

## Nanotechnology

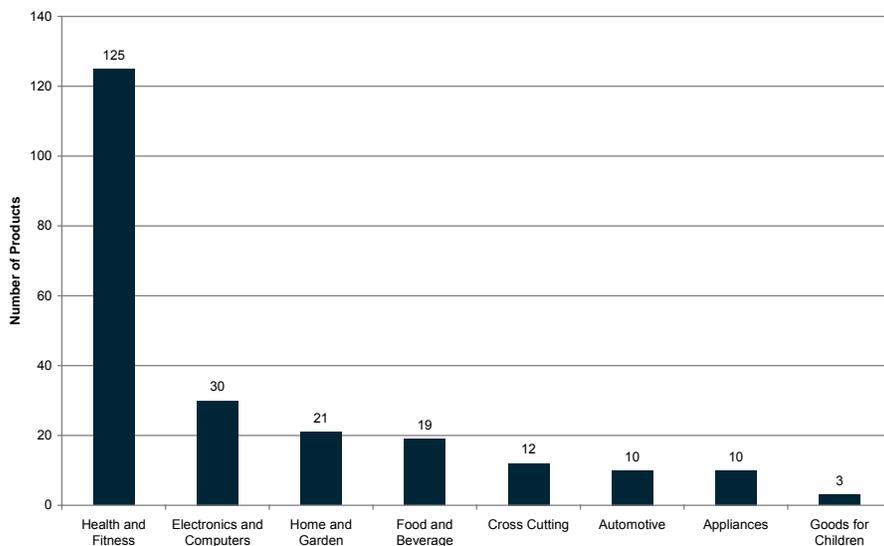
### Non-traditional Methods for Valuation of Nanotechnology Producers

October 2006

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Global Nanotechnology Consumer Product Inventory-March 2006



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## KEY ISSUES FOR STRATEGIC INVESTORS:

### Preparing for the Age of Nanotechnology

In our first report on nanotechnology issues in August 2005, we stated that quantum physics is shaping up to be the underlying science behind a significant portion of today's Gross National Product. Estimates of the global market for nanotechnology products stands at approximately \$9.4bn in 2005 and \$10.5bn in 2006 according to BCC Research. Growth projections vary but general consensus is in the range of \$25 billion in the next 4 to 5 years. This report focuses on issues that could limit those prospects if not addressed quickly.

### Hype is declining but products continue to enter the market

The nano "hype" may be dying down but investment and orders seem to be increasing. Most of this business appears to be in the chemicals sector where nano additives are actually one of the first and still profitable aspects of the market. While higher value added applications in electronics are right around the corner, profit is being realized primarily in personal care, sunscreens, polishing applications and antimicrobial products. Many drug and biomedical applications also are now on the market. Costs are coming...

### Go to page 8 for the full list of Key Issues for Strategic Investors

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# 1 The Innovest Nanotechnology Index and Research Group

National investments in nanotechnology worldwide increased over eightfold during the period from 1997 to 2005<sup>1</sup>. Experts agree that nanoscience will enable new technologies across a majority of industry sectors going forward.

Early testing reveals that some types of engineered nanoparticles may present risk in terms of human health and eco-toxicity.

Experts in the “nano” space are beginning to warn investors that this could result in perception risks that could affect markets for nanomaterials and end-products.

In light of this, Innovest has reviewed a set of 200 public companies and a set of 100 private companies listed on NanoInvestorNews.com for qualities that we feel will be appropriate in offsetting potential perception risk and in contributing to responsible nanotechnology development going forward. We have distilled this list down to an index of 15 companies, and a research group (watch list) of an additional 8 companies.

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<sup>1</sup> President's Council of Advisors on Science and Technology (PCAST). The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel. May 2005.

FIGURE 1 Assessment of Risk and Strategic Positioning for 15 Firms Selected for the Innovest Index.

		Product Strategy	Product Risk	Product Stewardship
Altair Nanotechnologies, Inc.	ALTI	Good Strategy/Practices	Moderate Risk/Average Practices	Product Risk
ApNano	IPO soon	Product Risk	Product Risk	Product Risk
BASF AG	BAS-FF	Product Risk	Product Risk	Product Risk
Biosante Pharmaceuticals, Inc.	BPA	Product Risk	Product Risk	Product Risk
FEI Company	FEIC	Product Risk	Product Risk	Product Risk
Flamel Technologies S.A.	FLML	Product Risk	Product Risk	Product Risk
General Electric Company	GE	Product Risk	Product Risk	Product Risk
Headwaters, Inc.	HW	Product Risk	Product Risk	Product Risk
JMAR Technologies, Inc.	JMAR	Product Risk	Product Risk	Product Risk
Lumera Corporation	LMRA	Product Risk	Product Risk	Product Risk
Nalco Holding Company	NLC	Product Risk	Product Risk	Product Risk
Plug Power, Inc.	PLUG	Product Risk	Product Risk	Product Risk
Spire Corporation	SPIR	Product Risk	Product Risk	Product Risk
Starpharma Group	SPL	Product Risk	Product Risk	Product Risk
Veeco Instruments, Inc.	VECO	Product Risk	Product Risk	Product Risk

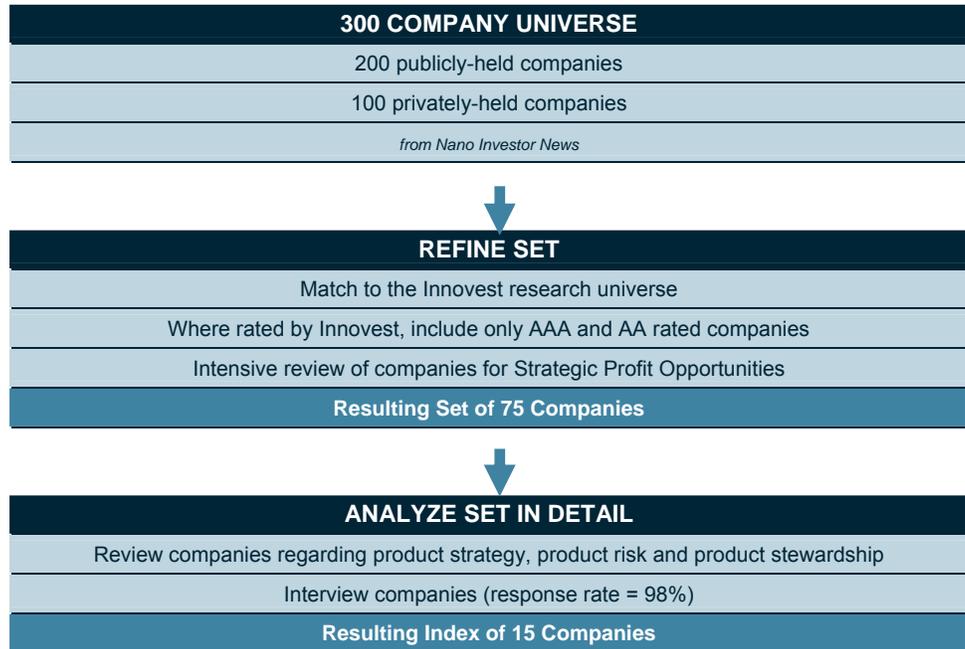
Good Strategy/Practices	Good Strategy/Practices
Moderate Risk/Average Practices	Moderate Risk/Average Practices
Product Risk	Product Risk
Not Applicable	Not Applicable

For monitoring purposes only. Source: Innovest

#### Research Group

MEMS USA	Nanosolar
NanoDynamics	Nanosys
Konarka	Ener1
Nanosight	NanoMix

To develop our analysis, we first started with a broad universe of 300 companies (200 public and 100 private) from NanoInvestorNews.com, ranging from a number of pure-play companies to large, diversified manufacturing and chemical companies (see Section 9 for a more detailed description of universe and the analytical process). We then matched this set to the Innovest research universe, primarily large-cap companies, and where rated, we included only those companies with high ratings, AAA or AA. We then subjected the highly-rated companies and the non-rated companies to an intensive search for firms offering **strategic profit opportunities in the fields of water technology, renewable energy resources/technology and innovations relevant to large scale medical needs**, resulting in an analytical set of 75 companies. Within this set, comparative analysis focused on product strategy, product risk, and product stewardship. The process involved product analysis, market review and company interviews, where we achieved a 98% response rate.



Rather than the typical Innovest methodology, which involves a best-in-class comparison *within* an industry sector (see [www.innovestgroup.com](http://www.innovestgroup.com) for our methodology), this report is an assessment of companies in different sectors and their early efforts to offset risk through product strategy, risk management and product stewardship. In each case, the company was evaluated based on a general understanding of risks and opportunities specific to that firm. Going forward, Innovest will conduct *comparative* analysis of strategy and approach within specific industry sectors such as chemicals, pharmaceuticals, personal care products, aerospace/defense, etc.

This index is for monitoring and is not available for investment. Detailed company profiles for each of the index constituents are in Section 7, starting on page 58.

In addition to the index, we have established a watch list of development stage companies (some are privately held) that also rate well on these parameters. Section 7 also includes shorter comments on these companies.

**In the following sections of this report:**

**Chapter 2** provides an overview of the investment landscape with particular emphasis on the toxicology issue and its relevance to our analysis.

**Chapter 3** discusses the market viability issue in light of the possibility that perception issues could play a role in healthy market development and in company performance. The focus is on products with large scale benefits relevant to the average person. These kinds of applications could help to offset any public perception risk issues that may arise.

**Chapter 4** provides a brief overview of early findings on some types of engineered nanoparticles. We survey recently completed work by well-known entities in the nano space and provide a few comments of our own for investors to understand before making investment decisions. Early developments on the regulatory front are discussed. This section also contains a description of the evolving regulatory climate.

**Chapter 5** provides an overview of company best practice and other value indicators.

**Fifteen company profiles are provided in Chapter 7** followed by brief comments on eight companies in our research group.

**Report appendices** cover characterization of the nanoparticles, detection methods, potential exposure routes, potential for environmental interaction, and an overview of the regulatory landscape in the US and Europe.

## Key Issues for Strategic Investors

### **Preparing for the Age of Nanotechnology**

In our first report on nanotechnology issues in August 2005, we stated that quantum physics is shaping up to be the underlying science behind a significant portion of today's Gross National Product. Estimates of the global market for nanotechnology products stands at approximately \$9.4bn in 2005 and \$10.5bn in 2006 according to BCC Research. Growth projections vary but general consensus is in the range of \$25 billion in the next 4 to 5 years. This report focuses on issues that could limit those prospects if not addressed quickly.

### **Hype is declining but products continue to enter the market**

The nano "hype" may be dying down but investment and orders seem to be increasing. Most of this business appears to be in the chemicals sector where nano additives are actually one of the first and still profitable aspects of the market. While higher value added applications in electronics are right around the corner, profit is being realized primarily in personal care, sunscreens, polishing applications and antimicrobial products. Many drug and biomedical applications also are now on the market. Costs are coming down now as well which could lead to even more nano applications in consumer products. As of March 8, 2006, the nanotechnology consumer products inventory contains 212 products or product lines

### **Due Diligence**

Some particles and processes may represent risk in certain applications and it is a matter of conducting sound due diligence. This issue is now given more attention relative to previous years. A full day was dedicated to the scientific and legal implications of this issue at the NanoBusiness Alliance conference held in New York this year. However risk remains. Since our last report we find that perception issues can be prompted even when the product in question does not actually contain nano particles as in the recent case of a recall in Germany of an industrial cleaning agent.

### **Drawing Parallels**

Industry's experience with synthetic chemicals and genetically modified organisms may provide historic lessons for investors interested in the potential impact that perception issues could have on the advancement of nanotechnology. Our concern is with healthy development of the market. Beyond traditional financial valuation, companies that have addressed this issue preemptively fare well in our rating.

### **2007 Will Be An Important Year**

We expect a number of EHS studies to be complete in that year. Moreover, officials in various markets tell us that they have set their sites on that timeframe for establishing a base level of regulation. Adequate funding to ascertain risks is necessary to **reduce uncertainty** and support the healthy development of nanotechnology markets. This report provides an update on recent hearings dealing with this issue.

### **The Right Technologies, Now**

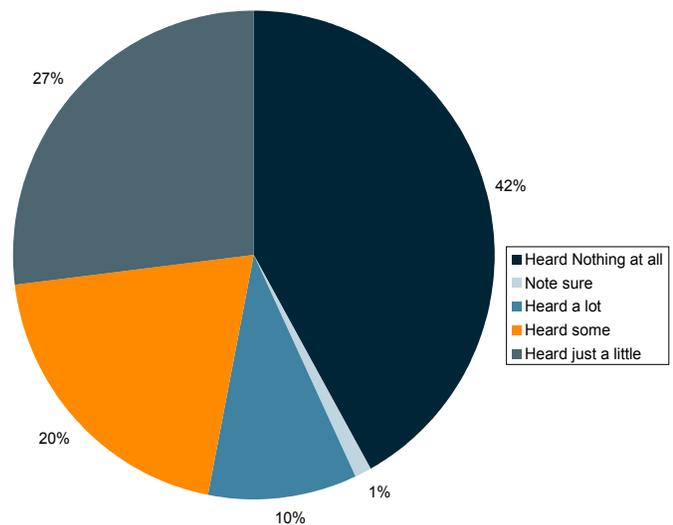
In August of last year, our report on the nexus between nanotechnology and cleantech was met with some skepticism. However we maintain that beneficial technology applications are more likely to offset public perception issues should any arise. Moreover it stands to reason that companies would want to focus R&D efforts on rapidly expanding markets. For example, the largest end-user market for nanotechnology in 2005 was environmental remediation at 33% of the total market (BCC Research).

Cleantech applications making news for some of our companies: Cleantech may be an investment buzzword but if that's what has the interest of investors then we are pleased that we were early on this trend. Our cleantech focus last year meant that we took prescient positions on companies that are turning out to have improved results this year. In particular, our interest in Altair Nanotechnology's Nanotitanate Lithium Ion battery seems to be getting some attention. ALTI's stock has seen a steady increase since last year and we anticipate that orders for its electric car battery drive train will be announced in the near future.

## 2 Overview: The Potential Materiality of Public Perception Risk for Nanotechnology

In our first report issued in August 2005, we raised the argument that while public awareness and understanding of potential nanotechnology risks was limited today, the situation could easily change as more products enter the market. Focus group studies are beginning to show increased awareness and limited trust in government to minimize nanotechnology risk. Whereas, similar studies in previous years have revealed very limited awareness, today the percentages are increasing.

Public Awareness of Nanotechnology



As such, our Nanotech Investment strategy takes into account:

- » **Traditional financial valuation when revenues are present**
- » **Product Information, Alliances and Deal Flow when its too early for DCF Valuation**
- » **Management's handling of this potential risk to the market**

## The Investment Landscape

### Counter-intuitive quantum properties

Nanoscience is the study of forces and matter at the scale of 1-100 nanometers. A nanometer is equivalent to approximately 1/80,000 the thickness of a human hair. At this scale, particles may adhere to the properties of quantum physics not present in classical physics. True nanotechnology makes use of these counter-intuitive properties specifically and may yield what we refer to in this report as engineered nanomaterials and particles. ***These attributes are part of the reason why nanotech has prompted the attention of regulators and the public. The safety of nanomaterials represents a significant uncertainty factor.*** At issue is the ability to identify and characterize the particle based on various factors such as size, chemical composition, and particle surface.

### Early findings

Chapter 4 and Appendices provide some brief details regarding what is currently known about certain types of nanoparticles under different scenarios. There is a body of technical literature to rely on but the best resource for the layperson is a report released by global insurance giant SwissRe which outlines risks related to inhalation exposure and describes experiments showing particles passing the blood-brain barrier<sup>2</sup>. Early analysis also demonstrates how certain kinds of particles (particularly those with functionalized surfaces) can exacerbate the mobility and bioaccumulative properties of toxins already present in the environment. Fullerenes, quantum dots, carbon nanotubes, nanowires and dendrimers are being studied at this time. While Rice University's Center for Biological and Environmental Nanotechnologies has been a central force in identifying these issues and devising technological solutions, it is now commonly recognized that product risk is a possibility that will require the financial community to conduct analysis on a case by case basis.

### Not everything that is nanoscale is nanotech

The best example that we have found for the layperson is the following: A nanoscale particle may make a better catalyst at the nanoscale simply because there is more surface area to create a reaction. True nanotechnology relates more to a scenario in which a material that is not a catalyst at the macroscale suddenly takes on catalytic properties at the nanoscale<sup>3</sup>. This analysis focuses on the risks and opportunities involved with the use of ***engineered nanoparticles, particularly those that are free as opposed to bound in materials.*** This differs from simple nanoparticles that are currently used to make surface coatings reflective and other similar applications.

### Products not Nanotechnology

Nanoscience will be applied across multiple disciplines and enable advances across a range of potential applications. As such, the investment focus is on

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<sup>2</sup> Hett, Annabelle. "Nanotechnology; Small Matter, Many Unknowns". Swiss Reinsurance Company. Zurich. 2004.

<sup>3</sup> Brookstein, Darrell. Nanotech Fortunes: Make Yours in the Boom. 2005.

products and not nanotechnology itself. As we stated last year, the bulk of nano profits remains in commodity type applications such as automotive coatings. This is relevant in terms of potential operational risks that could be associated with production involving nanoengineered particles.

### **Still Early**

The vast majority of companies who claim to be involved in nanoscience or nanotechnology development are still engaged in basic research. The universe of companies will eventually narrow to a few who claim to have product ready for the market. These will be bought by large cap firms or their technology will be licensed. Fewer still will remain who can survive as viable nano pureplay companies. To date the ratio of venture capital to government R&D spending is very low and the number of licensing agreements, IPOs and acquisitions is also low.

### **Near-term**

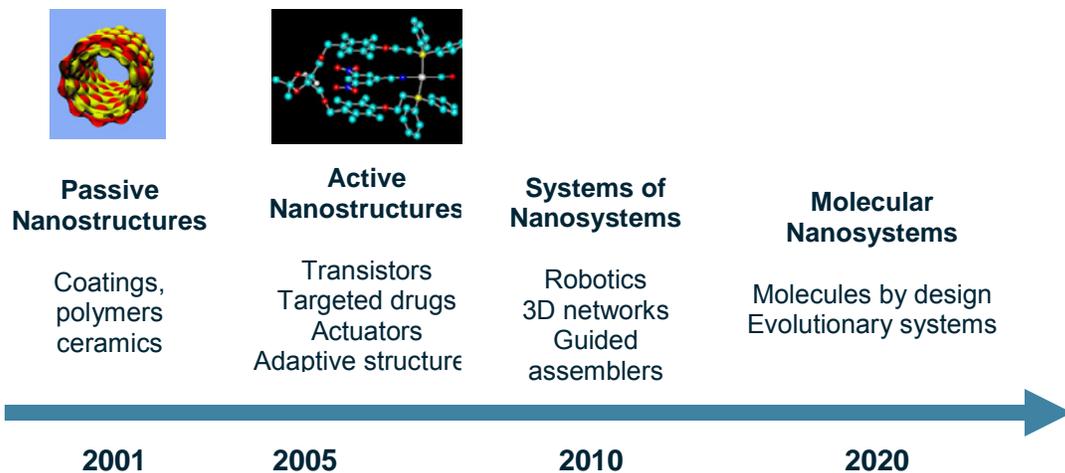
Lux Research predicts that 2007 will see more IPOs and consolidation between pureplays. In essence, while boom and bust cycles are likely to continue for companies grouped into nanotechnology portfolios, the overall level of venture and large cap investment seems to be improving and more products are entering the market daily.

### **Long-Term View**

Figure 1 shows a general timeline for various stages of nanotechnology development. Subsequent timelines provided in this report take into consideration the schedule for beneficial technology rollout, the regulatory outlook and a schedule for the release of new scientific findings that may be relevant to the perception risk issue for nanotechnology. The transition from passive to active is happening now. This and future transitions will change the risk picture both quantitatively and qualitatively. The convergence of nano and biotech may complicate risk assessment.

FIGURE 2 20 Year Timeline for Technological Development

## 20 Year Timeline for Nanotechnology



Source: Michael Roco<sup>4</sup>

### Nanomaterials in Products

The list of consumer applications containing nano particles of various forms continues to grow. As of March 8, 2006, a nanotechnology consumer products inventory launched by Woodrow Wilson Center for Scholars contains 212 products or product lines. This includes cleaning products, car wax, cosmetics, sunscreens and over the counter medical applications.

### Economies of Scale

Going from laboratory to commercial level production represents a primary challenge to the nanotech startup. The esoteric equipment required for large scale production is likely to significantly impact the cash burn ratio. Specifically, we are interested in firms that are partnering with equipment manufacturers to incorporate *life cycle* concerns into the production optimization strategy. Many firms provided information about closed-loop systems and other solutions.

### Cost and long lead time from technology to application

Given the extreme cost associated with research and development, there is little room in the budget for anything else. With uncertainty arising around the safety of nanoparticles, more companies may feel the need to submit their products for *independent testing* thereby representing an additional factor in the consideration of cost and time to commercialization. See Chapter 5, Product Stewardship, to learn about how firms are dealing with these issues.

<sup>4</sup> Adapted from Roco, M. National Science Foundation

### Large Corporations

Although estimates differ depending on the definition of nanotechnology, NanoInvestorNews.com shows that there are approximately 200 public companies involved in nanotechnology research and development about 77 of which are large corporations. Several of them have nanoscale particle products on the market or are marketing products enhanced with nanoscale particles. These products typically represent the most simplistic stage of development and are used for the enhancement of existing materials. Nanoparticles that impart reflective and strengthening properties for coatings or which make textiles stain resistant would be examples of this. This group includes large chemical manufacturers like Dow (DOW-NYSE) and DuPont (DD – NYSE). ***These firms have the resources and capacity to develop techniques to ultimately deliver nanoparticles at commercial production levels.***

### Pure Play

NanoInvestorNews.com lists about 700 private firms. Most of these firms are concentrating on the science and are not close to having a viable product in the near future. Some of them provide information for investors suggesting possible applications for their scientific pursuits. Note that while several companies may be working on the same technology, a firm selected for our index will have been tested for specific traits through our model.

