or not participating, in another round of financing?** In the second round, if the company hasn't hit its goals (maybe it is 10 cents on the dollar), it may be priced so that the existing investors either participate or get seriously diluted out. Some angels react very negatively to that, others just look at it as part of the business.

- **As an entrepreneur, is it possible to honestly accept the advice of this angel?** If the angel says "your business needs the following change to make it work, like maybe a new CEO," the entrepreneur needs to be able to recognize whether this is good advice and perhaps take it. While it may not be that dramatic, it may be just a change in marketing approach or a change in strategy, it is important for an entrepreneur to know that advice will be given and that he/she needs to decide what is appropriate for the situation.

- **Is there mutual respect and trust?** Personal compatibility is essential as well as professional. Obviously, if the entrepreneur is not able to take good advice from experienced people, he/she should, probably, for the sake of all involved, stay in the lab and license the technology.

As has been demonstrated, there are several factors to seriously consider when the time comes to finding the right angel. Check out the next issue of Phase III Commercialization to explore what a business angel looks for and how their deals are structured.

An entrepreneur must be pleasantly, cautiously, professionally skeptical about a potential angel investor, in the same way that an angel investor will be cautiously enthusiastic, yet skeptical about the entrepreneur, his ideas and vision for the future.

Visit these websites to find out more about angel investors and how to work with them:

www.angelcapitalassociation.org

www.angel-investor-news.com

www.inc.com/guides/finance/24011.html

A Window onto Manufacturing:
Title III of the Defense Production Act (DPA)

by Jenny C. Servo

Nearly 60 years ago, in answer to the domestic materials production needed for the building Cold War as well as the Korean War, the Defense Production Act (DPA) was signed into law. The purpose of the DPA Title III Program is to create, maintain, modernize, or expand the productive capacities of domestic sources for critical components, technology items, and industrial resources essential for national security and for which either no domestic capacity exists, it is insufficient to meet defense needs or it is in jeopardy of being lost (50 U.S.C. App. § 2061 et seq.). For example, in 2004 when the domestic supply of beryllium was in danger or being depleted due to closure of a primary metal production facility, Congress responded using Title III as a vehicle and by appropriating $10.8M for the design and construction of a new beryllium plant.

While the DPA and Title III have changed throughout the years, the main focus of ensuring the availability of resources needed for national security objectives has remained steadfast. This focus is stated in an amendment to the DPA in 1994 by President Clinton: "The United States must have an industrial and technology base capable of meeting national defense requirements and capable of contributing to the technological superiority of its defense equipment in peacetime and in times of national emergency. The domestic industrial and technological base is the foundation for national defense preparedness."

The Title III Program uses an Open-Ended Broad Agency Announcement (BAA) for project acquisition. In 2004 the Open-Ended BAA entitled Production Technology Partnerships was established which identifies 15 areas of interest (See right). Each DPA Title III Production Technology Partnership provides incentives to domestic manufacturers to develop, maintain, modernize or expand their critical production technologies and to develop and/or adopt best business and marketing practices to achieve joint manufacturing capacity, quality, affordability and economic viability requirements. The 15 areas of interest identified in the BAA are included below:

- High Performance Battery & Energy Storage Device Production
- High Performance Coatings Production
- Advanced Affordable Materials Production
- Wide Bandgap Material and Device Production
- Precision Navigation & Timing Device Production
- High Performance Quartz Oscillators Production
- High Temperature Superconducting (HTS) Wire Production
- Nanotechnology Materials and Device Production
- Advanced Electronic Device Production
- Advanced Mechanical Component and Device Production
- Biological and Chemical Sensor Production
- Advanced Structural Materials Production
- Micro-Electro-Mechanical Systems (MEMS) Production
- Electro-Optical Device Production
- Critical Infrastructure Protection and Production

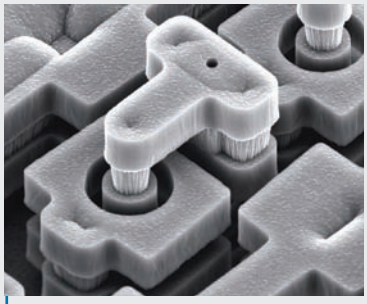
Department of Defense Management of Title III

Though available to all federal agencies, the Department of Defense is the primary user of Title III authority. The DoD Title III initiative has a mission to "create assured, affordable and commercially viable production capabilities and capacities for items essential for national defense." The program management of

Manufacturing Areas of Interest

Below are highlights of three of the 15 manufacturing areas of interest identified in the 2004 Open-Ended BAA.

