Blueprint for Maximum Nanotechnology Employment in California

Draft

May 30, 2005

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Issue

California is still struggling to adjust to the burst of the 1990s economic bubble. While the level of business has rebounded to near-boom levels, employment has yet to fully recoup losses. Manufacturing of information technology (IT) hardware has, for the most part, permanently shifted to Asia. ,. Some software development has shifted to Asia and Eastern Europe; this shift is just the start of the trend in software moving offshore.

There is little that can be done to bring back those lost jobs or stem the tide of losing more traditional IT jobs to Asia and other developing regions. California in general, and Silicon Valley in particular, has been through this before with losses in the defense, disk drive production and consumer electronics manufacturing sectors. In every case, the next boom involved development of different types of jobs and/or industries, and not the return of old jobs. But California's adaptability is its greatest strength. Each new boom entails even greater employment opportunities and better quality of life for participants. However, each cycle requires broad participation by all levels of government, industry associations, educational institutions, large and small companies and workers at all levels.

California is now at a juncture and must again face a major restructuring of its industry and workforce. The new technology is nanotech, which is likely to be California's greatest opportunity to date, but also the most difficult. Nanotech will impact every industry and therefore, either directly or indirectly, every career. This transition period is also the first time that several other regions of the world have organized and amassed huge resources in an attempt to take the lead from California, or at least grab a large share of the employment pie.

Because this is a large-scale and pervasive transition for California, the potential to get it wrong is great. Getting it wrong in a major technological shift means that some other region of the world would take the lead and reap the rewards of the improved quality of life that nanotech enables through profitable industries with large numbers of high-quality jobs. Gains or losses during these major transitions can impact a region for several decades to come.

Summary

The issues that impact employment by nanotechnology businesses overlap with employment by many other high-technology/life science businesses. Nanotechnology opens the door to both evolutionary and revolutionary products in most industries and markets, and, while not a business in itself, will become a key element in almost every business over the next century. The 21st century is the nanotechnology century, just as the 20th century was the electric/electronic century.

Some applications for nanotechnology, such as those in bulk chemicals, are not likely to offer many business or employment opportunities in Northern California and probably not in the US overall. Any market sector that can be addressed by mass manufacturing is likely to shift to a lower-cost region in a relatively short time interval[1]. Higher productivity in the US does provide some counter benefit, but data shows that in mass manufacturing there may still be a cost advantage in places, such as China, that can be as high as 10 to 1. Such cost savings are the result of cheap labor, limited regulations, limited enforcement of existing environmental restrictions, and a completely flexible workforce that can be directed to perform whatever job is needed regardless of training or individual desires.

Other fields, such as medical devices and equipment, biotech therapeutics, industrial equipment, and advanced sensors, open up a range of high-value products that can be tailored to the needs of individual users or small groups of users. In some cases those users will consist of groups with specialized needs such as medical devices dependant on several body chemistry factors in addition to the basic disease being addressed. In extreme cases the users will consist of groups of one individual who requires customized versions of therapeutic agents.

California in general and Northern California in particular should focus on technology and market sectors that require customization or need modest quantities of complex items that cannot be served by mass manufacturing. This approach allows a sustainable advantage for the teams of high-skill individuals in startup and emerging companies. Small

[1] Lowest cost in the case of manufacturing includes labor, capital, transportation, government regulation as well as the hidden costs of risk factors such as currency exchange rates, labor disputes, political upset and transportation delays.

business in California has been and continues to be rapidly adaptable to customer needs. Countries such as Japan have been slower to adapt but better at manufacturing cost reductions on mature technologies and products.

In many cases, nanotechnology-based products will require technology that covers multiple disciplines. It will be common to see developments that overlap physics, chemistry, biology and engineering. Products using nanotechnology, for the most part, will be complicated and difficult to create with the possible exception of certain mechanical components. Examples of mechanical components would be automobile segments such as bumpers or other body parts. California is not suited to the manufacture of large mechanical components but is ideally suited to cross-discipline products.

Given the low level of research and development spending in most enterprises (large companies), only a small portion of emerging nanotechnology will be created in those environments. Most raw and basic inventions in nanotechnology are likely to emerge from universities and federally-funded research centers. The largest companies tend to grow by acquiring small- and mid-sized companies that have developed new technology. Those mid-sized companies in turn develop from startups frequently built upon research at universities and federally funded research centers, or from spinouts of enterprises.

To ensure that new startups are generated with sustainable technological advantages, it is important to encourage all of these research centers to enhance collaboration between departments within each institution. It is also critical to have multiple institutions work together on most projects to allow a suitable fertile development environment that can take advantage of the technology contained within many research initiatives. Center such as CNSI, Cal IT2, QB3 and CBST should serve as the first wave of a new approach to regional cooperation for technology advancement.