### Academia

University research is an important part of the nanotechnology equation. Several of the venture capital firms and holding companies are working directly with research centers to deliver intellectual property straight to the market. This makes for a complicated risk profile. It is unclear where the accountability for safe nano development would lie in this situation. The role of universities with regard to the toxicology testing issue is examined in Chapter 5.

### Types of Investors

In surveying the ownership of the primarily nano-focused companies reviewed in our analytical set (See Chapter 9 for an explanation of the analytical set), we found wide variance in investment styles. The following table indicates the parts of this report that will be most relevant to each category respectively:

**FIGURE 3** Report Relevance to Various Investment Styles

VC/Private Equity	Market Viability of Products	Chapter 3
Momentum	Market Viability of Products;	Chapters 3, 6
Growth	Market Viability of Products	Chapters 3
Core Growth	Innovest Rating	Chapter 10
Core Value	Best practices reveal information	Chapter 4
Deep Value	Pure play companies in the Index	Chapter 2
Hedge Fund	Short positions; Timelines	Chapter 6
GARP	Market Viability of Products; Best Practices	Chapter 3, 4

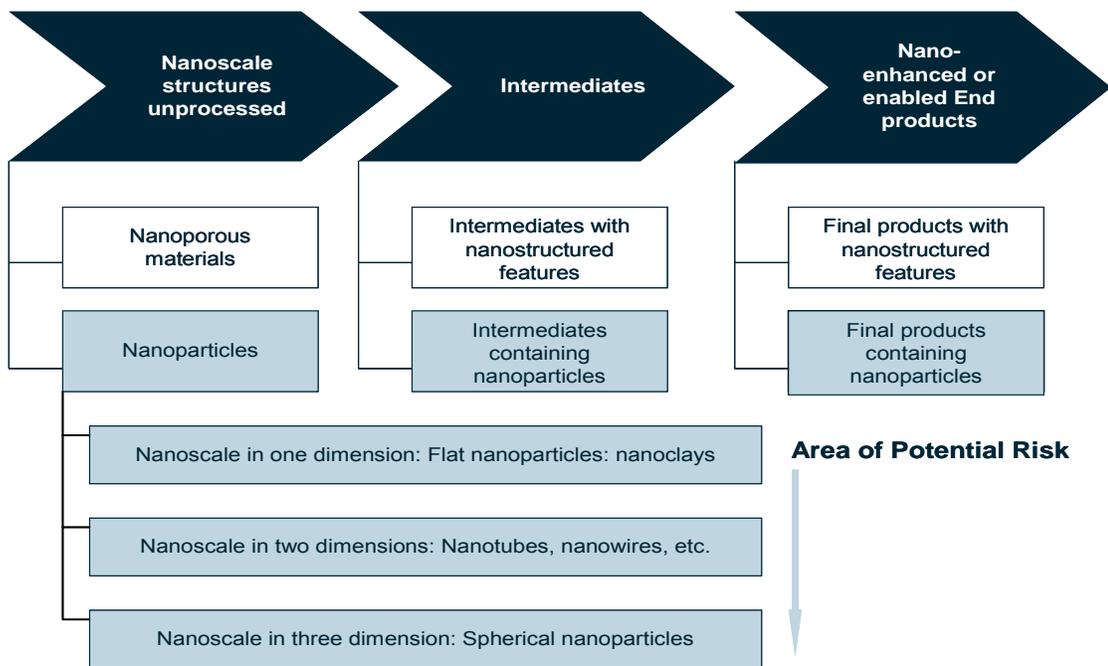
Source: Innovest

### Environmental Health and Safety Risk in the Value Chain

A recent report by the New York-based nanotechnology research firm Lux Research defines the basic landscape for risk with regard to present stage nano development. We use this to begin our evaluation of our analytical set. Figure 2 below provides a rough overview of the nanotech value chain and the most likely areas for environmental health and safety risks to manifest.

While we do not necessarily screen on the basis of a company's nanotechnology product, we take potential toxicology issues into consideration and monitor what programs and strategies are in place to minimize risk. **Comparative analysis reveals that some companies with similar risk profiles may vary with regard to awareness, approach and strategic development.**

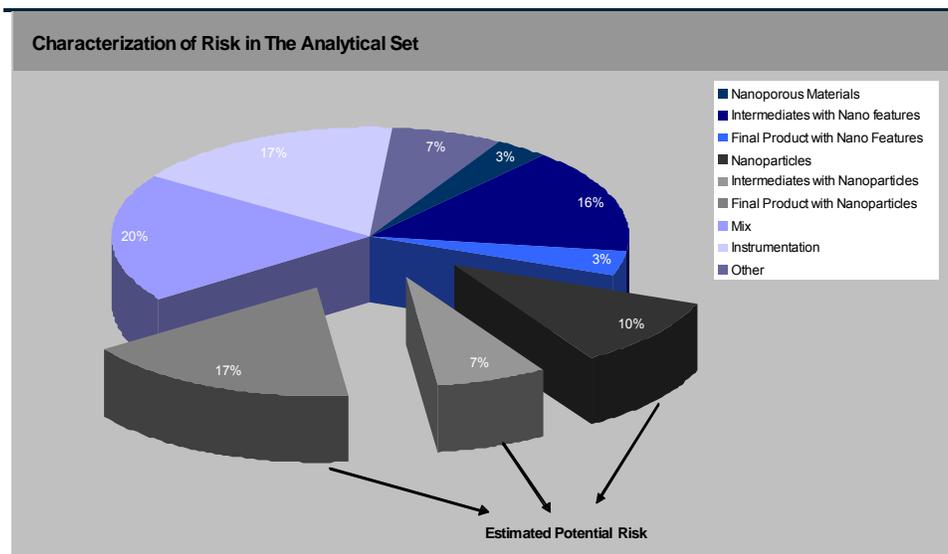
FIGURE 4 Overview of Potential Sources of Risk in the Value Chain



Source: Lux Research <sup>5</sup>

<sup>5</sup> Nordan, Matthew M. "A Prudent Approach to Nanotech Environmental, Health and Safety Risks." Lux Research. May 2005

**FIGURE 5** Characterization of Innovest Analytical Set of 75 companies According to Lux Definitions



Source: Innovest

### Wide Variation Between Firms

Our analytical set includes 75 publicly-traded companies ranging in size and business model from Nanophase Technologies (NANX-Nasdaq) to General Electric (GE-NYSE). The level of potential exposure to product risk varies accordingly. Several firms in the analytical set fall into the no-risk category. They produce nanoporous materials (gels, lab test surfaces, etc). Others are also low risk because they serve the nanotechnology research market. These firms supply labs with specialized equipment. In some cases, these firms are of interest because ***they will contribute to the ability to characterize and detect nanoparticles in the future – a key factor in reducing the uncertainty of using nanoparticles in production.***

### The Future of Risk Analysis

Microcap, pure play nanotechnology firms are not prevalent on most of the indexes being monitored today, but a host of privately held start-ups are waiting to be acquired and a few are positioning themselves for public offering. Interestingly, these firms appear to be cognizant of the risks and a number of them are conducting themselves in a manner that would be considered favorably in our analysis. Other firms are a cause for concern because in this early stage, ***poor handling of risk by any player could result in perception problems that would affect entire markets.***

### **Private Companies: More proactive but more risk**

We interviewed several private, development stage companies. Most of them are working with particles that would be noteworthy according to the diagram in Figure 2. While the technologies under development are interesting from an investment perspective, we keep in mind that they may also bear more risk. ***Our research revealed that investors should not assume that early or even late stage venture capital firms are conducting appropriate due diligence on the environmental, health and safety risks of the particles used or made by these firms.*** This report provides an outline of issues and a framework for analysis that could be used by investors who want to incorporate this into their analysis.

### **Where we are headed**

This year we take a broad view of risk, but in subsequent years of this analysis we will track nanotechnology development across many of the more than 80 sectors covered by Innovest. Food, pharmaceuticals and the three sub categories of the chemicals sector (Diversified, Commodity and Specialty) will likely be a starting point for this kind of benchmarking and analysis.

### **Beneficial alliances**

Innovest is connected with key resources in order to incorporate the latest in safety, legal and regulatory developments to the analysis. As we begin to scan through each of our sectors for nano-specific risk and opportunity, we employ these alliances to in a systematic way so that going forward; company profiles and thematic reports including nano-specific information will be available through the Innovest i-ratings client interface. Please see [www.innovestgroup.com](http://www.innovestgroup.com) for further information.

### **Four Scenarios**

There has yet to be any real indication of a surge in public awareness of nanotechnology. However, should this occur, experts interviewed for this review outlined four scenarios that could contribute to consumer backlash and product boycott:

FIGURE 6 Four Scenarios for Product Backlash

<b>Tipping the Scale</b>	
Mounting evidence of negative environmental and health impacts	Scant research to date reveals some early yellow light concerns
Continued flow of new nano-based products into the marketplace	Products are generally entering into the market at an estimated rate of 12-20 per month
Existing Frameworks prove inadequate in addressing risk and boosting public confidence	Summary of NGO responses to the EPA proposal to regulate nanomaterials through a voluntary pilot program Docket ID: OPPT-2004-0122. See Chapter 4.
<b>Nano Incident</b>	
Accidental release and exposure in a developing country	Scant research to date reveals some early yellow light concerns
Small business or research lab affected	Low risk but something to consider
Poorly handled emergency response followed by global press coverage	Low risk but something to consider
Low trust in industry undermines credibility of subsequent corporate interventions	A Santa Clara study recently asked respondents how much they trusted business leaders to minimize any risks potentially associated with nanotechnology; 60% said not much
<b>Popular Media</b>	
Release of film, embedded messages in advertisements offering a negative picture of nanotechnology	Michael Crichton's book Prey
<b>Market Reaction</b>	
Radicalized civil society actors raise concern	The recent T.H.O.N.G. protest in front of Eddie Bauer <a href="http://www.chicagohong.org">www.chicagohong.org</a>
Application of "precautionary principle"	Chapter 3 discusses developments in the UK and Europe
Actionable policy interventions	China establishes first nanotech standards in June
Protective regulatory spheres are established resulting in low public confidence in areas where protections are minimal.	If the UK and Europe apply any regulatory weight to the precautionary principle, this would effectively represent the greatest protections in any market. Already, chemicals regulation in Europe is moving to this. European chemicals regulation due to enter into effect in 2006 is a formal application of the precautionary principle. See Chapter 3 for further information on this issue.

Source: David Rejeski<sup>6</sup>

<sup>6</sup> Rejeski, David. Adapted from IOM talk 27, May 2004.

## Analytical Focus

- » General consensus and common sense holds that investors should focus their research on *revenues* and *products* with real applications, not pure science, in order to determine market viability for nano companies.
- » Management quality may be a key factor in determining a company's ability to generate revenues. Note that the Innovest model serves as a proxy for overall management quality. This may be useful even in the event that a development stage firm is purchased by a large cap company.
- » Part of the screening process involved the use of Innovest AAA and AA scores to identify companies that had already been screened for management quality. In addition, most of the firms analyzed are currently generating returns from other strategic business segments.
- » We favored these firms since this trait is likely to ensure that the company remains a viable investment while the nano product is still under development.

FIGURE 7 Innovest Report Focus

Investors are looking for <b>Revenues</b> and <b>Product Viability</b> , which is defined by Nanotech investment experts as:	This could be restated as:	With regard to Nanotech, Management Quality may be largely defined by how firms deal with:	This can be tested by evaluating how firms strategize for:
<b>Business Model Strategic Development</b>	<b>Management Quality</b>	<b>Perception Risk</b>	<b>Product Viability</b> <b>Product-Related Risk and Regulatory Developments</b> <b>Product Stewardship</b>

Source: Innovest

Given that the perception factor is deemed to represent a large portion of risk to nanotechnology producers, the companies that are first to offset risk through a comprehensive and proactive management strategy are not only more likely to minimize overall perception risk to the market but may generally be better investments over the long-term.

The following is a list of techniques used by venture capital firms and other investors to test for management quality in uncertain markets. We have modified them focusing on specific ways companies can address actual risks and public perception issues relevant to robust market development:

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...transparency is a key indicator

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### Signaling

Companies know more than investors at this stage of nano investment. Any information that a firm engaged in the research, development, manufacture and marketing of nanotechnology products can provide that differentiates itself from another is useful at this point. In the case of ApNano, the company's provision of data about its efforts to ensure that its product is safe went a long way in our estimation of management quality. In essence, **transparency** is a key indicator in this respect.

### Screening

The use of a filtering technique based on observable attributes that are associated with the desired unobservable characteristic. If revenues and product viability are the desired characteristic, then a cleantech product strategy is the observable attribute. The first cut of 300 stocks (public and private) was based on our assessment of **products targeted for the clean technology market** as the product viability component.

### Legitimacy

Creative action that provides symbolic significance of sophistication and quality. In conventional terms this may relate to the reputation of the venture capital firms providing funding and name recognition of the scientists/engineers involved in creating the product. As part of the prestige picture, our research focused specifically on a nano firm's ability to generate partnerships with universities and regulators in the interest of particle characterization and toxicology testing. In some cases companies may be able to take advantage of these opportunities at little or no cost. The benefit of **stakeholder coordination** for nanotechnology companies is considerable. In fact, many companies responded that by teaming up with regulators in order to conduct testing, there was minimal impact to the cash burn rate while simultaneously shedding light on the product liability question – a matter that could save the company money over the long-term.

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We identified several firms that indicated no awareness or appropriate strategy...

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### Socio-economic

External drivers that have perceived correlations with true but unobserved drivers of value. In our estimation, **regulation** provides a platform for observing differences between firms. Many of the firms that were interviewed demonstrated an early preparedness and awareness of developing voluntary and regulatory trends that would require them to adapt. These firms are growing with the regulatory picture firmly integrated with the innovation strategy. **Note: We identified several firms that did not seem prepared. In addition, some firms seem to be misinterpreting the rules for regulatory submission, representing possible risk for shareholders.**

## With Any New Technology, Revenues May Not Happen Right Away...

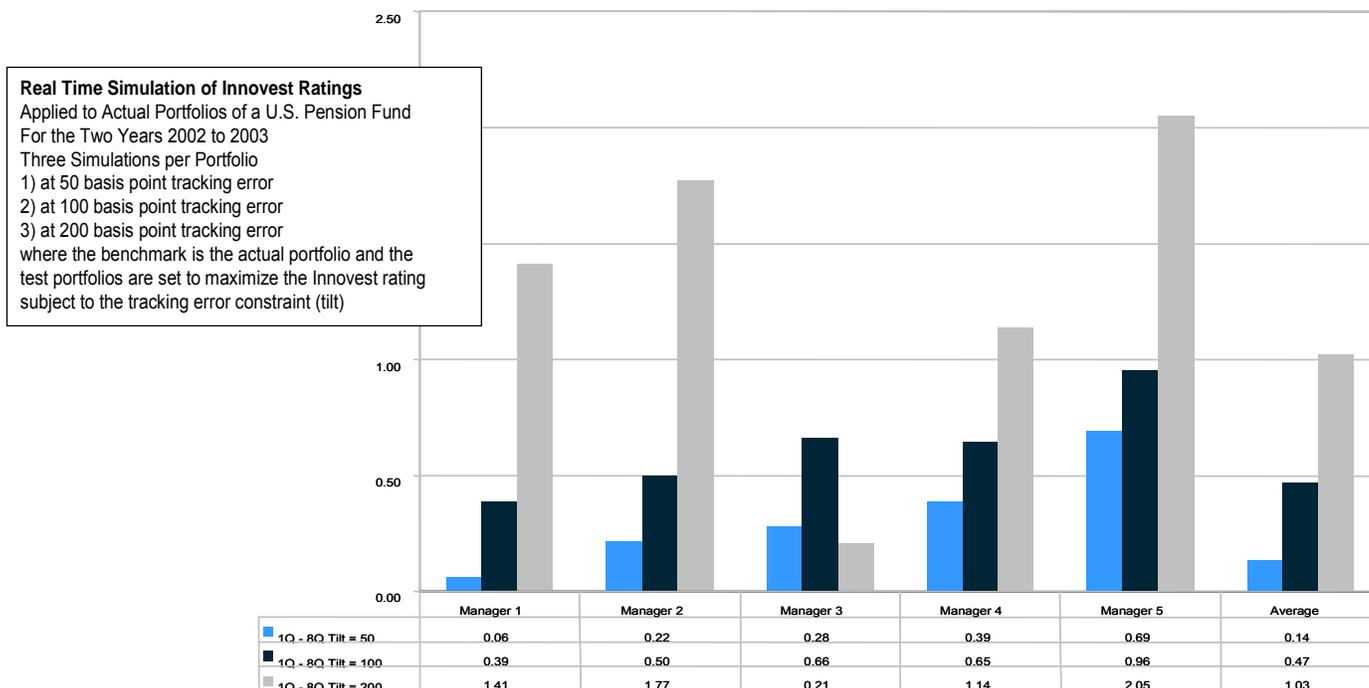
It may be relevant to consider the long-term value picture for a firm. Investors interested in nanotechnology, like Neil Gordon, President of the Canadian NanoBusiness Alliance<sup>7</sup>, find it important to consider business models and strategy when looking for companies with **long-term revenue generation potential**. The Innovest model is specifically designed to compare firms based on strategy and business model by evaluating more than 120 intangible value assets, which stand as a proxy for **overall management quality** – a key factor in the valuation of firms, particularly in uncertain markets.

The results are apparent. Across many sectors, we see that by looking at how companies deal with **macro drivers** and **plan for complex risks and opportunities** that take place over a period of one to three years, investors can understand more about a company's prospects today. For example, the chart below shows the results of an ongoing simulation wherein Innovest ratings were used to modify the actual portfolios of a variety of money managers (employed by a California public pension fund). The modified portfolios overweighted companies with high Innovest ratings and underweighted those with low ratings. The addition of this Innovest information added value ("alpha") to each of the portfolios. For more on this and other research and actual portfolios, please contact Hewson Baltzell (hbaltzell@innovestgroup.com).

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<sup>7</sup> Gordon, Neil. "Nanotech Sector Needs Study Business Model." Small Times. January 13, 2005. <http://www.smalltimes.com>

**FIGURE 8** Relative Performance of Innovest Enhanced Portfolios vs. Underlying Portfolios Over the Period 1/02 through 12/03



Source: Innovest

## Conclusion

Innovest has maintained since 1995 that the major portion of a company's value comes not from daily price fluctuations but from an overall picture of the company's long-term competitive prospects. Our methodology is specifically designed to test this aspect of corporate valuation through the assessment of forward looking rather than trailing indicators commonly relied upon by traditional valuation techniques.

More recently, Goldman Sachs has arrived at the same conclusion....

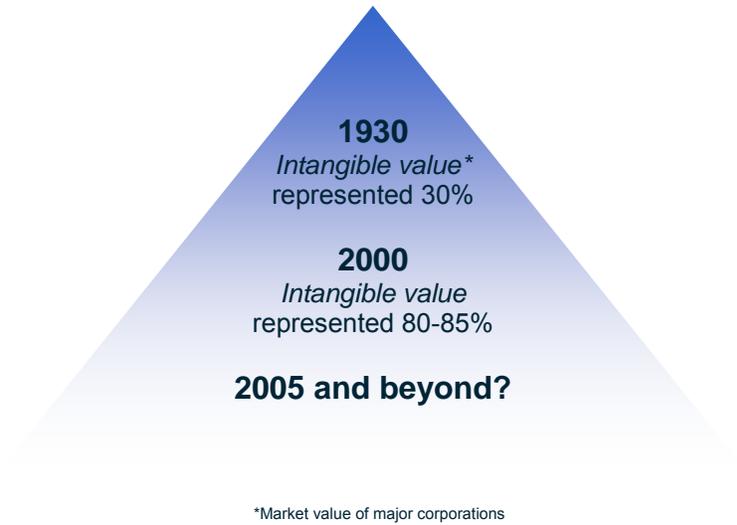
"...The bulk of the value (60%) of any company is determined by its long-run or sustainable returns, the next 20% by secular or cyclical change observed in the coming 12 months; and the remainder by longer term growth or other issues."<sup>8</sup>

<sup>8</sup> Goldman Sachs Energy Environmental and Social Report, February 24, 2005, p18

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**FIGURE 9** Growing Importance of Intangible Factors in the Valuation of Companies

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Source: Innovest

Our evaluation of strategy and business model focused on management's ability to deal with a variety of conventional and non-traditional factors. See Chapter 8 for a detailed explanation of our methodology for determining quality strategy and business model.