Nanotechnology works on the scale of molecules and atoms to build nano-scale machines and computers, or ordinary size objects, using machines called assemblers or fabricators. Advanced nanotechnology will enable manufacturers to build a wide range of products that are impossible to make today.



Micro-Electro-Mechanical Systems (MEMS) is the integration of mechanical elements, sensors, actuators and electronics on a common silicon substrate through microfabrication technology. This technology makes it possible to have complete systems-on-a-chip allowing for the development of smart products.

High Performance Coatings are coatings made from ceramic material, from nanotechnology engineered materials, and many other substances and are used to protect numerous products in countless industries from high heat, corrosion and other destructive environments.

Title III is provided by the Director of Defense Research and Engineering (DDR&E), with the DDR&E serving as the DPA Fund Manager while the U.S. Air Force serves as the Executive Agent.

Situated at the Wright-Patterson AFB in Ohio, the Title III Program Office—a component of the Manufacturing Technology Division of the Air Force Research Laboratory—is responsible for identifying and evaluating prospective Title III projects, submitting projects for approval by the DDR&E, structuring approved projects and implementing contracts and other business actions relating to projects. The Program office also oversees active projects, provides for sale and use of materials acquired through Title III contracts and provides planning and programming support to DDR&E.

> Funding for Title III Initiatives is normally provided by the Services or Defense Agencies in the form of funding offsets for specific Title III efforts.

How Title III Works

Title III is an authority and not a source of funds. In other words, it is not a funded program with its own source of funds with which to initiate programs. According to Mark Buffler, "Funding for Title III Initiatives is normally provided by the Services or Defense Agencies in the form of funding offsets for specific Title III efforts." Funds appropriated for Title III are placed in the DPA Fund, established in the Treasury for the Defense Production Act, Title III purposes. The DPA funds manager is the Director of Defense Research and Engineering.

In order for a Title III project to be initiated, a number of steps need to be taken. First, the Under Secretary of Defense (Acquisition, Technology and Logistics) [USD (AT&L)] acting on behalf of the President must certify that the proposed Title III project meets the DPA statutory requirements. Next, Congress must be notified of any proposed Title III project via the Budget or a Budgetary amendment submitted to Congress for review and comment. Finally, a period of 60 days must be allowed after Congress has been notified before any Title III action can take place.

The statutory criteria for use of Title III funds include: the industrial resource or critical technology item is essential to national defense; private industry cannot reasonably be expected to provide the needed resources or technology in a timely manner without incentives; the determination that Title III is the most cost-effective, expedient, and most practical alternative for meeting the need; and that the combination of U.S. national defense (military) demand and foreseeable non-defense (commercial) demand is greater than the total domestic industrial capacity.

For more information on Title III, contact:

Air Force DPA Title III Program Manager
(937) 904-4382
atl.dpat3@osd.mil
http://www.acq.osd.mil/ott/dpatitle3/

About Us ...

Dawnbreaker, Inc.

Dawnbreaker specializes in providing commercialization assistance to small advanced technology firms and their investors. Since 1990, we have worked with over 2,200 firms that have received funding from the Small Business Innovation Research (SBIR) program, the Small Business Technology Transfer (STTR) program, the Advanced Technology Program (ATP), and others.

Dawnbreaker's depth is in understanding the intent, method and objectives of the SBIR and STTR programs. Having worked within large corporations and small businesses, our staff understands the perspective and financial imperatives of both and is uniquely well-prepared to assist companies in planning for and succeeding in transitioning to Phase III (Commercial phase).

The success of our services is reflected not only in our track record, which includes a 60 to 1 return on investment, but also in the percentage of companies that receive investment and/or increased sales within 12–18 month of a programs' culminating Opportunity Forum®. To date, over $1 billion has been secured by participating firms. For more information, visit our website at www.dawnbreaker.com.

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