In the past only one department at one institution was typically involved in a new technology base needed for a startup. Many of those single- technology areas have already been mined for opportunities that can create large new businesses. It will become normal for large technology businesses to develop from multiple technologies. Similarly, single technology business opportunities will become more difficult to uncover or restricted to niche areas that offer opportunities for a small business that remains small. By encouraging cross-discipline and cross-institution interaction, the creation of new businesses with market potential to become large can be enhanced.

Background and Issues Regarding Employment Trends

The US is losing employment as more and more jobs are outsourced, mainly to Asia. This trend started decades ago with very low skill level employment. Initial areas such as textile manufacturing required little or no skill or education. The second wave included jobs of modest skills such as auto manufacturing, steel production and chemical manufacturing. Following that wave was a shift of semi-skilled jobs in a wide range of manufacturing for consumer goods such as electronics and the less capital areas of semiconductors such as assembly.

A political backlash in the US by unskilled and semi-skilled workers has led to demands that the US federal government protects these jobs. The government has tried to mollify these critics but not much can be done to keep those low-skill jobs in the US. In the distant past tariffs and quotas had been used to protect US jobs. This type of protection has little benefit to the overall US population and does tend to drive down US competitiveness.

In the last decade this outsource trend has encompassed greater skill levels and now includes many college-educated skills. In the last few years a large number of software programmer jobs, telephone technical support and chemical engineering jobs have been lost to Asia, particularly China. Many of these jobs entail education with a bachelor's degree. Today most technical support jobs have left the US never to return.

There is now a stronger backlash that includes skilled, semi-skilled and unskilled workers. However, there is little that any government can do for these jobs. With the global economy and global trade treaties, the US cannot unilaterally impose tariffs without harsh reactions from many other countries. Likewise quotas are also no longer permitted for the most part.

The US is using exchange rate shifts [2] as an allowed tool to maintain jobs. European countries have used exchange rates in the past. It is not evident that the US engineered the low dollar exchange rate as a balance-of-trade tool or if it is merely a side effect of low interest rates. The low dollar does provide limited assistance in reducing outsourcing. Unfortunately, the exchange rate most in need of adjustment for the US is the China-US rate. Many economists feel that China needs to re-value its own currency relative to the US dollar by 100%. This change may occur over a period of decades, but a change of that magnitude at one time would create economic shocks that could cause a worldwide recession. China has been strongly resisting a re-valuation of its currency since China's exceptional economic growth rate depends on a low currency value to expand exports.

A 100% change in the Chinese Yuan would undoubtedly help the US improve the balance of trade, but not entirely. China has such a large cost advantage relative to the US in areas like manufacturing and software that it would take a change much greater than 100% to allow a China-US trade balance on its own. In fact China is just one of a long line of offshore locations that will be picking up low-skilled, semi-skilled as well as skilled jobs in maturing industries. Over the next 100 years many jobs in all these categories will shift to the lowest cost country with available workers, infrastructure and access.

The US needs fresh approaches to developing full employment opportunities for its citizens. To ensure high value employment many of these approaches will require advanced education and re-education at advanced levels for a larger percentage of its citizens. Emerging fields such as nanotechnology offer opportunities where the US can keep its citizens trained ahead of other nations and improve both the level of employment and the quality of life of its workers.

Change is the Norm for Employment during the First Half of the 20th Century

Stable employment may someday be possible in the US but not for the next several decades. It will be rare for students in high school today to have one career for life. In fact as life expectancy rises driven by nanotechnology and biotechnology, we can expect most individuals to work more years. It seems reasonable to expect that by the end of this century most workers will work until the age of 80 with a typical age to enter the workforce of about 24 to 26. It seems likely that these individuals will have 3 careers of 15 years and ideally two re-education periods of about 2 years between each career.

The US has become just a small part of a global economy so stable employment in the US also requires stable employment worldwide. Stable employment worldwide implies worldwide stability and uniformity in many economic areas including: (a) currency exchange rates, (b) productivity growth, (c) interest rates, (d) tax rates, (e) manufacturing locations, and (e) consumption growth rates plus a (f) literate world population. Stable manufacturing employment requires additional elements: (1) stable populations in each region, (2) sufficient, stable and reasonably priced energy production, and (3) sufficient, stable and reasonably priced water supplies. In the first half of the 20th century none of these underlying factors to employment stability have much hope of constancy.