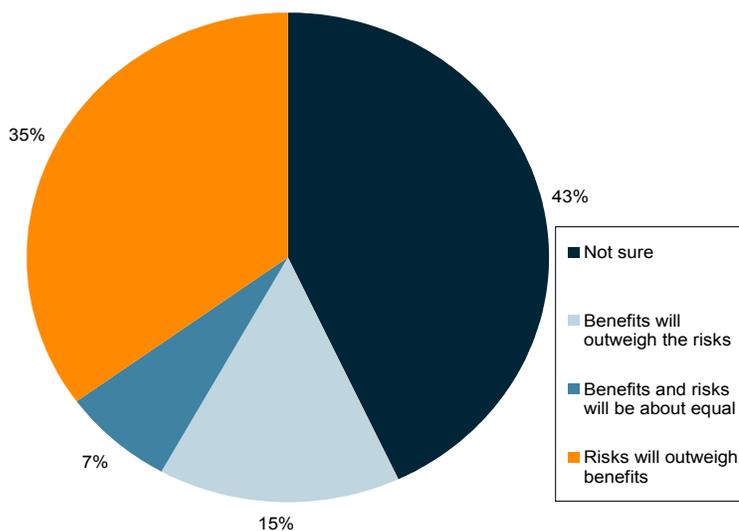
### 3 Perception Risk

## Perception Risk May Cause Delays in Lead Times and Diminished Demand

It is not difficult to identify many conventional barriers to market entry for nano-products (i.e. the challenge of devising commercial scale manufacturing capacity, long lead times, extreme expense of research and development). However, **perception risk** is considered to have the greatest capacity to impact both products and markets. In essence, the science may show little risk but if the public becomes nervous about the safety of nanotech, demand could be abated in certain markets such as personal care products, household construction materials, etc. The graph below shows the results of studies recently sponsored by the Woodrow Willson Center for Scholars Project on Emerging Nanotechnologies. Respondents were surveyed before being given information on nano risks and then after being given a very brief overview of the general science background.

FIGURE 10 Initial Impression of Risks and Benefits of Nanotechnology

Initial Impression of Risks and Benefits of Nanotechnology



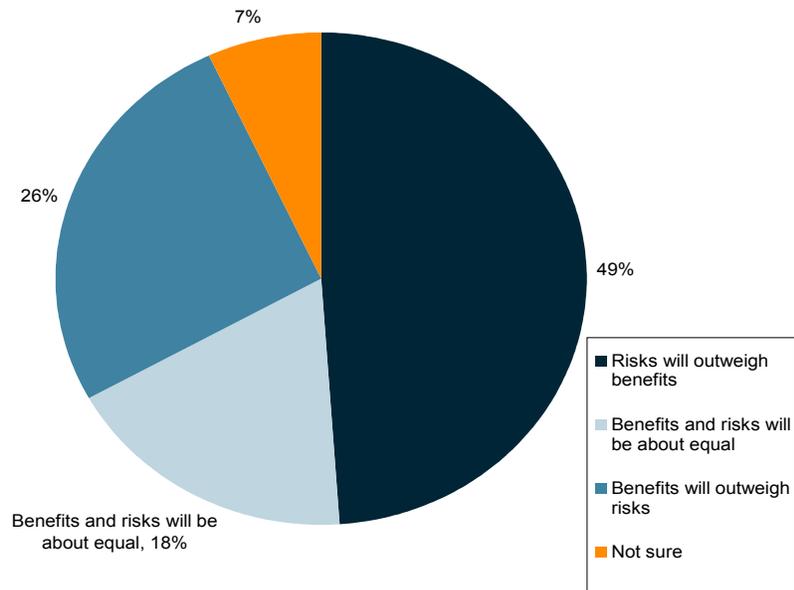
Source: "Public Awareness of Nanotechnology: What to Americans Know and Who Do they Trust?". 19 September 2006. Peter Hart Associates

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**FIGURE 11** Informed Impression of Risks and Benefits of Nanotechnology

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**Informed Impression of Risks and Benefits of Nanotechnology**



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Source: "Public Awareness of Nanotechnology: What to Americans Know and Who Do they Trust?". 19 September 2006. Peter Hart Associates

## PERCEPTION RISK IMPACT TO VARIOUS TYPES OF NANO FIRMS

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### **Diversified/Conglomerate**

All large capitalization diversified and end-user companies surveyed for the development of the index responded that they intended to apply nanoscience across all strategic business units. At least 10 of these firms have a significant portion of their market capitalization invested in “brand value”. Consistent with responses for the entire analytical set, these companies responded that they do not plan to specify that products are nano-enabled as part of the marketing strategy.

On one hand, the view may be that these large capitalization companies face very little risk in enhancing their products with nanotechnology. Any given activity represents only a fraction of the overall business. However, we posit that several of the diversified firms may face elevated perception risk. Civil society actors have proven to be very organized and motivated with respect to many of the various industries of interest. ***A diversified firm with 15 business units ranging from textiles to defense may face 15 different fronts for activism.***

We note that a year ago, only a few non-governmental organizations (Environmental Defense, Natural Resources Defense Council, ETC Group, and Greenpeace) had nanoscience on their radar ***Last month, 16 NGOs signed on to the comments that the Natural Resources Defense Council submitted to the United States Environmental Protection Agency on the EPA’s proposed voluntary program.***

### **Pure play**

Depending on the definition, approximately 17 of the companies in our analytical set are solely focused on nanotechnology. A significant number of firms in the set are sufficiently small to the extent that a nano “mishap” could have potentially material repercussions.

At a recent meeting of the Environmental Law Institute in Washington DC, several presentations proposed a scenario in which a small start-up has a production accident, which ultimately ends up exacerbating perception problems for large companies like Dow or DuPont. Innovest does not expect that this would be a problem mostly because of the significant expense associated with nanotechnology development. This expense would likely have a repressive effect on entrants with low operating standards. However, representatives of the American Chemistry Council responded that there was enough concern about this issue on the part of their members that the ACC is now trying to create a plan to work with start up nanotechnology firms to assist them with information and best practice.

***Perception is more likely to be a risk to pure-plays.*** Biotech is not a perfect analogy to what is happening with nanotechnology, however, there are lessons that can be extracted especially for certain nanotech sectors such as nano agriculture and nano-food applications. Investors in these sectors may have to exercise more precaution than those investing in semiconductor applications for example.

In June the United Kingdom failed in its efforts to convince the rest of Europe to lift the ban on genetically modified crops and food. The science, while in dispute, does not at this time appear to be sufficient to support the ban. ***Nevertheless, the mere perception that GM crops and food are a risk has resulted in a continuance.*** Ministers from the five countries (Austria, Luxembourg, Germany, France and Greece) simply did not accept that GM crops should be released, and the ban drew the backing of a sufficiently large majority of 25 member states to ensure that it remains in place<sup>9</sup>.

The EU ended a six-year moratorium on accepting applications for new genetically modified foods in May 2004, but efforts to bring about labeling rules are ongoing. Approximately 70% of the public is against GM foods and the “GM free” label has become a positive selling point<sup>10</sup>. This is further evidence that once public distrust has been initiated, it is very difficult to sell product even when trade pressures force governments to throw the doors wide open.

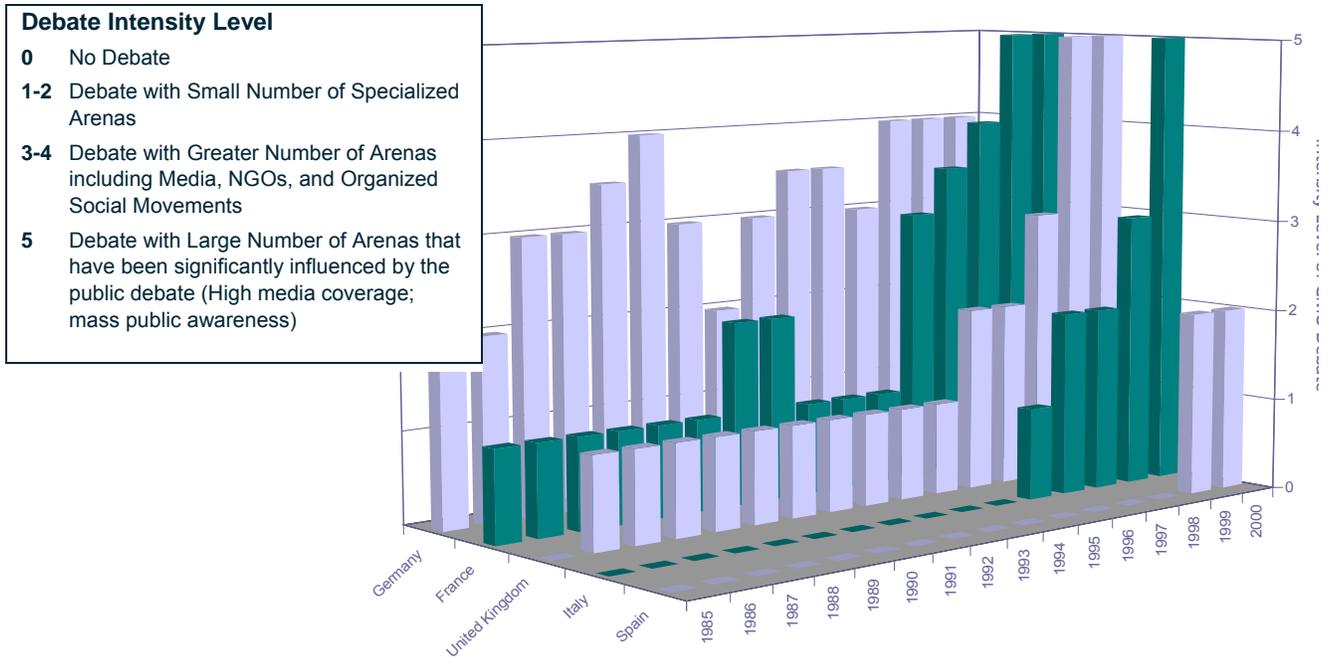
The following graph demonstrates the growth and evolution of public discourse on the issue of genetically modified organisms in Europe during the period 1996-2000.

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<sup>9</sup> Brown, Paul. “EU votes to continue ban on GM crops: Britain warns ministers of threat of trade war with US.” The Guardian. June 25, 2005.

<sup>10</sup> Brammer, Marc. “Risk to Investors With Regard to Genetic Engineering.” Innovest Strategic Value Advisors. 2004.

FIGURE 12 Intensity Level of GMO Debate in Five Selected European Countries



Source: PABE (2001) Public Perceptions of Agricultural Biotechnologies in Europe

## 4 Our Focus on Products

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“The Nanosys IPO was rejected for a very simple reason: Where’s the product? You’ve got a bunch of IP [intellectual property]... So what?”

—Tim Harper, President, Cientifica

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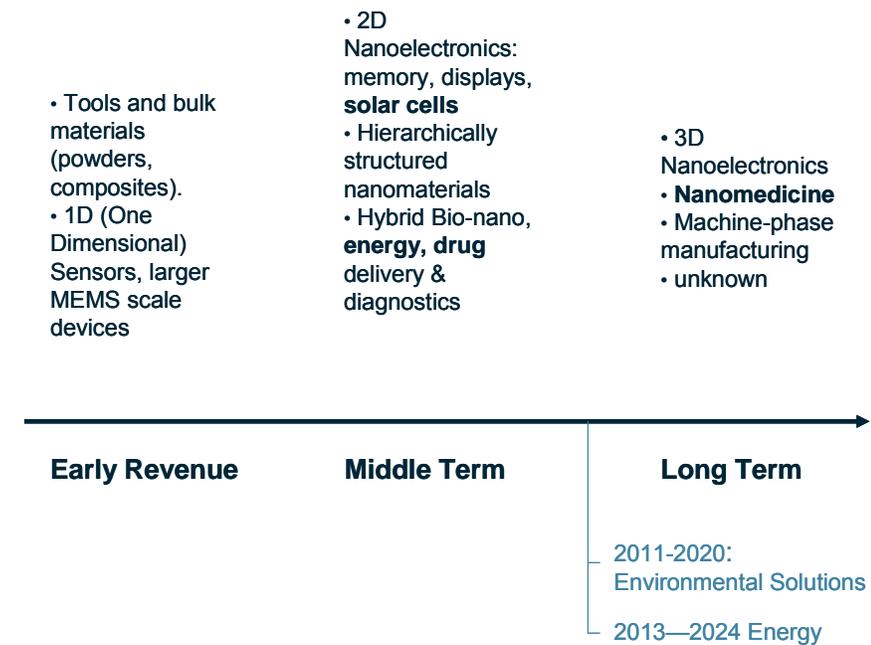
“Investors should try to distinguish between business plans with near-term commercial uses vs. long-term science projects...”

—David Aslin, Director, 3i Group

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FIGURE 13 Consensus timeline for commercialization of products

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Various sources: Darrell Brookstein<sup>11</sup>, Draper Fischer Jurvetson

<sup>11</sup> Brookstein, Darrell. Nanotech Fortunes: Make Yours in the Boom. 2005.

## Demonstrating the Benefits – A Key Aspect of a Viable Product Strategy

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**Question:** What are the biggest challenges for nanotechnology?

**Answer:** “The perception problem. Because people cannot understand nano, this technology is a little removed from the public domain... Companies and governments need to come together and make people aware of this technology...”

—Tim Harper, chief executive officer and founder of nano technology company Cientifica<sup>12</sup>

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### **Consumers and markets may be more willing to deal with risk if perceived benefits are clearly defined early**

Similar to biotechnology, the first applications of nanotechnology offer little in the way of obvious benefit to consumers. The Small Times database of over 500 commercially available products provides an interesting indication of where we currently stand in this regard. In summary, the majority of products are designed to enhance the properties of already existing materials making them stronger, lighter and more reflective. Others offer advantages for making industrial processes more efficient thereby providing direct benefit to business owners which are not necessarily an obvious benefit to the general public at this time. However, many companies we interviewed are targeting markets that we feel will help to offset any perception issues that might arise. How likely is this to be relevant to nanotech?

*Experts interviewed for this report felt that some of the same components that created a public backlash against biotechnology are already at work within nanotechnology<sup>13</sup>.*

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A study conducted by Santa Clara University demonstrates the public's prioritization for nanoscience<sup>1</sup>.

**57% of respondents want it to treat illnesses.**

**16% want it to clean up the environment.**

**Only 4% want it to produce enhanced products.**

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<sup>12</sup> Aparna Krishnakumar. 'Nano startups can take cues from IT'. The Rediff Interview/Tim Harper, CEO, Cientifica. July 04, 2005. <http://inhome.rediff.com/money/2005/jul/04inter.htm>

<sup>13</sup> "Much ado about almost nothing." The Economist March 18, 2004 print edition.

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Clearly, wrinkle-free pants are not high on the list of priorities.

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A growing body of literature suggests that nanotech companies need to be considering ways of demonstrating how the science will provide near-term opportunities for satisfying the wish list posted above. Clearly, wrinkle-free pants are not high on the list of priorities. Fortunately, many of the technologies that offer true benefit for the global poor in terms of energy use and storage, water quality and other relevant applications also happen to overlap with viable markets from an investment perspective. Escalating energy costs may make energy-related nano applications even more desirable in the future.

## INVESTMENT STRATEGY

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Interestingly, those technologies that offer true benefit may face lower perception risk have an improving investment outlook...

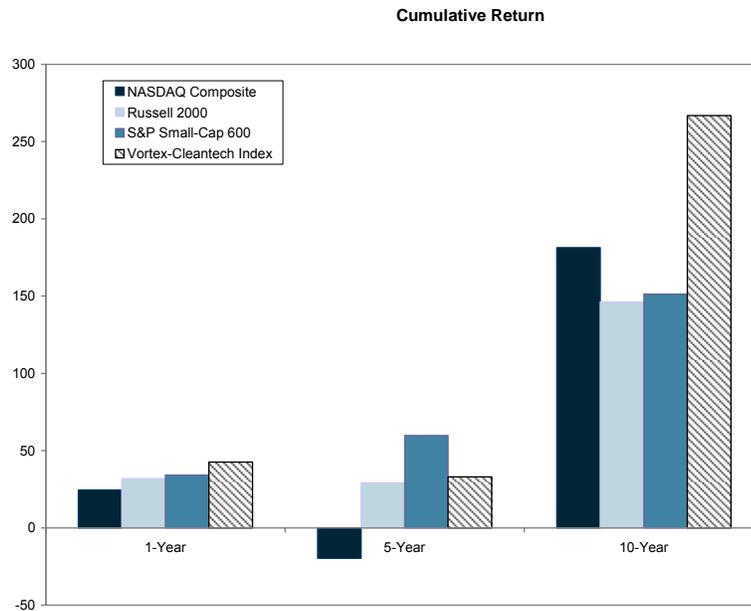
Innovest research is premised on the fact that large scale macro drivers such as carbon mitigation are creating a fundamental shift in economic need that is now relevant to the evaluation of publicly traded stocks. In our evaluation of over 2200 public companies across many indices we have noticed that this trend has led to a surge in cleantech strategy development and investment.

- » **Cleantech investment rose to a first-quarter record of \$335.9 million, which represents a 4.8 percent increase over the same a year-ago quarter and a 10.3 percent increase over 2003<sup>14</sup>.**
- » **The ten-year cumulative returns on the Vortex-Cleantech Index have beaten the following three indices.**

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<sup>14</sup> Cleantech Q1 Funds Grow 4.8% 3, August 2005. On the Internet:  
<http://www.redherring.com/Article.aspx?a=13030&hed=Cleantech+Q1+Funds+Grow+4.8%25>

**FIGURE 14** Vortex-Cleantech Index (VCI): One-, Five- and Ten-Year Returns vs. Market Indices



Source: Cleantech Venture Network LLC

### Macro Trends...

- » Increasing interest by major corporations in adopting clean technologies. General Electric is a recent example
- » Energy price volatility, carbon regulation in Europe
- » Advances in science and engineering that make certain clean tech applications more reliable and economically feasible
- » Local initiatives: green building standards, procurement strategies, tax subsidies etc.

### Institutional Investors...

- » The global solar market is growing by more than 30% annually with a current market of more than \$7 billion a year<sup>15</sup>.

<sup>15</sup> Carey, John; Aston, Adam, Hibbard, Justin and Grover, Ronald. "Alternate Power: A change is in the wind." Business Week. July 4, 2004 print edition.

- » This June, Goldman Sachs and Hudson United Bank entered into an agreement to oversee BP Solar's installation of 25 electric systems on Staples and Whole Foods Market stores.
- » In 2004, California State Treasurer Phil Angelides proposed the Green Wave Initiative; a four-pronged program for the state's public pension plans to support environmentally responsible investing. The proposal calls for the California Public Employees' Retirement System (CalPERS) and the California State Teachers' Retirement System (CalSTRS) to funnel \$1.5 billion into environmentally sound investments.
- » Shareholder interest has resulted in projects like the Carbon Disclosure Project. This year, the CDP attracted the support of 225 institutional investors globally, representing in excess of \$31 trillion in assets under management. This number increased by over 300% from 2003.

#### The implications of nanotechnology for cleantech development

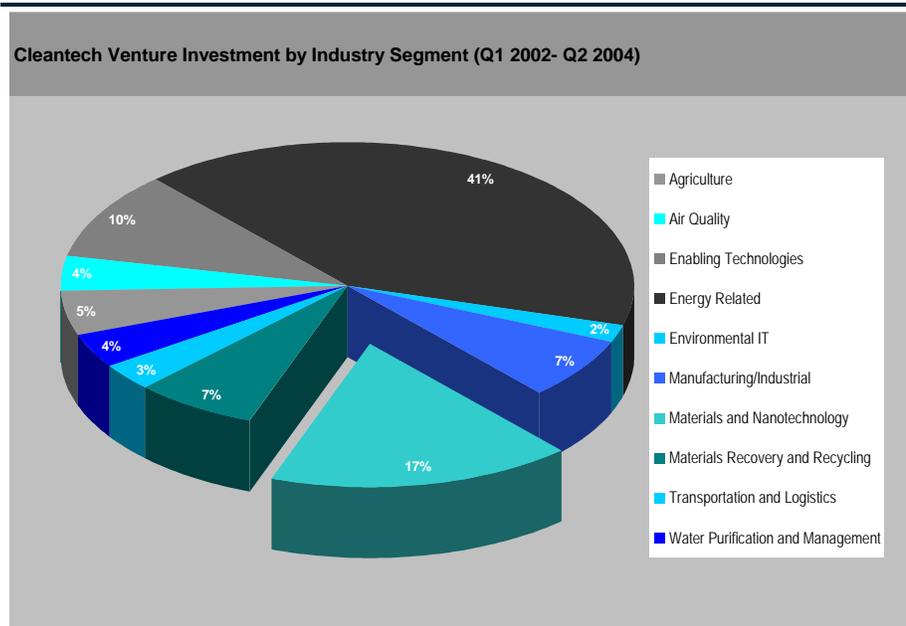
- » Advanced materials and *nanotechnology* investments increased in Q1 2005 to \$83.5 million from \$68.2 million in the same quarter a year ago<sup>16</sup>.
- » Energy, materials and *nanotechnology* accounted for more than two thirds of the capital flow into the cleantech industry during 1Q 2002- 2Q 2004<sup>17</sup>.

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<sup>16</sup> *Ibid.*

<sup>17</sup> LoGerfo, James. Co-editor Parker, Nicholas. Propper de Callejon, Diana. Cleantech Venture Investing: Patterns and Performance. March 2005. Clean Tech Venture.

FIGURE 15 Cleantech Venture Investment by Industry Segment (Q1 2002–Q2 2004)



Source: Cleantech Venture Network LLC<sup>18</sup>

## Strategic Profit Opportunity in the Analytical Set

For our index we looked for firms that not only offered a fully conceived and viable product strategy but one that involved a promising clean technology application.

### Market Need: Energy

Over 2 billion people today do not have access to energy services. Growth in demand for renewable energy in industrialized countries is leading to economies of scale facilitating increased access by the developing world. Experts believe that many new markets could sustain even higher rates of renewable energy penetration.

The good news for nanomaterials suppliers is that R&D funding for developing next-generation energy sources is on the rise. In the area of fuel cells and the associated hydrogen storage, governments worldwide have pledged more than \$4.5 billion over the next five years for development work that will deliver

<sup>18</sup> LoGerfo, James. Co-editor Parker, Nicholas. Propper de Callejon, Diana. Cleantech Venture Investing: Patterns and Performance. March 2005. Clean Tech Venture.

affordable fuel-cell solutions. Materials technology, and nanomaterials in particular, will play a crucial role in achieving that goal.