The nature of global economics in the 21st century is change. Change and sometimes-rapid change will continue until the world population stabilizes [3], energy sources and prices become stable and water becomes readily available in all regions of the world. An added requirement for slow and limited employment change is that most countries become moderately developed.

The United States has been a leader in promoting change and that is the greatest strength of the US. Most new industries start in the US driven by the combination of a culture of risk taking; excellent higher education; availability of risk capital; large domestic market; and a competitive environment that keeps markets open to newcomers. The best areas for new industries to start are Silicon Valley or the greater Boston area. However, these are expensive places to manufacture so it is only a matter of time before any industry shifts elsewhere. Manufacturing is the first sector that sees jobs go elsewhere. Over time creative jobs also shift to lower-cost regions as the skills needed for those jobs are

[2] The US dollar has a 90-day moving average value of about 107 Japanese Yen and about Euro 0.76. Many economists peg fair value of the US dollar about 25% higher.

[3] Steven Chu et al of Lawrence Berkeley National Laboratory have projected the world population to stabilize at 9 billion people.

developed in other elsewhere. Logically, the greater the new skills needed for a particular job, the longer it takes that job to shift to a lower-cost region.

Implications for California Employment

California has many similarities relative to other parts of the US. California also has some major differences compared to the rest of the US that impact employment.

Some of the major competitive advantages of California in general and Northern California in particular are:

- Greatest numbers of experienced technology /life science entrepreneurs
- History as the region with the most rapid adoption to new technology requiring new skill sets
- Greatest number of experienced startup executives
- Larger numbers of workers with advanced college degrees in all fields of science and engineering along with extensive experience in startups
- Most sources of venture capital funding and angel funding
- Greatest concentration of major research institutions (universities and federally funded centers)
- Largest number of professional service providers (lawyers, accountants, etc.) offering startup-specific services and deferred payment services to startups
- Access to major industrial customers in local area
- Access to global transportation networks

Some of the major competitive disadvantages of California in general and Northern California in particular are:

- Highest cost of real estate
- Highest cost of labor in all categories driven by cost of real estate.
- High levels of taxation, regulation and governmental restrictions that increase cost and slow development
- Local transportation problems that restrict access to workers outside a short range.
- Reduced access to and influence on the federal government driven by distance from Washington DC along with sharp political differences from the administration and a majority in congress.
- Limited supplies of electric power with potential for blackouts
- Limited supplies of water with potential for industrial rationing
- Frequent weather-related delays, especially for international air transport due to runway capacity restrictions during fog or rain at SFO.

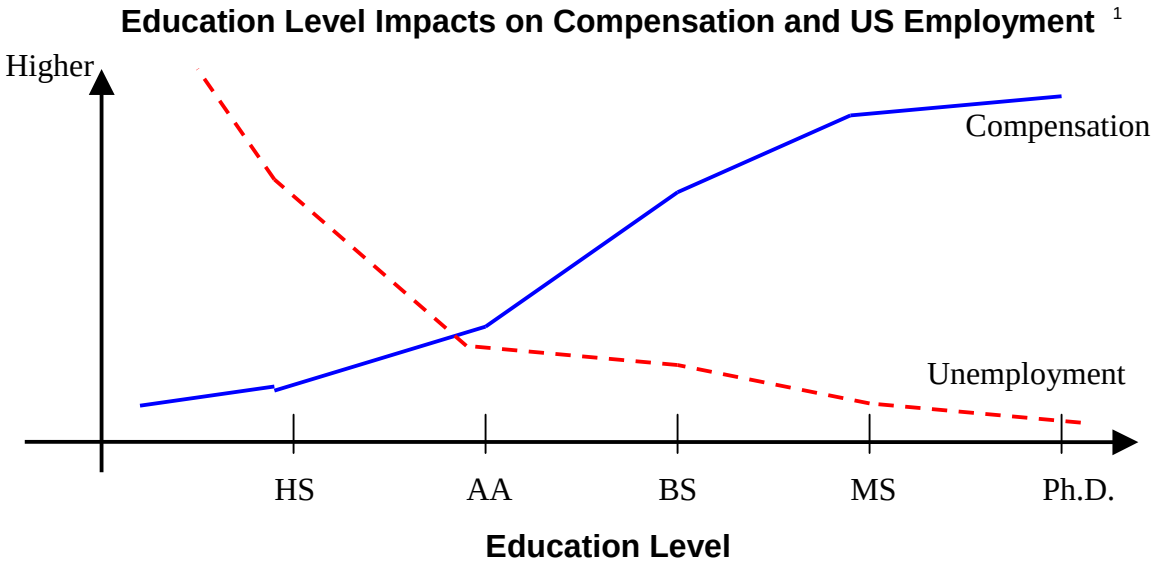
California can thrive in this challenging environment as long as it limits the disadvantages it places on itself through the state and local governments.

What this means for Northern California is that job creation should be targeted at emerging industries with high skill levels. There should be no attempt to return to past boom cycles or recreate prior industries in decline. Each boom cycle in California has been led by a new technology and market. We should learn from history.

This implies that even new high-skill level jobs in emerging industries have limited lifetimes in California. Workers, the state, and universities must plan on a re-education cycle for a large part of the workforce in cycles of about 10 to 15 years maximum. Fortunately, nanotechnology will provide a series of several cycles of new types of employment over the next century. California can become more successful than ever if we devise an approach that provides the education and skills needed in each successive wave of technology before other regions of the US and the world do the same. Given the history of California, this is a reasonable approach for the state and especially for Northern California. However, the implications for unemployed individuals needing to undergo extensive re-education that could last for two years every fifteen years are much more difficult to address.

Employment, Skill Levels and Education Impacts Employment Shift Offshore

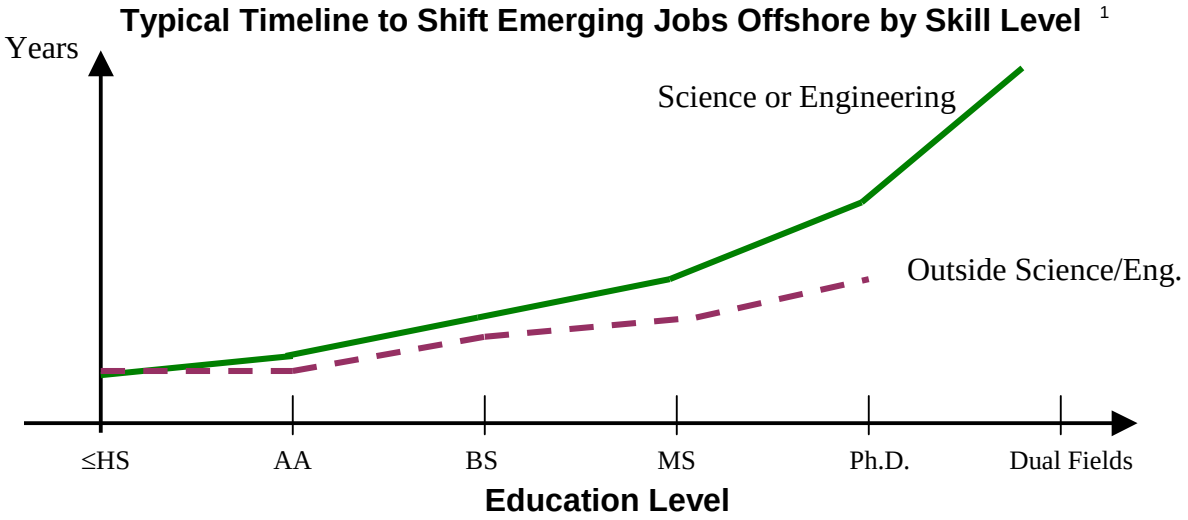
Traditionally, unemployment in the US has mainly been inversely related to education level. Also, compensation has been related to education level. The following chart illustrates that trend [4].



These relationships between education and earnings and education and unemployment are further enhanced for science and engineering education. For example, an engineer with a master's degree earns as much as 50% more during his lifetime than an individual with a master's degree in sociology.

With our global economy, jobs in each field of employment go to the location where a combination of costs, perceived risks and political factors yield the best risk-adjusted return to employers. Jobs have become fungible in our global society at all skill levels although changes in costs, political factors and risks take time to ripple through to employment. However, the time it takes for low-skill employment to shift is less than that to move high skill jobs as illustrated in the following graph.

[4] Data from US Census Bureau, National Science Foundation, Center for Economic Development, Department of Commerce, Bureau of Economic Statistics, National Institute of Standards and Technology, Helfrich interpolations



It must be noted that this shift of jobs to the lowest cost producer is not new and is not limited to the US. Even before this most recent trend hit the US, it hit Europe. This trend is even starting to impact China as jobs in China are starting to shift to other Southeast Asian countries. Europe took a protectionist path as could be expected.