A recent report titled *Nanomaterials for Next-Generation Energy Sources* provides an assessment of the possibilities for nanomaterials and nano-enabled devices for the energy sector<sup>19</sup>. The question is whether these products will truly offer viable benefits over existing energy sources. The report states that energy applications are increasingly popular with venture capitalists. Note that several of the venture capital firms we interviewed either have hired or are planning to hire specialists to help them assess the short and long-term viability of energy technology.

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<sup>19</sup> "Nanomaterials power next-generation energy devices." Friday, June 24, 2005. On the internet: <http://www.technology-tracking.com>.

## NANO APPLICATIONS FOR THE ENERGY SECTOR

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- » Photovoltaics inexpensive, light flexible
- » Hydrogen Storage Fuel
- » Fuel Cells
- » Batteries and Supercapacitors
- » Photocatalytic reduction of carbon to produce methanol
- » Direct photocoverion of light and water to produce hydrogen
- » Super-strong, light weight materials
- » Nanoelectronics
- » High current, hyper efficient cabling
- » Thermochemical catalysts to generate hydrogen
- » Carbon mineralization schemes
- » Organic light emitting diodes

## COMPANIES LISTING THEMSELVES AS HAVING NANO-ORIENTED ENERGY APPLICATIONS

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- » Nanergy Inc. (Nasdaq: NNGY)
- » Headwaters, Inc. (Nasdaq: HW)
- » US Nanocorp
- » DayStar Technologies, Inc. (Nasdaq: Dsti)
- » HERA Hydrogen Storage Systems, Inc.
- » Texion Solutions
- » GEMZ Corp. (Otc bb: Gmzp)
- » Hydrogen Solar Ltd.
- » Solaronix SA
- » Hydrocarbon Technologies, Inc.
- » Kainos Energy Corporation
- » Quantiam
- » Nanosolar, Inc
- » Konarka Technologies
- » PolyFuel, Inc
- » Adaptive Materials, Inc.
- » mPHase Technologies (Otc bb : Xdsl)
- » Nuclear Solutions
- » Axion Power Interantional (PS : AXPW)
- » Spire Corporation
- » Cymbet

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Ecoimagination is designed to take advantage of macro drivers such as carbon mitigation through GE's core capabilities such as lighting.

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### General Electric

While General Electric states that it does not plan on being able to commercialize a nano-oriented product anytime in the near future and while some non-governmental organization complain that GE appears to be actively opposing regulatory developments, we think the company's recently launched Ecoimagination campaign clearly defines the company's strategy and capacity to deliver nano products that offer significant benefits through cleantech. We count at least nine research platforms from advanced mechanics to polymers where nano is being studied and almost every core technology is a likely candidate for some type of nano application. It is not difficult to identify projects in the pipeline that would fit our requirement. For example, GE's light-emitting diodes, which may replace home lighting, could reduce energy consumption by an estimated

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An organic light-emitting diode (OLED) display comprises thin layers of individual carbon-based (hence "organic") elements that emit light when electric current is passed through them (electroluminescence).

These elements, or pixels, can be turned on or off independently and can create multiple colors and a fluid, smooth-edged display. They are self-emitting, requiring no backlight, and therefore are very thin and have low power requirements (in some applications, it will be approximately 2 to 10 volts). For electronics (think televisions) they also provide a wide viewing area, approximately 160 degrees, far superior to other available flat-panel displays. Because OLEDs do not need the backlighting, they do not face end-of-life concerns posed by the use of mercury.

**Source: Industry Week**

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10% in the U.S. saving \$100 billion annually<sup>20</sup>. GE may have to address these challenges to its reputation, but if it is first to deliver OLED technology at commercial scale, this should go a long way in offsetting public opinion.

### **Headwaters**

With a focus on efficient use of the world's natural resources, such as fossil fuels, Headwaters has developed nano-catalyst applications to improve natural resource utilization. The Company is the largest provider of technologies used to produce coal-based solid synthetic fuels, and is the industry leader in managing and marketing coal combustion products in the U.S. Headwaters is developing and commercializing its proprietary nanocatalyst technology, NxCat™, to convert or upgrade fossil fuels into higher-value products, to convert gas to liquid fuels and for use in direct coal liquefaction. The NxCat™ technology is also being utilized as a combustion catalyst in coal to reduce the release of nitric oxide by 20-30%.

### **Spire**

Targeting the solar electricity market, Spire has been meeting the demand for many years with both solar equipment and solar systems. Using their expertise in materials technologies, Spire has been utilizing nano for thin films and various surface technologies. The company's solar equipment which they develop, manufacture and market can be found in more than 150 factories in 42 countries. In fact, more than 90% of the photovoltaic modules on the market today were manufactured using Spire equipment. As for Spire's solar photovoltaic (PV) systems, they are used both for stand-alone emergency power back-up and for interconnection into the electric power grid. The most successful example of the company's solar PV systems in use is in Chicago, IL where Spire has worked with the City of Chicago, the local utility company and the State of Illinois to provide customers in the metropolitan area with grid-connected distributed photovoltaic systems. In fact, Spire's primary business unit is titled Spire Solar Chicago.

### **Plug Power**

Plug Power is aligning itself with the general trend away from large facility generation to on-site renewable energy solutions. The company's research platform is based on a proprietary proton exchange membrane (PEM) fuel cell and fuel processing technologies. Nanotechnology's role in manipulating the atomic building blocks of fundamental matter in a controlled and planned manner results in highly programmable fuel cell membrane technologies that significantly increase efficiency and durability. Plug Power is in collaboration with Albany NanoTech, an academic venture to research the use of nanoscience in providing proton exchange membranes that will be competitive with pre-existing energy solutions. While these applications are in development, the company is receiving orders for its GenCore® backup fuel cell systems. Tyco recently ordered 35 systems getting the firm ever closer to reaching its sales goal of 300 this year.

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<sup>20</sup> "Nanotech and the Poor: Opportunities and Risks." Meridian Institute. January 2005

## **MEMS USA**

Many of the companies we interviewed do not have a nano product ready for commercialization. However, several of them have identified the energy sector as the target market and are developing non-nano-related product to support cash flow while the nano products are in development. MEMS USA fits this description. The company recently announced a joint venture deal with Can-Am Ethanol One and Accelon® Energy System of Canada to establish a system that will convert 800 tons of Canadian wood waste per day into 160,000 gallons of clean burning fuel-grade ethanol. We understand that Merrill Lynch will provide a significant amount of funding upon finalization of the land deal. While the nano application is still in research, the company's current ventures fit well with our environmental strategic profit opportunity requirement. While certain dispersive applications of nano may represent risk (see appendices) we continue to monitor progress in the development of nano-based systems for use in detection and control for the energy sector.

## **Market Need: Clean Water**

The current size of the global water market is now \$287 billion and expected to be \$413 billion by 2010<sup>21</sup>. Experts predict that over half the world's population will face serious water shortage in the next 30 to 50 years and United Nations statistics show that water shortages could even be a problem in the United States. The industry has entered a period of rapid growth and consolidation not predicted even 10 years ago. The market faces a growing global crisis of an ageing water infrastructure insufficient to meet the needs of the world's swelling population. Regulation and a shift toward privatization have created new markets and investment opportunities are emerging as the global water industry restructures amidst these challenges.

Water purification and management represented only 4% of cleantech venture investment between 2002 and 2004.<sup>22</sup> However it is increasingly obvious that the industry is following the lead of companies like Nalco and General Electric in trying to solve this global problem. For example, Seldon Laboratories of Vermont has apparently developed a 'nanomesh' fabric made of fused carbon nanotubes, which can filter out all bacteria, viruses and other waterborne pathogens to US Environmental Protection Agency (EPA) potable water standards<sup>23</sup>. While we are concerned about some of the various applications being experimented with (mainly because they involve carbon nanotubes which are being studied for toxicology) we feel that firms who are looking to nanoscience to create inexpensive and highly functional systems for water quality have wisely chosen their target market.

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<sup>21</sup> UNSTATS. United Nations Statistics Division. Commodity Trade Statistics. <http://unstats.un.org/unsd/default.htm> June 26, 2005.

<sup>22</sup> LoGerfo, James. Co-editor Parker, Nicholas. Propper de Callejon, Diana. Cleantech Venture Investing: Patterns and Performance. March 2005. Clean Tech Venture. Page 21

<sup>23</sup> On the internet: August 5, 2005: <http://www.seldontechnologies.com/products/>

## NANO APPLICATIONS FOR WATER:

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- » **Photocatalytic materials - water passing through a nanomaterial is subjected to ultraviolet light**
- » **Nanofiltration based on the electrical charge of particles**
- » **Membranes and “fabrics”**
- » **Nanotube filters and porous aggregates**
- » **Detection systems**
- » **Soil remediation**

### **Nalco**

Nalco is the market leader in water treatment chemicals with a market share of 19% followed by General Electric at 11%. While nanoscience is likely relevant to almost all of Nalco’s various strategic business segments from paper to hydrocarbons, the Colloidal Technologies Group is the most relevant with regard to any future nano-oriented product. The nano-oriented water treatment applications (zeolite dendritic polymerization, membranes) are in development; however, given Nalco’s strong market position in the industry, the chances are significant that Nalco will have a nano product soon.

### **JMAR**

JMAR’s line of high-powered lasers and microscope products is relevant to our analysis for their possible application in bringing nanotechnology production to commercial levels. Moreover, these technologies may also be relevant to the detection and characterization of nanoparticles – an important factor in reducing uncertainty about nanoscience. These products are in various stages of development and when ready will allow for viewing the interiors of very tiny objects at the nanoscale, even organic material. In the interim, JMAR has wisely made water technology its target market. The BioSentry™ line of products is designed for continuous detection of microorganisms in water. While BioSentry is not part of the company’s nano platform sales from this product will sustain operations until the soft x-ray equipment is ready. The addressable market for BioSentry is roughly estimated to be \$500 million.

### **Argonide**

With a focus on water treatment, Argonide has developed a family of water filters developed from nano alumina fibers. The Company’s primary product is NanoCeram®, a highly electropositive filter that rapidly adsorbs particles at any size. The filtration technology utilizes attraction based on charges rather than separation through a membrane. The highly electropositive alumina attracts and retains sub-micron particles and is effective in removing bacteria, virus, cysts, DNA and endotoxins from water. The filters will also remove turbidity whose origin may be natural organic matter, colloidal inorganic or ultra fine metal particles. Applications include industrial water, chemical and pharmaceutical processing, biological sampling, pre-filters for reverse osmosis membranes, food and beverage manufacture and particulate removal in swimming pools and spas. This technology was developed with backing from the U.S. National Aeronautics and Space Administration (NASA).

## 5 Product Risk

The analysis of product related risk can be broken down into two major headings: **Product Safety** and **Regulatory Risk**.

### Product Safety

To date the science remains scant. The analysis of product safety involves a review of hazards and exposure. The following chart is a rough summary of some common particles and potential toxicity implications. While the chart below provides a useful introduction to risk in a simplified format, note that early findings are more complex than can be adequately covered in this manner. See the following page for a few of our caveats to this representation.

Characterizing Hazard: Different Nanoparticle Types Merit Different Levels of Caution

	Manufacturing weight	Use weight	End of life weight	In vivo imaging	Structural composite for automotive body	Sunscreen additive	Food additive	Display backplane	Polishing agent	Memory chip	Printer toner	Drug	Roof top flexible solar cell
Nanoparticles can get airborne in mfg.?	50%			◐	◐	◐	◐	○	◐	○	◐	◐	◐
Large volumes of nanoparticle used?	50%	10%	20%	○	●	●	○	○	◐	○	●	○	●
Nanoparticles free rather than bound?		40%	30%	●	○	●	●	○	●	○	●	●	○
Intended to go in or on the body?		30%	10%	●	○	●	●	○	○	○	○	●	○
Will be stressed during use?		10%		◐	◐	◐	◐	○	●	○	◐	◐	◐
Existing regulations apply to product?		10%		○	◐	◐	○	◐	◐	◐	◐	○	◐
Existing regulations apply to disposal?			40%	○	◐	●	●	◐	●	◐	●	○	◐

Potential exposure at manufacturing:	■	■	■	■	■	■	■	■	■	■	■	■	■
Potential exposure during use:	■	■	■	■	■	■	■	■	■	■	■	■	■
Potential exposure at end of life:	■	■	■	■	■	■	■	■	■	■	■	■	■



Source: Lux Research<sup>24</sup>

<sup>24</sup> Nordan, Matthew M. "A Prudent Approach to Nanotech Environmental, Health and Safety Risks." Lux Research. May 2005

## INNOVEST ANALYSIS ON HAZARDS

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While this provides a useful quick reference, our research takes into considering the following:

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This is interesting considering the limited amount of research...

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- » **Numerous reports attempt to characterize the environmental, health and safety risks associated with specific types of particles.** *This is interesting considering the limited amount of research and scientific review that has been published. Investors may note that many chemical structures have been approved by regulators and characterized as being safe. Only later do their toxic properties come to light resulting in significant liability.*
- » We have come across statements in our research on nanotechnology claiming that human exposure risk is measured in terms of volume. **This is incorrect.** In the case of nanotechnology, toxicity is likely to be *affected less by mass and volume and more by surface area, surface chemistry and particle structure.* **This provides real challenges for toxicology since many of the models used to predict the toxicity of materials relate toxicity to mass. The mass-based approach is the basis for most U.S. environmental regulations (air and water), which specify thresholds based on mass per unit volume.** *See Appendix 1 for further discussion of characterization issues.*
- » While titanium dioxide (TiO<sub>2</sub>) has been approved by the Scientific Committee on Cosmetics and Non-food Products (SCCNFP) in Europe and given a green light by the Food and Drug Administration in the United States, **we are cautious about these findings for the following reasons:**
  - » In February 2006 titanium dioxide was classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2B carcinogen "possibly carcinogen to humans". The evidence showed that high concentrations of pigment-grade (powdered) and ultrafine titanium dioxide dust caused respiratory tract cancer in rats exposed by inhalation and intratracheal instillation.
  - » A 1997 study suggests that TiO<sub>2</sub> may cause DNA damage, and the science is still uncertain regarding possible effects on damaged skin<sup>25</sup>.
  - » The SCCNFP used proprietary *company studies* to determine safety rather than setting preference for independent toxicity testing. Investors may note that the chemicals industry's credibility problem could be partly attributable to this and may explain the existence of programs like the OECD's High Product Volume Challenge, which **takes proprietary company data and makes it public for peer review.**
- » There should also be some caution surrounding nano-crystalline and nano composite drugs because many of them are going through the FDA on fast track (discussed later in this report) as an existing drug rather than a new structure that requires a more thorough review.

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<sup>25</sup> Dunford, Salinaro et al. "Chemical oxidation and DNA damage catalyzed by inorganic sunscreen ingredients," FEBS Letters , volume 418, no. 1-2, 24 November 1997, pp. 87-90.

## INNOVEST ANALYSIS ON EXPOSURE RISK

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The following table is a basic guide for incorporating particle risk into fundamental analysis. Note that due diligence will need to be continually updated as the science reveals new information on the risks associated with certain types of engineered particles. We provide a rough timeline on page 39 for completion of studies underway.

	products may involve a higher exposure risk. Investors may need to determine whether these applications are regulated. Moreover the toxicity of the particle is of significance in determining potential product risk. See page 42 for a timeline of scientific research to be completed over the next several years and <b>See Appendix 3 for details on exposure risk.</b>	use? Carbon black used in tires is currently being tested.  Is there a way for the product to be released through breakage or damage? One company told us that breaking the product would result in a burst of nanoparticles into the atmosphere. The company included this information as part of its marketing pitch. Remember that volume is not necessarily relevant to understanding exposures. Small amounts to could pose risk if inhaled.
<b>End of Life</b>	At the end of life, investors may consider the potential that nanoparticles will accumulate in the environment. The first level of environmental exposure will be related to applications that involve free nanoparticles i.e. contraception pharmaceuticals have now been identified as an eco-contaminant. Innovest research has identified a number of	Is the particle free or fixed? If particles are fixed it will be many years before anything is understood about how they succumb to the forces of nature i.e. in landfills.  What is the hazard of the particle? Coating may relieve some concerns with reactivity, however there is indication that

FIGURE 16 Exposure and Questions for Due Diligence

STAGE	NOTES	QUESTIONS FOR DUE DILIGENCE
<b>Resource Extraction</b>	This is likely a mining situation where, at minimum, there will be high levels of ultra-fine dust particles. Note that the U.S. National Institute of Occupational Safety and Health is currently conducting research on risks related to inhalation of these particles. Nanoclays are a low risk particle however in this scenario workers may have elevated exposure which could necessitate enhanced protection.	
<b>Manufacturing</b>	Manufacturing processes, procedures and equipment are the point of assessment here. Most development stage firms that we interviewed and who work directly with free particles appear to be cognizant of the issues and are taking appropriate precaution.  We did identify some variance among firms in the level of awareness and policy development. In some cases, companies appear to be shipping nanopowders in glass vials through overnight shipping services. Systems should be closed loop and involve some way of minimizing the amount of off-site waste that may contain particles. Regulators have not yet established workplace practices. Two chemical companies told us that toxic gas procedures are the most stringent and relevant standard that can be followed in the workplace right now. Keep in mind that some types of particles could potentially pass through most respirators on the market today.	What is the particle and the risks associated with it? Free or fixed?  Have the particles in question been externally tested?  Does the company utilize a closed production system?  What detection methods are in place? <b>See Appendix 2 for further discussion of detection technologies</b> and companies involved in the detection issue.  How well does the company rate with regard to overall operational and environmental management? There are ways to assess this. See Appendices on Innovest Methodology.  Has the company conducted a full Life Cycle Assessment (LCA)?
<b>Use</b>	The application of the nanoparticle is the point for consideration. Applications including cosmetics, food, aerosols, drugs, imaging and medical devices involve direct contact with the body. Common sense dictates that these products may involve a higher exposure risk. Investors may need to determine whether these applications are regulated. Moreover the toxicity of the particle is of significance in determining potential product risk. See page 42 for a timeline of scientific research to be completed over the next several years and <b>See Appendix 3 for details on exposure risk.</b>	What is the intended use? Will this involve free or fixed particles? If agglomerated what chemicals are used to minimize this?  What is the stress to the product during use? Carbon black used in tires is currently being tested.  Is there a way for the product to be released through breakage or damage? One company told us that breaking the product would result in a burst of nanoparticles into the atmosphere. The company included this information as part of its marketing pitch. Remember that volume is not necessarily relevant to understanding exposures. Small amounts to could pose risk if inhaled.
<b>End of Life</b>	At the end of life, investors may consider the potential that nanoparticles will accumulate in the environment. The first level of environmental exposure will be related to applications that involve free nanoparticles i.e. contraception pharmaceuticals have now been identified as an eco-contaminant. Innovest research has identified a number of evolving regulatory and market trends that may indicate that these types of liabilities are becoming increasingly expensive for firms.	Is the particle free or fixed? If particles are fixed it will be many years before anything is understood about how they succumb to the forces of nature i.e. in landfills.  What is the hazard of the particle? Coating may relieve some concerns with reactivity, however there is indication that nanoparticles may readily combine with toxins already present in the environment to enhance bioaccumulative properties. <b>See appendix 4 for further details on particle interaction with the environment.</b>  Can the material be recycled if it contains nanoparticles? Auto glass for example?

Source: Innovest

## THE INSURER'S PERSPECTIVE

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### Asbestos

There has been an exponential increase in asbestos claims and more than 6,000 independent entities have been named as asbestos liability defendants.

At least one company in every industry has been impacted, including non-producing companies.

An estimated 1.1 million claims have been issued with 75% of the plaintiffs not suffering any negative health impacts.

Approximate total cost to insurers and defendants will be \$200-275 billion.

Approximately 61 companies have filed for bankruptcy due to asbestos litigation.

**Takeaways: All companies involved in nano, including end users, may be held liable if nanoparticles are found to cause health or environmental hazards.**

**Source: American Insurance Association 2002**

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While most companies we interviewed, who are working directly with engineered nanoparticles, appeared to be cognizant of the risks, the fact remains that pressure to generate sales could affect responsible nanotechnology development in the future. By most accounts there are already 700 products containing fixed and free nanoparticles in the market. Most of these applications appear to be of low or no risk and our analytical set even includes a few firms with products that have obtained approval from the United States Food and Drug Administration. However, we have identified a number of product applications that raise concern according to early findings. In addition, this scenario leaves the majority of products unregulated. Many firms in the set responded that they are conducting their own tests on the nanoparticles that they are using. ***Investors may note that this information is largely proprietary making it unavailable to the public and to the scientific community for review.***

Insurers warn that this is an environment conducive to liability. Clearly European insurers have taken note of the potential for nanotechnology to create latent liability and are concerned about its capacity to create surprise. The four insurers SwissRE, MunichRe, GenRE and Allianz have all issued reports on this issue within the last two years. All are operating under the assumption that dangers will be chronic rather than acute. They are employing loss scenarios and loss limiting measures because "events" are deemed incalculable at this time.

In essence, commercial underwriters are already carrying the risks associated with early commercialization of nanotechnology. As more products are commercialized, insurers are taking on more risk to the extent that a large portion of an underwriter's portfolio could be nano-oriented within a five year period. Note also that companies are currently operating in an unregulated environment; the potential for a product to be brought to market without adequate screening is of concern.