The French have been the most extreme in attempting to fight the inevitable shift to low-cost areas. Before the GATT treaty the French were quick to impose tariffs on imports of many types. At one time the French attempted to protect semiconductor and electronic component manufacturing jobs in France by imposing import tariffs. After GATT restricted tariffs France continued to protect jobs by requiring excessive payments to workers by employers closing plants in France as well as hindering large scale imports with inane regulations. However, that did not stop large plants from closing as evidenced by IBM closing a plant in Essonnes. Even the large French company Thomson CSF closed a capacitor production facility in France and went offshore. Those companies found that to be competitive it was essential to move production offshore. Attempts to stop the shift of jobs offshore have resulted in a reluctance of any manufacturer to build new production capacity in France of any kind. The risk that such a plant may need to be closed in the future is too high for any company to incur the financial liabilities to workers hired at a plant.

Categories of Employment for Industrial Employers

Besides manufacturing jobs themselves there are many other types of jobs required to provide a total solution for a customer need by an industrial employer. These types of jobs exclude categories such as construction and retail that by their nature must be local.

The major types of jobs in major industries that employ large numbers of workers are:

- **Basic research (at company's location or could be at university funded by company)**
- **Proof of concept demonstrations (at company's location or could be at university funded by company)**
- **Development of prototype products (at company's location)**
- **Product design and development engineering (at company's location)**
- **Manufacturing engineering (at company's location or at third party subcontractor location)**
- **Mass manufacturing (at company's location or at third party subcontractor location)**
- **Customized manufacturing (at company's location or at third party subcontractor location)**
- **One-off manufacturing (at company's location or at third party subcontractor location)**
- **Product test and quality control (at company's location or at third party subcontractor location)**
- **Marketing (at company's location)**
- **Merchandising, Public Relations and Advertising for US plus some global market (at company's location or at third party subcontractor location)**
- **Telesales (at company's location or at third party subcontractor location)**
- Field sales (at buyers location)
- **Centralized customer service and support (at company's location**)

- Regional service and support (at sites near large groups of customers)
- Field service and support (at buyers location)
- **Service delivery (with physical interaction to buyer or at buyers location)**
- Customer finance (can be phone for small items or may be at buyer's location for large items)
- Accounting and Finance (includes invoicing customers, paying suppliers, collecting payments, accumulating financial data) (at company's location or at third party subcontractor location)
- Administration, Purchasing and Human Resources (at company's location and/or partially at third party subcontractor location)

Color Code

Green are functions that California can do well and in a cost-effective manner
Red are fields that California cannot perform competitively

Jobs requiring direct physical interaction of the supplier and the consumer have not been subject to shifts elsewhere. An extreme example is the medical doctor – patient interface that has required both be in the same room. However, even for the doctor-patient interface there is some element of potential for remote delivery of services such as telemedicine. Recent technology still at the experimental phase has shown good results for remote surgery using an expert surgeon connected to a robot surgeon thousands of miles distant. The remote surgeon is provided with stereoscopic 3-D vision and precision robotic remote hands that enable precise surgery from anywhere.

Both business people and scientists are also learning that mass market solutions may not be the answer to winning customers. This is becoming painfully apparent in pharmaceuticals. The major pharma companies have been totally focused on finding new blockbuster drugs. The big pharma companies have extensive sales channels with thousands of employees that visit practicing physicians [5]. The cost of this distribution channel is extremely high and exceeds the cost of all research and development at big pharma companies. The cost of educating those thousands of reps on a new drug to enable those reps to educate doctors is very high. Companies such as Merck claim that drug revenues must be at the billions of dollars per year level to justify the marketing and sales costs.

However, the rate of new drug introduction at big pharma has fallen. Many now claim that most drugs that work for mass markets have already been discovered and are in the market. Some biotech executives have emphasized that view [6]. In addition, drugs that save lives for some individuals have been later found to be deadly to others after those drugs were used in mass markets. While this is a tragic lesson, it illustrates that the one-size-fits-all model is not the only approach. Many in the biotech industry are coming to a conclusion that the days of drugs that can be sold to tens of millions of patients are nearly over. While this is not great news for big pharma, it could point the way to new businesses and new types of employment opportunities in California.

Customization has already developed in some fields that are easier to handle such as personal computers. All the major producers now offer customized versions of their machines direct from the production line. Some manufacturers offer units with many variations such as hard disk size, optical disk types, memory, networking, input-outputs, batteries, etc. The possible combinations for a given product can number in the tens of thousands. However, the skills needed to handle PC manufacturing customization are now common in less developed countries so even those jobs have permanently shifted offshore in most cases.

Critical Elements for Regional Employment in Emerging Technology Business

Energy, water, capital, skilled workers, experienced entrepreneurs, limited regulation, strong research institutions, clusters of related businesses and rapid access to global transportation are also critical for research, development and

[5] Companies such as Merck have large numbers of field sales employees that visit doctors. Merck has over 12,000 of these reps in the US alone. Merck claims that a Merck rep visits every practicing physician in the US every week to deliver information on new drugs as well as to provide data on other drugs and new findings on drug interactions.
[6] One biotech executive in a company working on a cancer vaccine has found that one of their promising products has mixed results against lung cancer. On careful review this biotech company discovered that their product was very useful for only one particular strain of lung cancer. Their research has uncovered 61 strains of lung cancer and their drug has not shown effectiveness against those other 60 strains.

production in most industries. California leads in the supply of skilled workers, experienced entrepreneurs, strong research institutions and clusters of related businesses. California's workers will require constant retraining as the skill sets demanded by employers evolve. California does well in capital compared to other regions but still falls short on capital for early stage startups and spinouts from universities.

The supply of potable water is limited and in many parts of the world most sources of potable water have been exploited to their limits or beyond. Someday when energy is cheap and plentiful, unlimited potable water can be made from seawater [7] or reclaimed from wastewater [8]. Unfortunately, energy is still an issue in most countries and the US in general and California in particular is no exceptions. Energy production is likely to undergo changes, as environmental pressures on the emissions of carbon dioxide are restricted. California has seen rapid growth in the demand for energy and water. California must build added infrastructure for water, energy, waste treatment and ground transportation and some or much of that may be enhanced by cleantech.

Detailed Recommendations for Nanotechnology in Northern California

Northern California has great strengths as well as several key weaknesses. Weaknesses driven by governmental bodies should be addressed to reduce or eliminate impediments. In addition, there are other vulnerabilities that can be addressed by some combination of regional and state government groups in combination with universities, federally-funded research centers, professional associations, and industry.

A - Make California as business friendly as possible
- Provide exceptions to less critical regulations for very small companies
- Provide special tax incentives to investors that place money in startups that bring technology out of California-based universities and federally-funded research centers

B - Promote businesses that use or spin out from California universities and federally-funded research centers.
- Take advantage of the billions of dollars spent on basic research by the federal government in California
- Provide incentives for California universities and federally-funded research centers to cooperate with other California universities and federally-funded research centers.
- Provide special tax incentives to investments in startups bringing technology out of California-based universities and federally-funded research centers**.**

C - Develop re-education programs for professionals who are unemployed and underemployed
- Use federal fellowship program modified to fit mid-career professionals
- Provide post-doc type fellowships plus expanded federal loan programs to allow workers supporting families to participate

D - Enhance science education at the secondary school level
- Attract cadre of teachers with industrial science experience and advanced science degrees with suitable differential compensation over standard teaching positions
- Enable a 2-year special program of science teachers with loan forgiveness from mid-career federal loan program
- Enable a 2-year special program of science teachers through partnerships with large corporations that lend professional workers

E- Improve California infrastructure
- Coordinate the planning of mass transit, airports, rail, highways, housing, retail, commercial and industrial development
- Create special startup zones immediately adjacent to research universities, with suitable zoning, adequate parking, public transit, and ease of permits for unusual materials in modest quantities

[7] Desalinization of salt water is done using polymer membranes in a process called reverse osmosis but the energy needed is high relative to other sources of water.
[8] Wastewater can be purified using reverse osmosis but most locations do not permit its use as potable water but can be used for functions such as irrigation of golf courses.

F - Focus on nanotechnology subcategories suitable for Northern California strengths

- Focus on high-value-added components and systems that can tolerate California's cost structure
- Avoid state and regional efforts to cover all fields
- Ignore activities requiring bulk manufacturing of materials for incorporation into other's components and systems

NanoBio - Using nano to enhance biology

1. Equipment and molecules for disease screening / diagnosis

Nano-bio-related research projects are underway at many UC campuses and national labs in California. These projects are tasked with the development of very advanced tools and equipment for the rapid detection of disease through the nanoscale properties of molecules. There also exist ancillary institutions, including the Center for BioPhotonics in Science and Technology, QB3, Center for Quantitative Biology. These centers are developing large-scale complex equipment suitable for rapid medical diagnosis. Critical for Northern California is that these sorts of equipment are likely to be produced locally due to the specialized and highly proprietary components used and the low to moderate volumes produced of each type of equipment. However, in many cases this equipment is so complex that individuals with engineering and science degrees (probably at the bachelor's level) will be necessary to make, test and verify them. There are likely to be limited numbers of each of several models produced so that there is no mass production likely, resulting in virtually no learning curve. This equipment will require FDA and other government approvals as well as certification for each and every unit.

In many cases, specialized bio-chemical agents will be used in conjunction with this equipment to enhance its sensitivity. Most of the agents being developed are customized synthetic nano reagents that mimic biological functions and add certain electro-magnetic properties. Development, production, and after-sales services for this type of equipment fits Northern California very well. These units follow a model similar to semiconductor production equipment (itself concentrated in Northern California), with specialized supplies.