For example underwriters for the chemical industry may initially count only a few companies involved in nano activities in the portfolio. But looking at the larger picture, we note that many of the large capitalization chemical firms are beginning to enter into venture deals with pure-play and micro-cap companies. This makes for a scenario where insurers may bear the burden for the entire supply chain. It is not difficult to make a correlation with an asbestos-like situation where any and all related firms are liable. Moreover, the small-cap, pure-play companies may need to consider whether this will result in a situation where underwriters are already fully loaded with nano-oriented risk from their long-standing relationships with the large-cap companies. These companies could find coverage to be costly under this scenario.

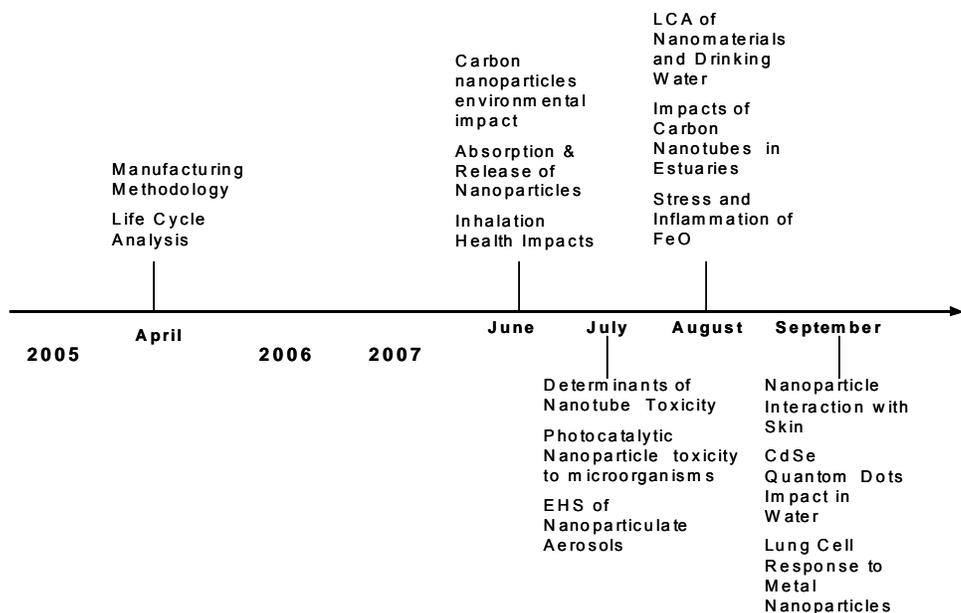
## Investment Strategy

Given that Europeans tend to be more emphatic about the precautionary approach and that major insurers are beginning to ask for it, we feel that companies that acknowledge this issue as part of their business model have greater chances for market acceptance and reduced liability over the long-term.

### INVESTORS WILL NEED TO REMAIN ABREAST OF SCIENTIFIC DEVELOPMENTS

Our research shows that venture capital firms are not necessarily conducting due diligence regarding the environmental, health and safety implications associated with the use of certain kinds of engineered nanoparticles. Investors concerned about potential liability will need to remain current on scientific developments and should look for companies that are teaming up with regulators and academia to increase the amount of scientific data available. The following is a schedule of U.S. Environmental Protection Agency (EPA) funded research that could have implications for investors going forward.

FIGURE 17 EPA Funded Research



Source: U.S. Environmental Protection Agency<sup>26</sup>

<sup>26</sup> <http://es.epa.gov/ncer/nano/research/index.html>

## EHS Science Funding is Critical to Limiting Uncertainty<sup>27</sup>.

- » According a 2005 study presented by the Project on Emerging Nanotechnologies, funding or “highly relevant nanotechnology risk research is just one percent of the annual NNI budget – totaling just an estimated \$11 million in 2005. More important than the level of funding is the fact that there is no coordination of the risk research.”<sup>28</sup>
  - » **Funds are only earmarked for EHS research and projects are buried within individual funding programs at each agency. There is no strategic direction for risk research. This leaves researchers and industry without clear guidelines for safe use and safe products.**
- » Many groups concerned about the lack of sufficient funding have spoken out about their concerns:
  - » The American Chemical Council (ACC) and other environmental groups have expressed a need to the EPA for more funding.
  - » Representatives of the NanoBusiness Alliance have also spoken on the issue and asked for more federal environmental research<sup>29</sup>.
  - » The Environmental Defense Fund (EDF) has called for \$100 million to be set aside to study potential health and environmental risks.
  - » Lux Research May 2005.

FIGURE 18 Annual Spending Estimated from the National Nanotechnology Initiative and the Project on Emerging Nanotechnologies (PEN).

US Federal Government Annual Spending on Nanotech Risk R&D (Millions USD)				
Agency	NNI-estimated risk-related annual R&D	PEN-estimated risk-related annual R&D (all relevant research)	PEN-estimated risk-related annual R&D (highly relevant research)	
NSF	24	19	2.5	
DOD	1	1.1	1.1	
DOE	0.5	0.3	0	
HHS (NIH)	3	3	3	
DOC (NIST)	0.9	1	0	
USDA	0.5	0.5	0	
EPA	4	2.6	2.3	
HHS (NIOSH)	3.1	3.1	1.9	
DOJ	1.5	0	0	
<b>Totals</b>	<b>38.5</b>	<b>30.6</b>	<b>10.8</b>	

Based on January-December 2005. Highly relevant means directly specific to risk research. Source: NNI<sup>30</sup>

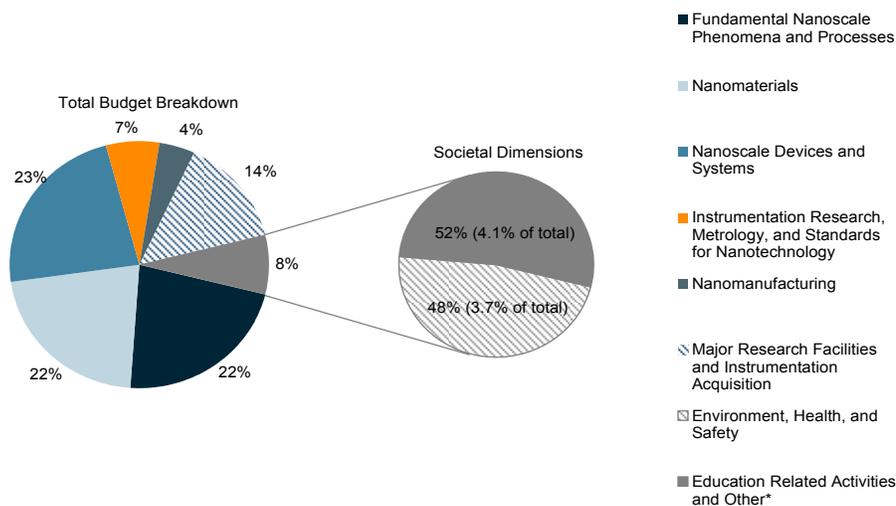
<sup>27</sup> National Nanotechnology Initiative. <http://www.nni.gov>. July 2006.

<sup>28</sup> Maynard, Andrew Phd, Rejeski, David. “Nanotechnology, A Research Strategy for Addressing Risk” Woodrow Wilson Center for Scholars

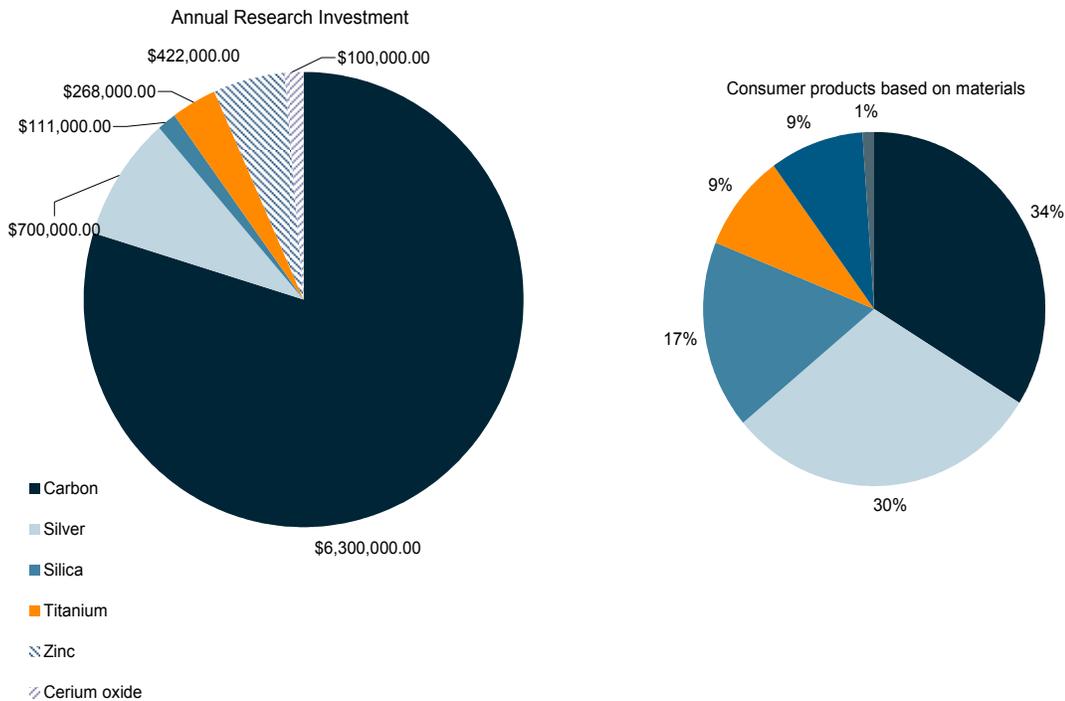
<sup>29</sup> *Ibid.*

<sup>30</sup> *Ibid.*

FIGURE 19 NNI Funding Breakdown



Nanotechnology ESH Research Funding for Six Classes of Engineered Nanomaterials, Compared to Consumer Products Using Those Materials



Based on January-December 2005. Highly relevant means directly specific to risk research. Source: NNI<sup>1</sup>

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This is effectively the first sign of a non-tariff barrier.

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...repeating many of the errors that were made with biotechnology.

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Shareholders are left with potential liability and poor returns.

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Current regulatory developments may pose risk to companies and their shareholders

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## Implication of Regulation for Shareholders

China announced in late June that it has developed the first batch of nanotechnology standards and stated its intentions to develop an entire set which could in their words “reshape world nanotech competition.”<sup>31</sup> Upon closer inspection the current set only covers first-stage nanomaterials already in commercial use; however, the message is clear and relates back to the concept of protective/regulatory spheres impacting the competitive landscape. This is effectively the first sign of a non-tariff barrier.

In comparison, the United States, which currently leads in the number and concentration of nanotechnology start ups, appears to be repeating many of the errors that were made with biotechnology. At this stage, the regulatory situation for Genetically Engineered (GE) crops in the U.S., the major market for both developers and sales, consists of a patchwork of outdated regulations and voluntary guidelines which have been widely criticized by the scientific community. Since the first introduction of these new crops in the early 1990s, there have been no new laws passed to regulate GE crops. ***Instead, all regulation has fallen under pre-existing laws.*** Public groups widely criticized the process because major players like Monsanto appeared to have an inordinate role in the development of controls.

In essence, markets operate properly when there are adequate checks and balances between corporate interests and protection of the public. When this is absent, the result is public distrust in regulators and companies to the extent that demand is abated and ***shareholders are left with potential liability and poor returns.***

It appears that all interested parties (both corporations and regulators) are cognizant of trying to avoid past mistakes. However, counter to the intuition that regulation is bad for healthy market development, and given our conversations with companies for the development of this index, we raise the argument that well-conceived science-based regulation may in fact support viable markets. In light of this we feel that current regulatory trends may pose risk to companies and their shareholders as frameworks become solidified:

- » **In June, the U.S. Environmental Protection Agency proposed a voluntary reporting program. NGOs have written a formal response pointing out a number of faults with the proposal (see Figure 16). There is concerted discussion about the possibility of exhausting *pre-existing* statutes under the Toxic Substances Control Act (TSCA) for nanotech.**
- » **The Food and Drug Administration has already approved several nanotechnology-oriented structures and has recently established a new Office of Combination Products for multiple-component nano pharmaceuticals.**

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<sup>31</sup> Zheng, Yu. “China Surpasses traditional scientific powers in standardizing nano-tech.” Xinhuanet. [www.chinaview.cn. http://news.xinhuanet.com/english/2005-06/20/content\\_3110882.htm](http://news.xinhuanet.com/english/2005-06/20/content_3110882.htm).

Depending on the type of structure, companies can opt for the lengthy process for submission or a more streamlined process which does not necessarily involve a toxicology review<sup>32</sup>. Several cosmetics and personal care items containing nanoparticles that have been recently targeted for study are already on the market.

- » The National Institute of Occupational Health and Safety website states that a set of “best practices” were supposed to have been released in 2004. They have not been released. Moreover the agency’s position statement does not result in any actionable guidelines for companies at this time. This could result in a situation where an increasing number of workers are potentially exposed to nano-engineered particles and materials with little or no guidance concerning proper handling and protection procedures.

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FIGURE 20 Summary of NGO Responses to Proposed EPA Voluntary Reporting Program

**Summary of NGO Responses to the EPA Proposal to Regulate Nanomaterials Through a Voluntary Pilot Program**

**The EPA proposed voluntary program is inadequate and inappropriate:** We conclude that all engineered nanomaterials are “new chemical substances” under TSCA because they are new or “organic or inorganic substances of a particular molecular identity,”....therefore the pre-manufacture notice (PMN) reporting requirements under TSCA section 4 are triggered prior to their commercial manufacture or import.

**Immediate Regulatory Objectives:** EPA should use its authority under the Toxics Substances Control Act (TSCA) section 4 and other authorities to require adequate toxicity testing of engineered nanomaterials and to evaluate these materials so as to prevent unreasonable risk to the population, by preventing the release of potentially harmful nanomaterials into commerce.

**Adequate Information:** Testing on nanomaterials should be performed in a transparent manner by a credible independent agent, and all findings made public as required by various statutes under TSCA.

**Long-term regulatory objectives:** The burden of proof should be reversed essentially requiring the manufacturer to demonstrate that nanomaterials are safe prior to commercialization. Those materials deemed unsafe should be prevented from entering commerce unless they can be used in a highly controlled manner in order to prevent human exposure.

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Source: Docket ID: OPPT-2004-0122

## RELEVANCE OF NGO COMMENTS FOR SHAREHOLDERS

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In trying to understand this from the perspective of shareholders, we consider these responses in the following manner:

- » Clearly the NGO community is activated and cognizant of the implications of the science.

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<sup>32</sup> Till, Marc, Simkin, Michele, Maebius, Stephen. “Nanotech Meets the FDA: A Success Story about the First Nanoparticulate Drugs Approved by the FDA.” Nanotechnology Law & Business Volume 2.2 (2005). Page 166.

- » The EPA is taking a more open approach this time and inviting commentary we feel will favor companies and shareholders over the long-term.
- » We are concerned about the various interpretations of existing regulation and the fairly vague rules that currently govern the way companies submit chemicals for review.
- » Results of focus group studies will be launched in September showing a low level of public support for voluntary approaches by government and industry and desire for more pre-market testing of nanotech-based products and materials. In essence voluntary programs may be useful in providing some initial data, but in light of this, we wonder how useful they will be in instilling public confidence over the long term.
- » If regulators fail to take into consideration the concerns outlined above, nanotech companies could face the same perception and market rejection problems that affected biotechnology companies.

## REGULATORS' RETICENCE TO ACT, IMPACT TO FIRMS

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Closer examination of the regulatory environment for genetic engineering in the United States shows ***a significant lack of oversight that places the risks taken by the industry squarely onto shareholders.*** Regulator's reticence to act with regard to biotechnology resulted in a lack of public trust in government and a chilling effect on the European market for genetically engineered food products. The following table is a sample list of food companies representing in excess of \$450 billion in yearly revenues that have publicly committed to remove GE ingredients from their supply chains in key countries or regions.

**FIGURE 21** Market Rejection of GE foods

Aldi	Coop	Hip	Sapporo
Alpro Soya	Corona	Kirin	Soya Hellas
Amadori	Dannon	Kraft Jacobs Suchard	Spar
Asahi	Delhaize Le Lion	Marks & Spencer	Super Quinn
ASDA	DUC	McCain	Tegel
Barilla	Edeka	McDonald's	Tinglemann
Ben & Jerry's	Esselunga	Migoros	Tesco
Bodin	Ferrero	Nestl'	Trader Joe's
Burger King	Findus	Nutricia	Unilever
Cadbury's	Friki	ParkinShop	VitaSoy
Carrefour	FujiOil	Perdigao	Waitrose
Coca-Cola	Gerber	Sadia	Wiesenhof
Coluryt	Heinz	Safeway	Wimpy Fast Foods

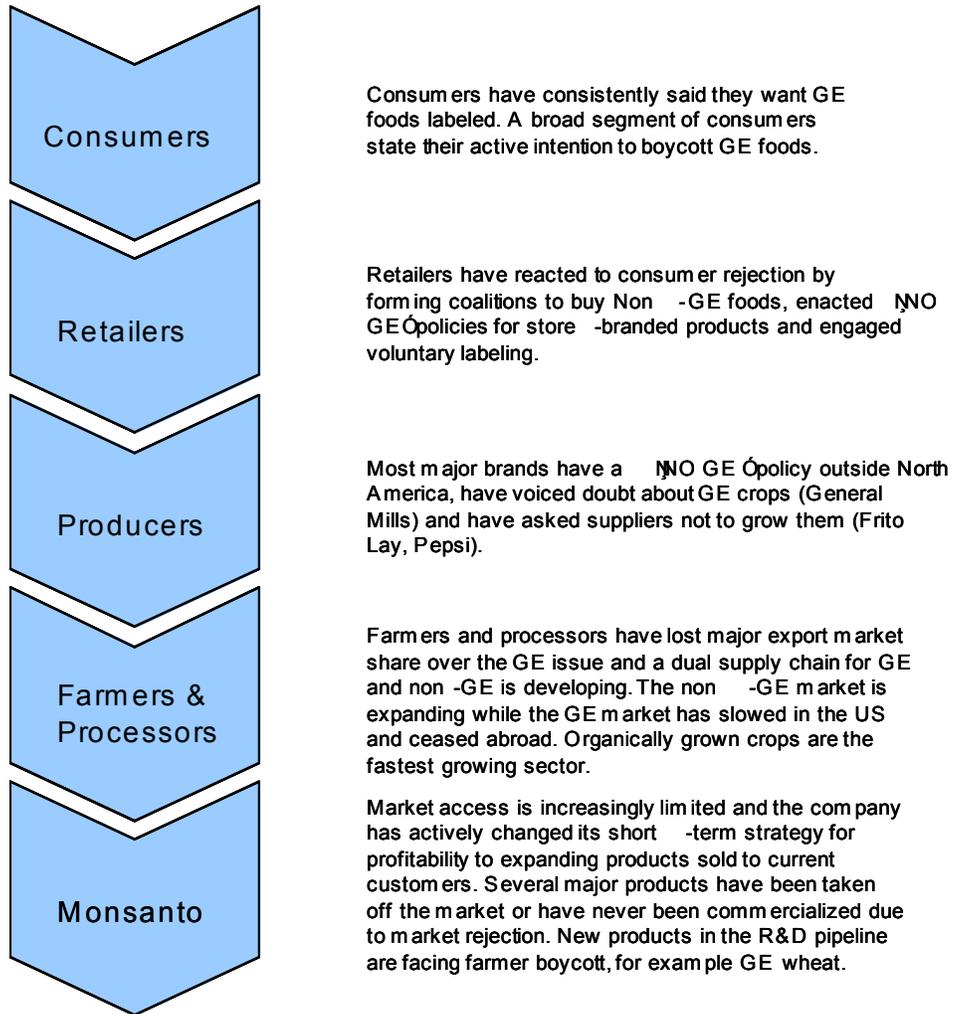
This is a sample list of food companies representing in excess of \$450 billion in yearly revenues that have publicly committed to remove GE ingredients from their supply chains in key countries or regions. The scale of rejection by each company varies from those who have removed only GE ingredients from food for human consumption in products sold in one or more countries, to companies who have an international or global policy to remove GE ingredients from their supply chain and also to exclude the use of GE crops as animal feed. Source: Innovest

### Market Rejection

Below is a flowchart showing the development of market rejection for genetically engineered foods. Many of the companies we spoke with believe that a lack of adequate and timely regulation could result in similar situation for nanotech.

FIGURE 22 Flow Chart of Market Rejection for GE Products in Europe

**Flow Chart of GE Market Rejection**



Source: Innovest

## A Model to Support Viable Markets: Cambridge, MA

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### Chinese Standards Announced in May include:

#### Nomenclature

Two testing methods: Gas adsorption  
BET and the granularity of nano powder

Four Sets of Specifications for Existing  
Nano materials currently on the market.  
This includes: nickel powder, zinc oxide,  
titanium oxide and calcium carbonate.

They will be effective from April 1, 2005

Li Zhonghai, Director of Standard  
Administration of China, disclosed that  
research on 15 nano materials  
standards were underway and the 7  
items released this time was only the  
first batch.

Liu Zhaobin, spokesman for General  
Administration of Quality Supervision,  
Inspection and Quarantine, confirmed  
that preparation for certification of nano  
materials has begun. The training of  
personnel has also been initiated.

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Wall Street tends to react unfavorably to regulation in most circumstances. However given our findings above, we sought to find examples of situations that demonstrate how regulation could be viewed by the investment community as necessary for supporting viable markets. The following anecdote may be helpful in this regard:

Very early in the national debate about recombinant DNA the Cambridge City Council created the Cambridge Experimentation Review Board (CERB) and developed its own regulatory framework for biotech research including an ordinance regarding the use of rDNA. Counter to intuition, biotech leaders specifically chose to locate their R&D headquarters in Cambridge because the city's established review and regulatory process, and mature understanding of the field, were in fact part of the community's appeal. Regulation there was seen as being clear and predictable. Cambridge is now a haven for biotech research, development and cross-licensing with 50 biotech licenses held by leading firms in the area<sup>33</sup>.

Investors may note that the Cambridge Model worked largely because the National Institutes of Health (NIH) had already established a scientifically-valid set of biosafety guidelines and continually updated them in response to new scientific advances. The city would never have had the intellectual capacity to develop the guidelines otherwise. As shown on the following pages of this report, nothing remotely similar currently exists for nanotechnology

We interpret this as being a signal that countries like China, who are developing standards very early in the game, may see a competitive edge as the international race to win superiority in nanotechnology ensues. China and India are gaining ground. China currently ranks third in the world behind the United States and Japan in terms of nanotech patent applications. An as yet unpublished article in the journal Research Policy places Chinese researchers second in terms of the number of papers published in nanotechnology journals. It also estimates that the U.S. government spent \$1 billion on nanotech research in 2004, just ahead of China, Europe and Japan, which each spent about \$900 million<sup>34</sup>.

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<sup>33</sup> Lipson, Sam. "The Cambridge Model: How public Oversight of biotech is good for everyone – even business." GeneWatch. Volume 16, Number 5 pg. 7-10.

<sup>34</sup> "Developing Global Nanotech" Red Herring. 12 April 2005.

## CHINESE OFFICIALS BELIEVE STANDARDS SUPPORT VIABLE MARKETS

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In May the General Administration of Quality Supervision, Inspection and Quarantine and the National Committee for Standards jointly held a news conference to announce the coming debut of China's national standards for nanomaterials. This includes a nanomaterial nomenclature. While it is unclear how binding these standards are and while there are no definitions for subjectivity, rapid action by China should indicate to other countries the competitive reasons for moving quickly to develop their own standards. Chinese officials expressly state that the standards were intentionally designed to support the "healthy development of nanotechnology". ***Chinese officials state that these standards might serve as a useful model for international standards***<sup>35</sup>.

### Standards Setting

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We note that several of the firms in our analytical set are in talks with overseas joint venture partners

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Activities being undertaken by bodies like the International Council on Nanotechnology (ICON), ASTM International, and the International Standards Organization (ISO) will be the tipping point for countries seeking guidance on how to develop their own regulation. Indeed, this factor has a critical role in technological development and market growth of nanotech products and companies. On one hand, the Cambridge Model discussed above suggests that this could spur development in certain markets. Conversely, it could create regional barriers to entry.

The activities of the standards-setting organizations will effectively result in a base-line set of instructions for characterization and nomenclature for nanomaterials. We predict that once this occurs, the basis will be set for the development of regulation and trade industry policy.

The chart below indicates the flow of developments toward standardization as it progressed last year.

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<sup>35</sup> Interview with Embassy of China 21 May, 2005 and People's Daily "World's First National Standard for Nanotech to Be Effective in China." On the internet: 2005-03-03<http://www.edu.cn/20050303/3130013.shtml>.

**FIGURE 23 2005 Schedule of Activity Toward ISO standardization**



Source: Innovest

### 2006 Update

The process shown above generally reflects the flow of information in the United States in 2005. Similar processes took place in many countries. All this activity culminated in the November 2005 meeting resulting in twenty-four countries participating in the technical committee developing **ISO TC 229**. To date, three primary activities have been delineated and leadership assigned.

- » **Terminology and Nomenclature led by Canada**
- » **Measurement and characterization led by Japan**
- » **Health, safety, and environment led by the United States**

## REGULATORY OUTLOOK: UNITED STATES

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...reporting program will be  
in place by end of year

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### Environmental Protection Agency

On June 23, the U.S. Environmental Protection Agency (EPA) conducted a public meeting on nanoscale materials to discuss a potential voluntary pilot program. The pilot would require companies (both large and small) to report toxicological and eco-toxicological data on certain nanoscale particles. Some of the nanoscale materials are new chemical substances subject to notification requirements under section 5 of the Toxic Substances Control Act (TSCA) Industry and non-governmental parties provided comment. At issue is the concern that companies have to guess whether a certain nanoparticle represents an existing or new structure under this regulation. ***We note several instances where firms have made potentially risky judgment calls on this already. Experts predict that the reporting program will be in place by end of year.*** Certain factions in Washington are proposing that pre-existing EPA statutes under TSCA may already be applicable (See Appendix 5).

### Issues to consider

One carbon nanotube structure was submitted in January for consideration of its exemption status under TSCA 5. This may have implications for other CNT producers but this depends on the specific features of interest listed in the submission document. ***More importantly, there could be a more general affect on CNT companies if the analysis leads to negative judgment.*** We continue to monitor the progress of this submission.

### 2006 Update

The voluntary pilot program has been postponed and will now begin at the end of 2006.

### Food and Drug Administration

The first approval for a nano-based pharmaceutical went to Merck for Emend® on March 26, 2003. Companies focused on pharmaceutical applications are less subject to speculation over the regulatory issue at this point in that each structure must be evaluated on a product-by-product basis. According to research undertaken by NanoBiotech News, 61 nanotech-based drugs and delivery systems and 91 devices or diagnostic tests have entered pre-clinical, clinical, or commercial development<sup>36</sup>.

If the nanoparticulate drug has a different pharmacokinetic profile than its larger particle original then it must be submitted as a new chemical entity. However, a drug that is simply the nanoscale version of its larger analog still needs to prove bio-equivalency but the process is a more streamlined approach that ***does not***

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<sup>36</sup> 2005 Nanomedicine, Device and Diagnostics Report National Health Information, LLC <http://www.nanobiotechnews.com>

**require firms to submit both the New Drug Application (NDA) and the Investigational New Drug (IND) screening.** Conducting both is a costly and time consuming process<sup>37</sup>.

### Issues to Consider

Drugs involving nanoparticles are taking two forms; nano-crystalline forms of existing drugs and nanoparticle delivery mechanisms for new and existing drugs.

For nano-crystalline forms of existing drugs investors may need to consider that particles at the nanoscale may not necessarily be identical to their macro analog.

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Recognizing this confusion, the FDA has recently created a new Office of Combination Products.

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In addition, several companies in our analytical set are utilizing nanoparticles as delivery mechanisms. We identified a significant amount of variance between firms in how they decided to submit (see above). Recognizing this confusion, the FDA has recently created a new Office of Combination Products. Note: we have some concern about the decisions taken by a few firms in our analytical set and are monitoring the potential for risk. Note that some recent public perception studies have found a very low level of trust in the FDA to manage the risks associated with nanotechnology. This may be grounded in perceptions of the agency's record with regard to Vioxx and other drugs that proved harmful once in wide use by the public.

### 2006 Update

In August 2006, Food and Drug Administration (FDA) announced the formation of an internal Nanotechnology Task Force that will develop regulatory approaches to encourage the development of safe, agency-regulated products that use materials developed with nanotechnologies. The task force will identify research and policy gaps to enable the agency to evaluate possible adverse health effects. We continue to monitor the developments of the task force for further developments.

The FDA's current defines nanotech products as involving all of the following:

- » **Research and technology development, or products regulated by FDA, that are at the atomic, molecular or macromolecular levels, and where at least one dimension, that affects the functional behavior of the product, is in the length scale range of approximately 1-100 nanometers.**
- » **Creating and using structures, devices and systems that have novel properties and functions because of their small and/or intermediate size.**
- » **Ability to control or manipulate at the atomic scale.**

Note that while most companies responded that they do not plan to identify their products as being "nano-enabled" public concern could develop into a demand

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<sup>37</sup> Till, Mary C.; Simkin, Michele M.; Maebius, Stephen. Nanotechnology Law & Business Volume 2.2 (2005) page 66.

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### Uses of Nano in Food

Companies are using nanotech to change the structure of food and food packaging:

“Interactive” drinks that contain nanocapsules that change color and flavor.

Spreads and ice creams that have improved texture due to nanoparticle emulsions.

Nanocapsules that carry nutrients and flavors into the body increasing the bioavailability of the product.

Nano-sized self assembled structured liquids (NSSL) that integrate free phytosterols into food products. The phytosterols will compete with cholesterol for entry into the micelle, bloodstream.

Nanomaterials that extend food shelf life and signal when a food spoils by changing color.

Clay nanoparticles that make plastic less likely to shatter and seal in carbon dioxide to keep carbonated drinks fresh.

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for labeling. Experts expect the “nanofood” market to rise from US\$ 2.6bn today to US\$7bn next year and to \$20.4bn in 2010. Approximately 200 companies are currently active in research and development. The US is the leader in the sector followed by Japan and China. By 2010 Asian countries are projected to be the sector leader in the market for nanofood<sup>38</sup>.

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**FIGURE 24** Companies Engaged in Nano Research and Development

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Nestlé	McCain Foods
Altria (Kraft Foods)	Nippon Suisan Kaisha
Unilever	Nichirei
PepsiCo	BASF
Cargill	United Foods
General Mills	La Doria
Sara Lee	Goodman Fielder
H.J. Heinz	John Lusty Group Plc
Campbell Soup	Northern Foods
Maruha	Astrofina
Associated British Foods	Nutralease
Ajinomoto	Mars, Inc.
DuPont Food Industry Solutions	

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Source: Food Engineering Magazine and Helmut Kaiser Consultancy<sup>39</sup>

<sup>38</sup> “Nanotechnology sales increase to €687.5m in 2004.” Food Production Daily. Com <http://www.foodproductiondaily.com/news/news-ng.asp?n=60283-nanotechnology-sales-increase>. 27 May, 2005.

<sup>39</sup> “The World’s Top 100 Food and Beverage Companies,” Food Engineering Magazine, 1 November, 2003 and Helmut Kaiser Consultancy.

## OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION

OSHA is likely the first agency to come up with actionable requirements for firms regarding the use of nanoparticles in the workplace.

The National Institute for Occupational Safety and Health (NIOSH) is the research body serving OSHA, the regulator in charge of workplace standards in the United States. NIOSH is in fact the only agency involved directly in scientific research at this point. All other agencies may utilize funds to sponsor research, but **OSHA is likely the first agency to come up with actionable requirements for firms regarding safety standards affecting the use of nanoparticles in the workplace.** While there does not appear to be any major developments in the pipeline, we expect a round of NIOSH research to be ready within the next several months and that could result in OSHA rule development. Studies on the propensity for carbon nanotubes to form an aerosol while being handled and the toxicity of nanotubes were recently published. The following is a list of studies underway. Representatives of NIOSH expect a few of these to be **finished in the very near future.**

**FIGURE 25** National Institutes of Occupational Health and Safety H&S Studies Underway

### Current Projects of the NIOSH Nanotechnology and Health & Safety Research Program:

Generation and Characterization of Occupationally Relevant Airborne Nanoparticles
Pulmonary Toxicity of Carbon Nanotube Particles
Role of Carbon Nanotubes in Cardio-Pulmonary Inflammation and COPD-Related Diseases
Particle Surface Area as a Dose Metric
Ultrafine Aerosols from Diesel-Powered Equipment
Monitoring nanoparticle exposures with respect to aerosol surface area concentration.
Risk assessment for nanoparticle exposure
Bypass leakage, and nanoparticle recirculation in the workplace
Surface activity of inhaled particles
Evaluating occupational nanoparticle exposures
Characterization and control of beryllium ultrafine aerosols
Characterizing metallic nanoparticles from diesel combustion
Ultrafine particle intervention studies in automotive plants

Source: NIOSH

### **2006 Update**

On August 8, 2006, NIOSH posted a document which intends to review what is currently known about nanoparticle toxicity and control. The document listed several potential health and safety concerns, including precautionary measures regarding worker exposure. The document serves to exchange information that may prevent material impairment of safety or health as nanotechnology develops.

## **Regulatory Outlook: International**

Europe is decidedly more emphatic about the use of precautionary principle in reference to nanotechnology. To date the consensus in Europe appears not to be centered on whether nano-materials should be regulated, but rather when and how they will be regulated. The European Framework Program on Research and Technological development has already developed a formal outline of pre-existing regulation that could be applicable to nanoscience. There has already been a formal request to the European Union Senior Toxicology Committee to have nanomaterials regulated.

The following is our updated information on the European regulatory landscape:

### **U.K. Department for Environment, Food, and Rural Affairs (DEFRA)**

In September 2006, DEFRA announced its Voluntary Reporting Scheme, an initiative aimed at addressing any potential risks posed by the products of nanotechnology. Industry, research organizations, and other stakeholders may provide DEFRA with information on the nanomaterials they are using. The initiative will provide information on the potential risks that these materials may pose to the environment and human health. Currently, the Scheme is voluntary and has been given a two year time frame.

### **European Union**

In September 2006, the European Parliament rejected a recommendation from its Committee on Industry, Research, and Energy for certain nanomaterials to be subject to rigorous safety checks foreseen in the pending REACH legislation. Members expressed concern that due to the size of the particles, there would be room for exemptions given the threshold defined by REACH. However, lawmakers endorsed the committee's view that the understanding of potential damage to health and environment by nanomaterials is limited and should be investigated, in accordance with the precautionary principle, before such particles are put into production and placed on the market. Attention to safety is expected to receive additional emphasis in both the 7FRP and nanotechnology action plan.

## Unanswered Questions

We understand that as many as 17 carbon nanotube structures and other particles have been submitted for review as a new chemical under EPA TSCA Section 5. We think that this may have implications for other CNT companies, but it will depend significantly on the specific characteristics being submitted for and this could leave room for speculation. Moreover approximately 17 general nanotech submissions may currently be going through some sort of TSCA review.

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### Fundamentally new characteristics

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It is widely recognized that particles at the nanoscale do not adhere to the principles of classical physics. This suggests the existence of a particle with fundamentally new characteristics that need to be screened as *new chemicals*. We continue to identify firms that appear to be interpreting their product as being a preexisting chemical and we wonder what liability this may represent should research underway reveal a specific risk regarding nanoparticles that have been submitted in this way as opposed to the new chemical review process.

Investors may consider that regulation may not be the only necessary protection for firms, particularly given the number of cases like MTBE (methyl tertiary butyl ether) that have occurred over the years. Hazards were identified in 1954 but MTBE was approved by the US Environmental Protection Agency in 1991. The clean up of MTBE in water systems has been estimated to be in the range of \$25-\$85 billion according to American Water Works Association (AWWA). We identified a few firms that set their own internal moratoriums on certain types of particles because early analysis led them to believe there would be risks. It may be relevant to inquire about this when conducting due diligence.

## 6 Product Stewardship

The following list of best practices that may be of relevance in evaluating a firm's ability to prepare for potential perception issues and new developments in the scientific and regulatory landscape.

### Testing

Testing of the nanoparticle in question may represent the most proactive and given the extreme expense of providing "extra" particles for research, perhaps the most costly option that can be undertaken by a firm.

#### Agency

Some companies are teaming up with the National Institutes of Occupational Health and Safety (NIOSH) to take part in the establishment of regulation and standards. This may involve the donation of nanoparticles for use in research and some companies are providing information to NIOSH and/or other agencies about lab and operational procedures for study and evaluation.

#### University

Companies that team up with universities may have the opportunity to offset the expense that might otherwise be incurred by contracting with an independent testing laboratory. The results are mutually beneficial and help to build the body of publicly available data on the EHS implications of nanotechnology – something that ultimately benefits all companies. Some companies that we interviewed explained that working with universities may also have the side benefit of reducing toxicity testing costs. In this case the primary cost is related to providing batch particles for study.

#### Independent

A few firms have paid independent laboratories to analyze the particle in question. Our research shows that this is indeed a costly option and the results are private. Given the expense, this may be relevant to the evaluation of cash flow for a pure-play company. This may also indicate the level of priority that a firm has placed on responsible development. Companies targeting sensitive markets such as the UK and European Union may feel added pressure to submit structures to a lab even if they are relatively certain that there are minimal risks. Examples of two firms that are providing these services are Harlan Laboratories and Intertek Group plc.

#### **Companies that have had their products tested include**

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- |                           |              |
|---------------------------|--------------|
| » Altair Nanotechnologies | » Nalco      |
| » DuPont                  | » ApNano     |
| » Carbon Nanotechnologies | » Starpharma |
-

## Disclosure

A variety of laws and regulations in both Europe and the United States could be interpreted as being relevant to the enforcement of disclosure about nano related risks. Sarbanes Oxley's Management Discussion and Analysis, Rule S-K 303 is a likely candidate in this respect. Under S-K 303, companies are:

- » **Required to provide historical and prospective analysis of the financial condition and results of operations**
- » **Required to disclose any known event or uncertainties known to management reasonably likely to have a material effect on the financial condition or operating results.**

It is widely recognized that SK 101, 103 and 303 require the reporting of information about operational risk such as environmental issues. This may include information on climate change, site contamination or chemical product liability. The large majority of firms across all three sub-sectors of the chemicals industry have begun to comply.

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Stakeholders request a full disclosure of life cycle implications.

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At this early stage, any level of transparency about nanoparticles in use would be considered highly proactive. Investors may note that several companies have opted to provide basic chemical composition, structure and size information relating to the particles in use. Going forward, the scenario could change, particularly if there is an incident (note that certain nano powders can be explosive) or dramatic finding. We heard from several stakeholders that it would be desirable for firms to provide information about the entire life cycle of the product in question.

### **Companies currently disclosing particle information:**

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- » **BASF AG**
  - » **Altair Nanotechnologies**
  - » **Headwaters**
  - » **Most of the carbon Nanotube companies**
- 

## Life Cycle Analysis

In the case of nanotech, a notable benefit stems from a detailed understanding of where potential liabilities may lay in production, use and disposal. In certain markets such as Japan and the European Union this is an increasingly relevant concern as new statutes require companies to take responsibility for their products at all stages. Innovest specializes in assessing the financial exposure to companies related to these regulatory changes.

To date, only a few life cycle assessments (LCAs) on nanotechnologies have been completed. Although few LCAs have been completed, others are underway or are in the early stages of development<sup>40</sup>.

We note that the NGO community is placing a particular priority on encouraging firms to disclose the results of the LCA to the public as part of their fiduciary reporting requirements. Discussion has centered on whether aspects of Sarbanes-Oxley could be interpreted as requiring this.

We have identified approximately 11 companies in our analytical set who are likely to have conducted some sort of LCA on their products. In some cases this is because the company has a standing policy to conduct an LCA as an inherent aspect of the innovation strategy. Contact the analyst for further information.

## Operational Quality

We noticed that a few companies in our analytical set appear to be announcing their affiliation with the Good Laboratory Practice standards of the European Union as part of their nanotechnology marketing platform. The GLP is essentially a “seal of approval” that certifies the results of lab data. This will be particularly important for companies that may need to submit structures to European regulators. A few examples of GLP certified companies include: ApNano and BASF AG.

## Small Business Innovation Research

Investors may want to look for pure-play companies that are recipients of the Small Business Innovation Research grant. The program is competitive and is designed for innovative projects that have strong commercialization potential. So far, of the 75 companies that we reviewed, Altair Nanotechnologies is one of three recipients of an SBIR grant in our analytical set. The company was awarded both a Phase I and Phase II grant that in total provide an estimated \$550,000. At minimum, the SBIR indicates that a set of government selected reviewers consider the company’s efforts to be scientifically and economically promising. At present, there are no requirements that firms receiving Phase II SBIR grants submit information regarding EH&S practices. Nanomix and Nanosolar are also recipients.

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<sup>40</sup>“Analysis of Nanotechnology from an Industrial Ecology Perspective.” Lekas, Deanna. Yale School of Forestry & Environmental Studies. 26 May 2005.

## Teaming up with Environmental Defense – An Update

Environmental Defense (ED) is an NGO that specializes in developing beneficial partnerships with companies in order to establish best practice and disseminate such data to other companies dealing with similar issues. Partnerships have been formed in the paper, chemicals, utilities and other sectors.

Following ED's announcement of its intentions to work in the area of nanotechnology in 2005, it has since launched its cooperative program. Due to the complexity of the task at hand, ED has elected to initially collaborate with only one company, DuPont to identify of risk, establish best practice, and monitor performance for responsible nanotechnology development. The partnership is intended to result in a process that's viable for companies, NGOs, academics, and government with a final goal of providing a model for government policy. Throughout this process feedback is solicited from a variety of representatives from the stakeholder groups mentioned above. The first draft of this framework is expected in the first quarter of 2007 and the last draft expected later that year.

Due to the scale of the industry, some believe that such agreements fundamentally undermine the ability to push through more formal regulations. Concerns were previously raised about the ability of such programs to reach all players. The common complaint is that such one-off agreements can only reach a small fraction of the existing and potential nanomanufacturing base. However, through the feedback that Environmental Defense continues to solicit, a large number and type of organizations have been involved and modifications to the framework have been made accordingly.

## HPV

A company's faithful adherence to the High Product Volume (HPV) program can be an indication of how transparent a firm will be with regard to nanomaterials manufacture. HPV is a voluntary reporting system established in 1998 to encourage companies to submit structures in order to increase scientific understanding of the toxicity implications of the more than 2,200 chemicals currently on the market. At the time, more than 70% of top-volume commercial chemicals lacked publicly available screening data. Companies make voluntary commitments to the program in order to contribute to the body of knowledge regarding inorganic chemicals and their toxicology profiles.

There is wide variance in on-time submission of robust summaries to the HPV program and there are many "orphaned" chemicals. Note that BASF was rated by Environmental Defense as being in the top ten performers in submitting robust

summaries on time in 2003 while 3M and General Electric were classified among the 10 worst submitters<sup>41</sup>.