2. Devices for disease treatment and management

The long-term use of therapeutic agents is becoming common for a range of medical conditions. The number of prescription drugs used for extended periods or entire lifetimes is becoming common. For instance, one of the shortcomings of orally-administered drugs is lack of patient compliance. Several universities in California and a handful of startups are already pursuing the development of devices to deliver doses of drugs on a programmed schedule. Even more ambitious projects are underway to test for the need of additional drugs every few minutes and then administer the required dose as needed. In some cases, these delivery systems will be worn as a patch on the arm or leg. In other cases, these devices will be implanted inside the body with sufficient supplies of concentrated agents to last several years.

These types of drug delivery systems are using nano-encapsulation on many of the therapeutic agents to preserve them for longer periods. Some of them use functionalized nanopores that keep bacteria out of the storage elements but allow passage of therapeutic agents as needed.

These devices are very high value, small in size, long lasting, and may contain 1,000 days' drug supply. They must be produced and filled in clean room environments under FDA-approved monitoring. Since each small unit may contain thousands of dollars' worth of drugs there would be little need to move production offshore, resulting in lower risk. Labor costs would be a small percentage of the total costs. This model is similar to high-value semiconductors, such as Intel microprocessors that are still made in the US. This is a highly desirable type of business for Northern California since it will employ a mix of high-skill and mid-skill people. While this business is likely to stay in the US, California should make any governmental changes needed to induce these companies to locate here

3. Molecules and organisms to correct environmental problems

Research projects to find ways to remedy environmental problems using nanotechnology and nanobiotechnology are being performed around the world. Developments include microorganisms that eat and digest toxic materials, catalysts that break down toxic molecules, and nanocoatings that encapsulate toxic chemicals rendering them harmless.

This is a broad field that can provide high-value products. No one region is likely to dominate this field. However, Northern California has many research projects underway at federally-funded research centers and universities that are showing promise. To enable these projects to become real businesses will take a challenging commercialization effort. Even after successful laboratory demonstrations, commercialization is not assured. Most investors are not comfortable

with this type of project and there is little funding available to carry these projects from laboratory success to field trials. Building these business in Northern California is possible from the economic side but will require a creative new approach for commercialization.

4. Targeted delivery of therapeutic agents

Most therapeutic agents work well on diseased cells. These same agents tend to impact healthy cells in undesirable ways. Nanotechnology finally offers potential solutions that can deliver those agents to diseased cells but bypass healthy cells. Targeted drug delivery also opens the door to using highly toxic agents that otherwise cannot be used on humans.

A large number of startups are working on nanotech coatings, natural or artificial antibodies and other nanomolecular targeting and delivery techniques. Some researchers and startups are working on nanocoated molecules that can penetrate cell membranes before delivering an agent.

Northern California has its share of these targeted drug delivery research projects at universities and has more than its share of startups in this field. Volume production has not been addressed yet so it is not certain that production fits with Northern California's strengths. It is possible that production will be capital-intensive and require FDA monitoring, making Northern California a suitable location. (The FDA lacks experience for this type of clinical trial so timelines to production are uncertain.)

It is likely that these products, like many other pharmaceuticals, will achieve large revenues quickly once they are on the market. Therefore, Northern California should work to commercialize research at its universities and to attract relevant startups. Even if these companies become capital-intensive by using expensive machines, their California location improves the potential that those expensive machines will be made locally. The manufacture of the costly machines used in nanotech medicine production fits very well with Northern California's strengths.

5. New and customized therapeutic agents

Pharmacogenomics [9] is just starting and show promise as a cost-effective step towards improving health care. Northern California companies such as Genomic Health are providing testing services that enable physicians to select more effective breast cancer therapies based on genetic sequences. Other tests are in the pipeline to allow the selection of drugs and/or selection of surgery types and intensities for a range of diseases.

Therapies based on group classification are just the first step. There are numerous research projects underway at several California universities that will develop tests that allow physicians to target therapies for each individual. These initial projects are developing tests that use a limited portion of a person's genetic code to make these decisions. The next step is to look at longer sequences of genetic code to determine how to make specialized molecules based on each individual's DNA. The promise of fully custom drugs is the elimination of safety issues, reduction or elimination of side effects, and improved effectiveness.

This customized product model is a nearly perfect business type for Northern California. This is one area where Northern California can take advantage of its strengths to ensure that startups in this field start their business here. During the startup phase these companies will employ Ph.D.s and M.D.s, along with chemists, physicists and engineers, to develop their products and services. These businesses will employ many people in semi-skilled areas as their customer bases grow. The cost of labor is not a critical factor so that these companies are most likely to expand wherever the business first starts.