## Environmental Certification

Nanophase Technologies Corporation (NANX-Nasdaq), which specializes in nanomaterials and nanoengineered products and which is a major supplier of titanium dioxide nanoparticles to BASF, recently announced that it has been certified as having met the international standards of ISO 14001:2004. This is a very general audit of overall environmental managerial capacity. It is highly unlikely that the audit was conditioned to be specific to nano-oriented production. However we understand that ISO is in the process of forming convention on responsible nanotechnology development. When this happens, companies like Nanophase will be in good standing with regard to their next audit.

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<sup>41</sup> Environmental Defense On the internet: [http://www.environmentaldefense.org/documents/2685\\_HPVBestandWorstFinal.htm](http://www.environmentaldefense.org/documents/2685_HPVBestandWorstFinal.htm)

## 7 Conclusions

### Knowledge is Power

Investors are gearing up, and venture capital spending is expected to recover by end of 2005. Comparisons between nanotech and the advent of the information technology era abound. But the analogy is not exact. Product safety was not a concern for software. Investors need more information.

- » Most companies we spoke with expressed concern over the fact that so little priority has been placed on toxicity research by the National Nanotechnology Initiative.
- » What we do know is that a number of toxicology studies are scheduled for completion in 2007. The results will hopefully provide better information allowing investors to make more informed decisions about which technologies are safe for investment. At minimum, the information may point to questions that need to be asked.
- » Currently the focus is on fullerenes, carbon nanotubes, dendrimers, quantum dots and nanowires. The analysis of risk is complex involving many parameters. It should be undertaken on a case-by-case basis with an understanding of production processes, product use and end disposal.
- » In many instances there are mitigating factors that reduce the relative risk of a product. For example, Rice University's Center for Biological and Environmental Nanotechnology (CBEN) has revealed that it can minimize the reactivity of particles with functionalized surfaces by coating the particle<sup>42</sup>.
- » Detection of particles in production, and potentially in the environment, is critical to the safety issue. Companies engaged in providing detection technologies will be sound investments.

### Perception and Market Development

Perception of the risks of nanotechnology is mostly limited to the academic community and policy makers at this stage, but the possibility of public backlash cannot be completely discounted.

- » Companies have a role in working to offset the potential for perception issues to impact markets.
- » Transparency, involvement in the science and a commitment to product stewardship are important indicators of corporate quality.
- » People may be more willing to accept risk if nanoscience yields the right products now. This means renewable and clean energy technology, resource efficiency, clean water and vaccinations.

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<sup>42</sup> "Rice University Researchers Reduce Toxicity of Water Soluble Buckyballs by 10 Million Times." On the Internet: <http://www.Azonano.com>. Posted 24 September, 2004. Retrieved 6 June, 2005.

## Regulation

- » A significant portion of the more than 60 companies we interviewed indicated an interest in having some sort of standards in place. In many cases, they felt that science-based regulation would provide a more level playing field. The lack of adequate funding for toxicology research is, again, an issue here.
- » Looking at the international picture, the rapid response to the possible risks of nanoscience has prompted a movement toward standards development and establishment of nomenclature.
- » Off the record conversations with regulators indicate that Europe, the UK and China are expecting to have some sort of binding requirement for companies within the next 2 to 4 years. China clearly states that its standards were designed to create a robust foundation for nanotechnology development in that region and they expect their standards to impact the competitive landscape for nanotechnology.
- » A regulatory timeline for the US is less certain given what appears to be a concerted effort by the legal community to exhaust all existing statutes. This is very similar to the way that U.S. regulators dealt with genetically modified crops and food. With regard to nanotechnology, the U.S. is gearing up for the initiation of a voluntary reporting scheme. Investors may note a growing level of discord regarding this option.
- » We continue to monitor the possibilities for risk related to the fact that a few nanotechnology companies may have already improperly interpreted existing law.

## Investors Play a Role

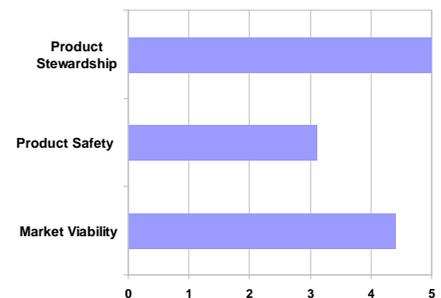
- » We strongly support calls made by others in the investment community for increased government funding of toxicology research. The NNI's lack of priority for this issue represents a missed opportunity to minimize uncertainty.
- » There is always a fine line between lax policy development and market chilling risk aversion. Counter to intuition, our research shows that robust, science-based regulation can contribute to healthy market development.
- » We interviewed 12 venture capital firms specializing in nanotechnology. Very few of them indicated adequate attention to this aspect of due diligence. To the extent that a given environmental, health or safety issue can delay commercialization or result in perception issues and/or latent product liability, we believe that asking the right questions will be important.
- » Responses to these questions may reveal hidden value, particularly for development stage firms.

## 8 Profiles of Index Constituents

### Altair Nanotechnologies, Inc.

<b>Country</b>	United States
<b>Ticker Symbol</b>	ALTI
<b>Industrial Sector</b>	Specialty Chemicals
<b>Combined IVA Rating</b>	N/A
<b>Sub-Factors</b>	
<b>Market Viability</b>	4.4
<b>Product Safety</b>	3.1
<b>Product Stewardship</b>	5.0
<b>Analyst</b>	Heather Langsner (646) 237 0212 hlangsner@innovestgroup.com

#### Sub-Factor Performance



#### Rating Outlook

We recently sat down with management and posed some questions about the future of Altair's business model. Our interests have been mainly centered on the high value added product lines as opposed to the titanium and pharmaceutical/verterinary applications. While Altair is seeking to capitalize in the nearterm on these units, the long-term view is that the company will eventually want to spin those activities off and will concentrate on just the battery business.

Followers of our nanotechnology index know that we took an early position on Altair Nanotechnologies (Nasdaq: ALTI) in 2005. The company has suffered from previous years with inefficient and lackluster management. However in September of last year, we met with ALTI's management and began to work out a different picture on the company. Investors may note that Motley Fool and Lux Research have also just recently begun to change their tone regarding this stock. We will go one step further. First, the company's Nano Titanate battery resolves the lithium ion battery dilemma over safe operating temperatures. This is not news for us. We detailed ALTI's battery advantages in our report last year. This information has been reiterated by the company in light of recalls made by Dell and Apple last month. The company is likely to announce that it will be raising more funds. Normally this would be taken as a bad sign, however, in our view the company needs to do this in order to fill orders for its battery technology. Two deals are in the works that may see a ramp up in auto battery orders that require the company to scale up and even outsource production in the near term. We remain positive about a two month projection based on the company's success in promoting its cleantech offerings, however investors may note that the company's burn rate is still quite high.

While we continue to monitor the possibility that toxicology studies on nanoparticulate metal oxides underway could impact Altair's model and while certain applications ready for commercialization give us pause, ALTI has consistently come out in front of the nanosafety issue since the arrival of CEO Dr. Alan Gotcher who has testified before Congress on this issue. The company is known for standard setting performance in the area of transparency, risk management and product stewardship. The company's business model is based on a diverse range of product platforms (too many in our

estimation) but the company has revenue coming from research grants and Department of Defense funding and is one of the few public nano pure-play companies focusing on cleantech product applications. ALTI provided complete particle information and has submitted particles for testing through academic institutions and governmental agencies. Finally, the company displays a competitive approach to operational quality and information sharing regarding possible nano-oriented risks relative to other companies in the analytical set.

## Company Overview

ALTI is an industrial nanotechnology company that specializes in developing and commercializing nanomaterial and titanium dioxide pigment technologies. It also has collaborative ventures with industry partners and leading academic centers which have allowed them to pioneer an array of intellectual property and products. Most of the company's existing products, potential products and contract research services are built upon its proprietary nanomaterials and titanium dioxide pigment technology.

ALTI is applying its proprietary development platform to two divisions: life sciences and performance materials. The Life Sciences division is pursuing market applications in pharmaceuticals, drug delivery, dental materials and other medical markets. The Performance Materials Division is pursuing market applications in advanced materials for paints and coatings; titanium metal manufacturing, catalysts, air and water treatment, and alternative energy including advanced battery electrode materials.

Currently the company has three different revenue streams: research contracts and grants, commercial collaborations, and licenses, royalties and product sales. Year 2004 sales of \$1.15 million increased due in part to a commercial collaboration with Titanium Metals Corporation funded by the Department of Defense, a license agreement with Western Oil Sands and a grant from the National Science Foundation (NSF). The top institutional investors with positions in ALTI are Barclay's Global Investors, Hussman Econometrics Advisors, Hauck & Aufhäuser Investment Gesellschaft S.A., Merrill Lynch & Company, Inc., Vanguard Group, Inc., and Gabriel Capital L.P. ALTI holds over 30 patents and has more than 50 pending. The company has 43 employees.

## Market Viability

ALTI has the ability to minimize perception risk for nanotechnology products because of management's focus on environmental applications and an above average commitment to sourcing manufacturing technology that minimize environmental impact. ALTI has six platforms that are divided evenly between the two divisions. In the Life Sciences division, ALTI's three platforms include: pharmaceutical drug candidates, controlled chemical delivery systems, and biocompatible materials. The Performance Materials division has many applications targeting the cleantech market. The three platforms include: advance materials, water and air purification, and materials for advanced energy. The current status of the market viability for each division is described below.

### Pharmaceutical Drug Candidates

The Company has licensed a drug candidate, RenaZorb™, to Spectrum Pharmaceuticals and states that it is receiving milestone payments. The target market for this drug is patients with end-stage renal disease (ESRD), a \$600 million market, which is expected to grow to over \$1 billion in the next four years because of increasing evidence that earlier prevention of high blood phosphate slows the progress of renal failure. Spectrum Pharmaceuticals is completing testing and seeking approval from the FDA for commercial use in humans. The drug may also be used for cats and dogs as 21 million suffer from renal disease worldwide. This untapped market is estimated to be in excess of \$100M per year. The licensing and commercialization of Renalan for animal indications is currently underway.

### **Chemical Delivery Products**

For the chemical delivery platform, ALTI's TiNanoSphere™ product is targeting drugs with (a) poor bioavailability and (b) which need to be introduced into cells to effect their therapeutic action. Treatments that require targeted delivery are cancer therapies and vaccines. This platform is being tested by third parties and is expected to be a long-term project for the company.

### **Biocompatible Materials**

This platform consists of dental materials and prosthetic coating materials. The dental material, made of a nanozirconia, is expected to be commercial by next year whereas the orthopedic implant coating materials that stimulate osteoblast growth should be commercialized within three years.

### **Advanced Materials**

This platform has applications for paints, coatings, sensors, and the production of titanium dioxide pigment utilizing the Altair Hydrochloric Pigment Process (AHP). The company is completing a Phase I feasibility study for Western Oil Sands to produce titanium dioxide from tar sand tailings. They are also in discussions with other companies and should have licensing agreements by year's end. ALTI has a collaboration agreement with Titanium Metals Corporation, TIMET, (NYSE:TIE) which requires them to supply their TiO<sub>2</sub> micro porous electrodes for titanium metal production using the FFC process. They are currently shipping materials to TIMET. Finally, ALTI produces thermal spray grade powders. They are currently supplying nominal amounts of their TiO<sub>2</sub> coating materials to F.W. Gartner and are in early stage discussions with several companies for their yttria stabilized zirconia coating powders.

### **Air and Water Purification Systems: Air**

ALTI has a strategic alliance with Genesis Air to supply specialized surface-activated nano-sized titanium dioxide compounds for use in HVAC air cleaning systems, specifically Genesis Air's GAP Photocatalysis technology. This system is currently in 12 beta sites worldwide and is expected to be commercialized in the fourth quarter 2005. This application addresses a new, unique solution in the \$45 billion HVAC market.

### **Water**

ALTI's water purification system, NanoCheck™, removes phosphate (the food for algae) from water and has been in field trials for over one year. This product represents some potential for risk in our estimation and this would not be a relevant application for our index. However, the company demonstrates a leading approach to product stewardship and we will continue to monitor the potential for risk. Applications for this product include swimming pools and aquariums as it is effective in providing an algae-free environment. The company is currently in contract negotiations and expects to launch NanoCheck™ by the end of the year. This first NanoCheck product addresses a key problem of the 10 million plus installed recreational pools. Additional applications for NanoCheck range from treatment of aquariums to municipal water systems.

### **Materials for Alternative Energy**

ALTI is targeting the alternative energy market by producing 1<sup>st</sup> and 2<sup>nd</sup> generation Lithium Ion Battery Electrode Materials and Hydrogen Generation Electrode Materials. The company has a development partnership with Advanced Battery Technologies where the batteries are in Phase II testing. ALTI expects its partner, Advanced Battery to have the batteries using Altair's battery materials commercialized within Q4 2005 to Q1 2006 and in road test in electric sedans and buses by the end of 2005. The company is also in discussions with battery manufacturers, providers of battery material, and companies within the automotive industry concerning their technology. The company is halfway through a Department of Energy (DOE) sponsored program with UNLV on a hydrogen filling station project and has produced nanometer scale metal oxide electrode films for use in a photochemical hydrogen generation device. These materials are a fundamental building block for the multi-billion dollar electric vehicle market.

## Product Safety

ALTI is cognizant of the potential risks and impact of regulation on their business and the company is taking a proactive approach by working with government agencies such as National Institute for Occupational Safety and Health (NIOSH) and the DOE as well as teaming with academic institutions to develop "best in class" documentation and procedures for nanomaterial production and handling.

The company has submitted particles opting for a new chemical designation under EPA chemicals regulation. This is critical as we found several firms that seem to be misinterpreting existing rules for submission. We continue to monitor the potential for risk for those firms since those products are now commercially available and have not undergone a thorough review.

## Product Stewardship

ALTI appears to be a market leader in the area of product stewardship, representing one of the few transparent companies we screened. Their proactive approach towards product stewardship is likely to yield real value in the future as they are better prepared to deal with a possible binary event, market freeze, or regulatory change. They also stand to have global acceptance and market reach due to the use of the precautionary principle. When interviewed, CEO Dr. Alan Gotcher spoke to every issue; disclosure, life cycle analysis, testing, operational quality, and small business grants, we examined in this area of our due diligence.

## Disclosure

Altair Nanotechnologies sets the standard for disclosure. The company provided the chemical formula, structure, and particle size for each of their platforms. While many pure plays selling particles such as carbon nanotubes provide particle characteristics, the companies applying particles to products were reluctant to provide this information. More importantly, ALTI is also providing particles and characterization information to governmental agencies and academic institutions.

## Life Cycle Analysis

While ALTI is cognizant of the need for Life Cycle Analysis (LCA), this remains an area for improvement as the company is currently relying heavily on its partner companies to perform this task. Innovest research heavily weights for LCA performance and will be looking for ALTI to enhance operations in the future by conducting thorough LCA's on their products. We do note that the company is working with partner firms to conduct efficiency review in the supply chain.

## Testing

ALTI has opted to submit particles to NIOSH for exposure and toxicity testing. By doing this the company may be bypassing the added costs associated with contracting with independent testing facilities.

## Operational Quality

ALTI has invested in closed system manufacturing to produce high-quality, controlled particles. Note that other companies in the analytical set are struggling with these issues. CEO, Dr. Alan Gotcher, is staying abreast of any potential problems with worker and customer safety and industrial hygiene through collaborations with academic institutions. Due to the company's concern for industrial hygiene and the nature of the manufacturing process, the exposure risk to employees should be minimal. Given the company's proactive approach to stewardship and an operational quality, it is expected that the company can minimize any general exposure issues that may be specific to commercial production of nanomaterials.

## Small Business Innovation Research

ALTI was just awarded its second SBIR grant of over \$470,000 provided by the NSF. The company is using the grant money for continued development of nano-structured electrodes for the next generation of batteries and super capacitors.

**FOR PROFILES ON THE OTHER INDEX CONSTITUENTS AND RESEARCH  
GROUP OF PRIVATE FIRMS, PLEASE CONTACT HEATHER LANGSNER AT  
212 421 2000 EXT 212**

## 9 Explanation of Analytical Set

Our research focused on 200 publicly traded companies and 100 private companies listed on NanoInvestorNews.com.

We identified all the companies in this universe that had corresponding Innovest ratings and made sure that all companies listed on the Lux Nanotech Index™ were also included on that set. Lux is an internationally recognized leader in nanotechnology research. The ("Index") is a modified equal dollar weighted index comprised of 26 publicly traded companies which seeks to measure the performance of securities in the nanotechnology field. The Index was created by, and is a trademark of, Lux Research, Inc. The American Stock Exchange serves as the calculation agent for the Index.

To be included in the Lux Index, components must meet the following eligibility requirements:

- » **Be listed on the New York Stock Exchange or American Stock Exchange, or quoted on the NASDAQ National Markets or Small Cap Market systems.**
- » **Have a minimum \$75 million market valuation.**
- » **Have a minimum average daily trading volume over the preceding three months of 50,000 shares.**

We held our universe to different criteria:

- » **We matched the Innovest coverage universe with the list of the 200 publicly traded companies listed on NanoInvestorNews.com. Of that set, we selected for our AA and AAA firms.**
- » **The list of publicly traded and private companies was also subjected to an intensive search for firms offering strategic profit opportunities in the fields of water technology, renewable energy resources and innovations relevant to large scale medical needs.**
- » **A list of 75 companies were contacted and interviewed. The non-response rate was approximately 2%.**

Companies meeting our criteria for product strategy, risk management and product stewardship were eligible for the index.

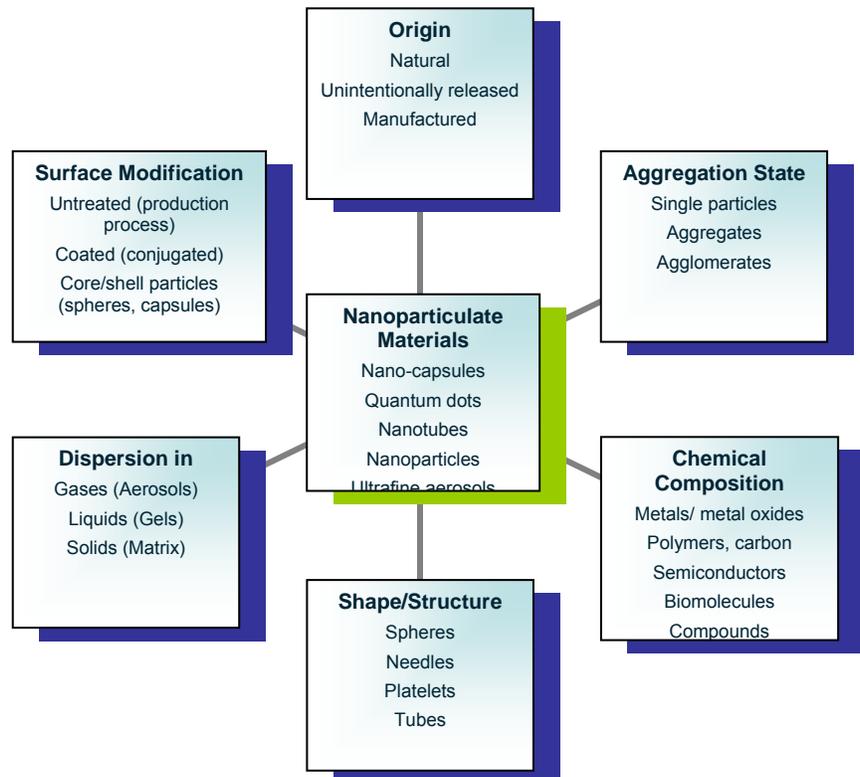
Ten private development stage companies were also selected for their cleantech applications. Innovest will monitor their progress over time and update coverage in 2006. In the interim, comparative analysis will begin in the Aerospace/Defense, Chemicals, Semiconductors, Pharmaceuticals, Biotechnology, Healthcare and Equipment, Personal Care and Household Products sectors.

## 10 Appendices

### Appendix 1: Characterization of the Nanoparticle

Unlike established chemical assessments, nanotoxicity is different and more complex. The important characteristics to identify and assess in bulk engineered nanoparticles are **structure, surface, and size** along with traditional chemical parameters of volume and life cycle analysis. Variation in these three characteristics impacts toxicity requiring toxic assessments to be done on a **case by case basis**. This is not only burdensome but also expensive for companies (impacting their cash burn rate) and governments. Furthermore, the physical or chemical property that is most closely correlated with toxicity and therefore should be measured is unknown. Figure 22 below categorizes the various parameters for nanoparticle characterization.

FIGURE 26 A Look at The Relevant Parameters for Characterization of Nanoparticulate Materials.



Source: Future Technologies Division of VDI Technologiezentrum GmbH<sup>43</sup>

Currently, toxicity assessments are being conducted in university laboratories and governmental agencies throughout the world. In examining the existing body of research, it does appear that some nanoparticles are more toxic than others. However, the research has also shown that altering the size, the surface or the structure can significantly impact the toxicity<sup>44</sup>. Moreover, particles can be coated with other substances to reduce reactivity. Based on this current information, proper characterization of nanoparticles is likely to be a long and expensive process.

Globally accepted nomenclature and characterization standards are currently being addressed by a consortium of scientists, regulators, and governmental

<sup>43</sup> Luther, Wolfgang. Industrial application of nanomaterials chances and risks: Technological Analysis., August 2004.

<sup>44</sup> Warheit, David. "Nanoparticles: health impacts?" Materials Today. February 2004.

agencies from around the world to assist in toxicological identifications and regulatory frame working. Acceptable identification and characterization standards are also under construction and should be set within one year. Some companies, such as ApNano, are anticipating the risk associated with particle characterization and are mitigating it by having independent laboratories complete EHS screenings and particle identification on their products.

The figure below is an outline of the characterization needs to thoroughly assess nanoparticle toxicity going forward.

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**FIGURE 27** The future characterization needs of nanoparticles

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**A group of science experts discussing characterization of nanoscale materials at the University of Florida suggests the following characteristics are needed to assess toxicity:**

**Ex vivo**

**Physical:** size, shape, surface area, surface porosity, roughness, morphology (agglomerate vs. primary particles, stability of agglomerates), crystallinity, magnetic properties

**Chemical:** stability (dissolution), chemical composition, surface chemistry [zeta potential, acidity/basicity, redox potential, functional groups, reactivity (catalysis, redox, and photosensitivity)]

**In vivo**

Images, dispersibility, dosage (number density for materials with narrow size distribution; mass dosage for materials with wide size distribution)

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Source: NanoTox Workshop<sup>45</sup>

## Appendix 2: Detection Methods Available

The nanoparticle detection and quantification methods needed to determine workplace exposure levels and risks are not available because current detection, quantification, and characterization equipment is not applicable to large scale production or manufacturing systems. Detection methods for gases and solids are needed to address workplace exposure issues while detection methods for liquids are needed to assess biological tissue and living organism exposures.

Companies, such as NanoSight and Nanomix, which are beginning to enter the detection and nano instrumentation businesses show promise in expediting exposure information. NanoSight, Ltd. has recently launched a nanoparticle

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<sup>45</sup> Final Report: Developing Experimental Approaches for the Evaluation of Toxicological Materials. NanoTox Workshop. November 2004.

detection instrument that should enable rapid and cost effective detection and analysis of nanoparticles. This appears to be a high growth area for nano companies due to the need for workplace exposure reduction as economies of scale improve and more companies begin manufacturing nanoparticles and commercializing nano-products.

**FIGURE 28** Nanoparticle measurement parameters and techniques

Parameter	Measurement Techniques
Number concentration	Condensation Particle Counter (CPC)
Particle number and number-weighted particles size distribution	Scanning Mobility Particle Sizer (SMPS) Electrical Low Pressure Impactor (ELPI)
Submicron particle surface area	Epiphaniometer Diffusion Charger
Size, morphology and surface properties	Scanning Transmission Electron Microscopy (STEM) High Resolution Transmission Electron Microscopy (HRTEM) Scanning Near-field Optical Microscope (SNOM) Atomic Force Microscopy (AFM)

Source: Future Technologies Division of VDI Technologiezentrum GmbH<sup>46</sup>

The following is a list of companies commercializing the equipment that may be relevant for future detection needs: FEI Co, Veeco Instruments Inc., Symyx Technologies Inc., JMAR, Accelrys Inc, MTS Systems Corp.

## Appendix 3: Potential Exposure Routes of Nanoparticles

The possible routes of human exposure to engineered nanoparticles include inhalation, contact with the skin and mucous membranes, and ingestion. The

<sup>46</sup> Luther, Wolfgang. Industrial application of nanomaterials chances and risks: Technological Analysis., August 2004.

respiratory system and intestinal tract would act as transporters of foreign objects whereas; the skin would attempt to provide a barrier to a foreign object. Environmental dispersal routes include the air, land, and water. An interaction linking environmental exposure with human exposure may be possible through bioaccumulation in the food chain.

### **Inhalation Exposure**

Any product that may release nanoparticles into the air either in the finished product or manufacturing phase is susceptible to liability dealing with inhalation. Many of these products are already in the market place and include disinfectant and air-freshener sprays, paints and dyes, coatings, textiles treatments, and sprays for porous materials such as woods and clays.<sup>47</sup>

***Nanometer particles caused an increased inflammatory response, pathological response, and may have different distributions relative to larger particles in the lungs.***

- » **The respiratory tract and the lung are the major targets for nanoparticle-induced effects following inhalation exposure but particles can also be inhaled through the nose.**
- » **The lungs consist of airways and alveoli, with the alveoli being more susceptible to environmental damage due to their large surface area and intense air-blood contact. The alveoli would also be the location of nanoparticle transportation into the blood stream. Rat studies show exposure to the brain via the olfactory nerve.<sup>48</sup>**
- » **Size Matters: Particles smaller than typically 10 nanometers can penetrate to the deepest parts of the lungs. Penetration to the deepest parts of the lung is > 50% for particles smaller than 4 µm.**
- » **At a size less than 4 µm particles can reach the alveoli.**
- » **Fibers, with small diameters can also penetrate the deep lung.**
- » **Published studies on the inhalation of ultra fine particles suggest that *size is a determinant of reactivity in the lungs*<sup>49</sup>**
- » **A large body of evidence, in rats, indicates that *nanometer particles of a given composition are more potent (in mass terms) than micrometer particles in inducing pulmonary toxicity.*<sup>50</sup> Potency was equalized when surface area instead of mass was the metric of measurement.**

Surface Area and Chemical Reactivity Matters: Under overload conditions, large surface area of nanoparticles may overwhelm phagocytes, the cells responsible for eliminating foreign objects from the lungs, and trigger a stress reaction which increases inflammation in the surrounding tissue.

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<sup>47</sup> Hett, Annabelle. Nanotechnology: Small matter, many unknowns. Swiss Reinsurance Company. 2004.

<sup>48</sup> Oberdörster, Günter. "Extrapulmonary translocation of ultrafine carbon particles following whole-body inhalation exposure of rats." *Journal of Toxicology and Environmental Health*. 2002.

<sup>49</sup> National Toxicology Program Headquartered at the National Institute of Environmental Health Sciences. "Fact Sheet." 2005.

<sup>50</sup> Nanoscience and nanotechnologies. Chapter 5. The Royal Society & The Royal Academy of Engineering. July 2004.

- » **Generally speaking, increased inflammation, particle accumulation in the blood, DNA damage, and oxidative damage could conceivably lead to arteriosclerosis (blood clotting)**
  - » **Research has shown that both nanospheres and carbon nanotubes may increase blood clotting after exposure.<sup>51</sup>**
- » **Surfaces of some nanoparticles may be able to generate oxidative stress on cells or organs.<sup>52</sup>**
- » **Some nanoparticles will generate free radicals that can damage DNA.**
- » **Variations in surface treatments may cause differences in pulmonary inflammation but this research has not yet been peer reviewed.<sup>53</sup>**
  - » **Lung diseases attributed to poorly soluble particle exposure, which may apply to nanoparticles, include: *pneumoconiosis, bronchitis, emphysema and asthma.***
  - » **Another health effect not seen in micrometer particle exposure that is related to inhalation exposure at the nanometer scale is 'fume fever'. This acute condition is associated with exposure to freshly formed metal fumes. The systemic response typically resembles influenza-like symptoms that develop a few hours after exposure**

### Surface Contact

A heightened level of caution may be necessary with regard to products that will come in direct contact with the skin either during use or manufacturing. Once again, many of these products are already in the marketplace, including: cosmetics, suntan lotions and silver coated wound dressings.

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...surface modification creating a fullerene derivative had substantially less toxicity.

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- » **Water-soluble fullerenes have shown to be toxic in small levels to both human skin and liver carcinoma cells, whereas, surface modification creating a fullerene derivative had substantially less toxicity.**
- » **Again some particles may be able to penetrate the skin and if the particles or radicals can enter cells, could cause damage to DNA.**
- » **Based on limited toxicology studies, titanium dioxide has been approved in Europe for use in sunscreens whereas, zinc oxide which showed phototoxic results on cells and DNA, has not.<sup>54</sup>**
- » **NIOSH is currently conducting research on the permeability of engineered nanoparticles with skin. The study should be finished by April 2007. Other studies are taking place at the National Toxicology Program and the NANODERM project in Europe is also conducting research.**

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<sup>51</sup> <http://www.nature.com/cgi-taf/DynaPage.taf?file=/nbt/journal/v21/n10/full/nbt875.html>.

<sup>52</sup> Nanoscience and nanotechnologies. Chapter 5. The Royal Society & The Royal Academy of Engineering. July 2004.

<sup>53</sup> Warheit, David. "Nanoparticles: health impacts?" Materials Today. February 2004.

<sup>54</sup> Nanoscience and nanotechnologies. Chapter 5. The Royal Society & The Royal Academy of Engineering. July 2004.

## Ingestion Exposure

The products likely to be involved in liability surrounding ingestion exposure include most of the drug applications, drug delivery systems, imaging applications, and food enhancements. Unlike dermal and inhalation exposures, most of the products that involve ingestion exposure are not yet commercialized. Nanoparticles cleared from the lungs may also be swallowed, and enter the stomach.

- » **There are indications that manufactured nanoscale materials may distribute in the body in unpredictable ways, and certain nanoscale materials have been observed to preferentially accumulate in particular organs.<sup>55</sup>**
  - » **The spleen, the liver, and the kidney seem the most likely targets for nanoparticle accumulation.**
  - » **Once in these organs, the nanoparticles may not be cleared by normal mechanisms.**

## ENVIRONMENTAL HAZARDS

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Nanoparticle properties such as size, reactivity and mobility will likely create environmental exposure and risk related to nanoparticle transfer (which given their size, the transfer will be invisible) and potential environmental persistence. The environment may be exposed to free or fixed nanoparticles via the air, land or water (including ground water).

### Air

Release to atmosphere is one of the most likely scenarios. Nanoparticles have the potential to escape through filters during manufacturing and also have the potential for release at the end of the lifecycle when the products containing engineered nanoparticles are decomposing.

- » **The best scientific parallel to the hazards associated with air exposure is ultra-fine particles which are nanoscale or near nanoscale already present in the atmosphere.**
- » **Ongoing research suggests that ultra-fine particles increase air pollution, thus impacting climate change, and pose a danger to humans.<sup>56</sup>**
- » **Scientific research is associating increases in lung diseases and deaths to ultra-fine particle exposure.<sup>57</sup>**
- » **Currently, there does not appear to be any research into the impact or the potential for bioaccumulation of ultra-fine particles to living organisms besides humans.**

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<sup>55</sup> Colvin, Vicki.

<http://www.environmentalfutures.org>

<sup>56</sup> Nanoscience and nanotechnologies. Chapter 5. The Royal Society & The Royal Academy of Engineering. July 2004.

<sup>57</sup> *Ibid.*

## Land

Environmental exposure via land is likely to be associated with disposal of products containing engineered nanoparticles or the intentional use of engineered nanoparticles for land contamination treatment. There is a less likely chance that land exposure could come during disposal in the manufacturing phase.

- » **Some engineered nanoparticles are mobile creating the potential for widespread soil and land contamination.**
- » **Environmental risk is increased if the nanoparticles are not broken down in the ground or if the particles impair the vital role of bacteria.**
- » **It has been suggested by scientists that a few particles may be able to combine with pre-existing toxins and thereby increase the bioaccumulation of the toxin.**
- » **The limited amount of research conducted on bioaccumulation of engineered nanoparticles has shown the ability for certain nanoparticles such as carbon nanotubes, to penetrate the skin of worms and enter several other invertebrates.<sup>58</sup>**
  - » **These observations suggest the real likelihood of bioaccumulation of engineered nanoparticles.**
  - » **Nanoparticles of titanium dioxide are highly reactive and have been shown to kill bacteria in the soil.<sup>59</sup>**

## Water Exposure

All water sources, including ground water, have the potential for widespread nanoparticle exposure during every life cycle stage. Free nanoparticles used in applications such as drug delivery systems or food additives have the greatest potential of impacting water (Note: Many conventional pharmaceutical drugs are found in municipal water systems.)

- » **Several types of engineered nanoparticles appear to be non-biodegradable.**
  - » **For example, carbon nanotubes are completely insoluble in water and are biologically non-degradable.**
  - » **Studies also suggest buckey balls or fullerenes can cause harm to aqueous environments.**
- » **Nanoparticle properties are of significant importance to their environmental risk to aquatic ecosystems.**
  - » **They are highly mobile in aqueous environments.**
  - » **Their properties contribute to their ability to be absorbed, to form aggregates and to be accumulated in aquatic organisms.**

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<sup>58</sup> *Ibid.*

<sup>59</sup> <http://www.terressentials.com/nanotech.html>

- » In aqueous environments, many nanoparticles undergo agglomeration. If the particle aggregates with a toxin, the entire conglomerate could be toxic.

## Appendix 4: Nanoparticle Potential for Environmental Interaction

Nanoparticles may interact with the environment in three ways: absorption, aggregation, and biotic uptake.<sup>60</sup>

### Absorption

- » Many molecules will absorb to nanoparticles in various environments.
- » Biological interactions and bio-uptake may be influenced by these absorbed molecules.
- » Nanoparticles that penetrate cells will allow entrance of absorbed molecules.
  - » Toxins and other molecules unable to enter cells under normal conditions may be able to enter, thus causing the potential for toxicity and bioaccumulation.

### Aggregation

- » Nanoparticles may undergo aggregation in certain aqueous environments.
  - » Biological interaction with aggregated nanoparticles will be similar to bulk materials.
- » Aggregated nanoparticles that can enter the cell may cause extensive damage and induce cell death.

### Biotic Uptake

- » The surface of nanoparticles needs to be bound to cell-interacting or targeted molecules in order to interact with cells.
- » Nanoparticles may bioaccumulate if they are unable to be degraded or excreted.
  - » Most nanoparticles are not biodegradable.
  - » Studies have shown the ability of nanoparticles to enter lower level organisms, a threat for bioaccumulation.

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This raises concern about the ability of nanoparticles to combine with toxic chemicals already present in the environment increasing the development of bioaccumulative properties of the in situ toxic chemical.

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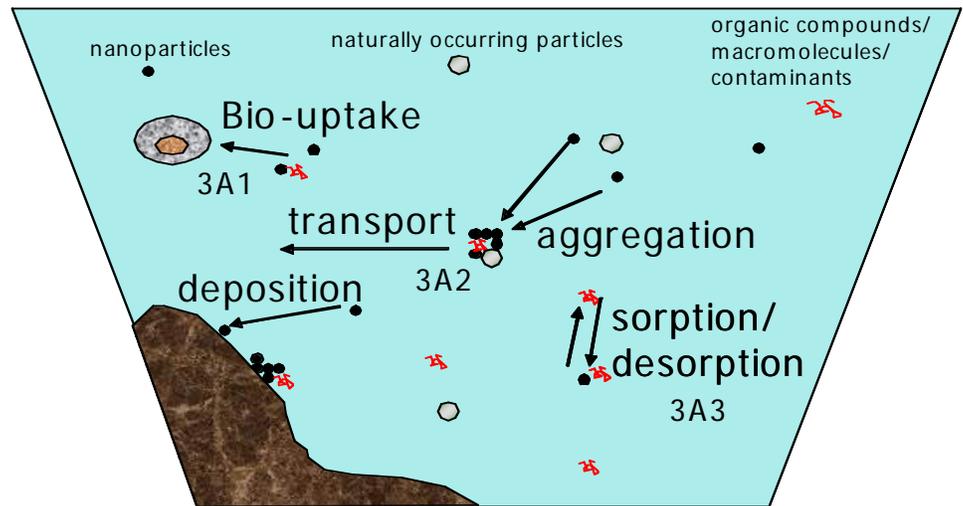
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FIGURE 29 Nanoparticles interactions with the environment

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<sup>60</sup> Colvin, Vicki. "Nanotechnology: Environmental Impact." Presentation.



Source: Dr. Vicki Colvin, Associate Professor, Rice University<sup>61</sup>

## Appendix 5: Overview of Regulatory Landscape

### UNITED STATES

#### Toxic substances control act

Enacted nearly 30 years ago, TSCA is the central law governing industrial chemicals.

TSCA authorizes EPA to screen and regulate “new” and “existing” chemicals.

Legal experts have identified several aspects of TSCA that can be interpreted as being relevant to the regulation of nanoparticles. These experts have also identified several reasons why attempting to do so might be problematic under current law. The following is a rough overview of the issues and possibilities for company confusion related to these statutes<sup>62</sup>.

#### TSCA Section 4 Testing

- » **The Low Volume Exemption is triggered in amounts exceeding 10,000 kg. This would obviously exclude many nanoparticle manufacturers.**

<sup>61</sup> *Ibid.*

<sup>62</sup> “Applicability of U.S. Environmental Laws to Assess, Applicability of U.S. Environmental Laws to Assess, Prevent, and Control Risks of Nanotechnology: TSCA.” Lynn Bergeson. Bergeson & Campbell P.C. present on May 25 in Washington DC for the Environmental Law Institute and the Woodrow Wilson Center For Scholars Dialogue on Nanotechnology. On the Internet: <http://www2.eli.org/research/events/nanotech5.25.05.cfm>

- » Processors do not have to submit unless risks are related to processing. Since there is no data on the process related risks for nanomaterials. Many manufacturers might be confused about whether to submit.
- » Experts indicate that there has been a significant amount of litigation concerning Section 4. Moreover, promulgating section 4 is known to take years.

### **TSCA Section 5 Existing Chemicals and New Chemicals**

- » Section 5's distinction between existing and new chemicals based on size is unclear.
- » A particle at the nanoscale may not necessarily be identical to its macro scale analog. Does this make the material in question a new chemical?
- » Rules associated with this would govern whether a company has to submit to regulators before commercializing. Confusing for companies and confusing for regulators.

### **TSCA Section 6 Unreasonable Risk**

TSCA Section 6 authorizes EPA to prohibit/limit the manufacture, import, processing, distribution in commerce, use, manufacture, import, processing, distribution in commerce, use, or disposal of a chemical if there is a reasonable basis to conclude the chemical presents or will present an unreasonable risk of injury to health or the environment

- » Section 6 states that unreasonable risk has to be based on “substantial evidence”. Only a handful of studies have been done to date. This makes us wonder about products already in commercial use.
- » The burden of proof is heavy on the EPA in relation to a court ruling in 1991. (Proof Fittings v. Fittings v. Fittings v. Fittings, 947 F.2d 1201 (5th Cir. 1991)) , 947 F.2d 1201 (5th Cir. 1991))

### **TSCA Section 9 Other Federal Agencies**

This statute lays the ground work for harmonization with other agencies. In essence, if another agency's ruling limits or reduces an “unreasonable risk” ruling by EPA then that agency must inform the EPA. Specifically EPA has a memorandum of understanding (MOU) with the Occupational Safety and Health Administration and Consumer Product Safety Commission regarding the “working relationship” process under which formal referrals will be made.  
[http://www.osha.gov/pls/oshaweb/owadis.show\\_document](http://www.osha.gov/pls/oshaweb/owadis.show_document)

### **TSCA Section 12B Authority**

The EPA will notify foreign governments if chemical substances are subject to the following TSCA rules or orders:

- » TSCA Section 4 test rules and Enforceable Consent Agreement Final TSCA Section 4 test rules and Enforceable Consent Agreements;

- » **Data required under Section 5(b); Data required under Section 5(b);**
- » **Order issued under Section 5; Order issued under Section 5;**
- » **Proposed or final rules issued under Sections 5 or 6; or Proposed or final rules issued under Sections 5 or 6; or**
- » **Actions pending or relief granted under Sections 5 or 7 Actions pending or relief granted under Sections 5 or 7**

The problem is that there must be a rule under 5, 6 or 7. In the case of nanomaterials there is nothing applicable.

In essence, this means that there would be not export notification and nanomaterials could be exported for use, distribution, processing, or disposal to anywhere in the world with no way of tracking its movement

## EUROPEAN UNION

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The European Union is in the process of overhauling its chemicals policy. The new policy currently under development known as REACH (Registration Evaluation and Authorization of Chemicals) is under constant state of flux. Companies want less regulation and regulators are trying to remain as close to the original proposal as possible. Two issues are relevant for nanoproducers; 1) should rules be designed for nanoparticles that would take into consideration the volume issue (REACH is triggered by the use of conventional chemicals in volumes exceeding a ton), then there are aspects of REACH that may require manufacturers to prove that the product is safe. This runs counter to pre-existing chemicals regulations in the United States and Europe. 2) We make the general assessment that bureaucratic systems tend to be flawed. Backlog, oversight, inefficiency are characteristic of pre-existing systems for chemicals regulation. Given this, we wonder to what degree nanoproducers will be able to safely rely on regulatory scenarios to prevent the commercialization of products that later prove to be harmful. Any incident of this nature could have negative affects across markets. We identified a few companies in our analysis who, after conducting their own studies, decided to terminate work in one technology or another based on early indications of risk. Ultimately, it will be companies that need to make decisions about risk. This is an interesting topic for due diligence.



### **Chemical Safety Report**

A Chemical Safety Report must be compiled for substances of > 10 t/a. This contains physicochemical, toxicological and eco-toxicological data, risk assessments for all uses and measures for risk management.

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FIGURE 31 Notes Regarding the Index Methodology

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The August 2005 version of the Innovest Nanotechnology Index focused on the technology, product strategy and product stewardship issues. Going forward a backed Innovest fund would follow a buy and hold strategy involving two groups of stocks: large cap companies concentrating on nano R&D, licensing and acquisitions and a small cap group for the start up, pureplay, and development stage firms. The following would be our process for security selection.

**Macroeconomics**

May impact tech stocks in general

**Industry**

Positioning in nano value chain  
Market potential Innovest valuation  
Time to market, ramp up of orders  
Industry connections

**Business Characteristics**

Identify nano value for large caps  
Non-nano activities generating profit

**Financial Health**

Revenues may not yet be present  
Burn Rate  
Traditional review for large capitalization companies

**Value**

Discount for Product Risk  
Strategic Profit Opportunity in markets already tracked by Innovest

**Management**

Innovest specializes in Management Quality Review through interview process  
Useful determinant of potential in the absence of significant revenues