Individualized medicine is likely to develop from the initial "group medicine" just starting to hit the market. In these businesses, precision of testing services, medical data security, and speed of results are far more important than labor costs. So far it seems that most companies in this field are located in California, predominately in Northern California. Extensive efforts should be made to locate these startup businesses here.

[9] Medical treatments targeted to populations of individuals with certain DNA polymorphisms that cause those populations to react the same to particular therapeutic agents within that population while other groups with different polymorphisms have substantially different reactions to the same therapeutic agents.

Nanodevices - Enhanced devices using nano

1. Specialized sensors with wireless for environmental monitoring

California is a leader in wireless technology, with both Northern and Southern California participating. California is a leader in MEMS and NEMS research, and many new sensors are at the lab demonstration phase in California universities. The combination of sensors and wireless on tiny devices opens up great potential for medical, industrial, commercial and residential markets. Chemical companies have publicly indicated that chemical plants could be made safer, emit less pollution hazardous to humans and become far more energy efficient if literally millions of sensors were installed. This is true of most industrial operations. Wires are not possible. The combination of nanosensor and wireless is a natural fit for California, especially Northern California.

There will be stiff competition on the wireless nanosensor field. Some devices will evolve from MEMS sensors on semiconductors. Massachusetts is the current leader in this field with the top company being Analog Devices. For California to take the lead will require broad cooperation between major Silicon Valley semiconductor companies, universities, national laboratories and startups.

2. Cost-effective solar energy systems

Solar energy has been a dream of environmental groups for decades. Solar energy provides electric power without carbon dioxide and avoids transmission towers and electric substations. Solar energy also offers a compelling advantage over all other alternative energy systems. Solar panel output peaks at the same time electric demand peaks. Wind, wave, geothermal and other alternative sources are either constant or have up and down production cycles that do not match demand.

Solar energy is not economically viable at current pricing. The cost of an in-home solar system is high. The solar panels themselves are expensive but that is only half the total cost of an installed and tested system. Even if solar panels were free, the remaining costs are sufficiently high to make solar power unattractive without government subsidies.

Cost-effective solar energy must be able to not only provide low-cost solar panels but also technology to connect the output of those panels into the home at equally low cost.

Energy prices show no downward trend from their current high levels. In the short-to-medium term governmental subsidies are needed and likely to continue. The issue of energy dependence on the Middle East is also likely to keep subsidies alive.

Under the subsidy scenario it makes sense to pursue more cost-effective solar cells. The overall sun conversion efficiency is not important in economics. What is important is the cost per peak watt. Current panels made with Silicon and protected with glass in a panel are sold at about $4 or more per watt. Recent research in Northern California using a biomolecular technique that could drive that down below $0.50 per watt is showing promise. Current government subsidies and high residential electric rates allow homeowners to install solar with a 5-year payback time or less with panels at $0.50 per peak watt.

Production of these solar panels could be done in Northern California but not likely in the Bay Area. This type of production is likely to require more space, water and utilities than fits with conditions in the Bay Area. Plants could possibly be located in the Sacramento Valley if suitable water and power were guaranteed.

One very long-term approach that offers promise for cost-effective solar power without subsidies is bio-based. Research in this area is centered in Northern California and funding for this research should be enhanced.

3. Medical Nanomaterials

This stage is now in progress, with research, testing, and most recently the first approval of functionalized nanomaterials for medical use. This stage takes advantage of current research at UCSF, UC Berkeley, Stanford, and other nearby universities, as well as local strengths in pharmaceuticals, biotech, and nanomaterials.

4. Nano membranes and nanoparticle binding for efficient environmental cleaning.

There are many sites that require extensive environmental cleanup. First, there are dozens of closed or soon-to-be-closed military bases.

Local governments can make good economic uses of the land and possibly the buildings on these bases. Most of these bases have extensive cleanup needs. Many bases stored large quantities of fuel and other chemicals underground. Studies comparing fuel deliveries with fuel consumption have shown that large fractions of fuel leaked into the ground.

Local governments have strained budgets at best. (For instance, some local governments are already being forced to consolidate primary, middle and high schools due to budget limitations.) There is no possibility that local agencies can pay to clean up environmental problems at former military bases.

Likewise, the federal government has record deficits that are not about to dissipate. There is no way that the federal government can afford the hundreds of billions of dollars needed to clean up all the military bases using existing technology.

Existing technology sometimes requires removal and replacement of 10, 20 or as much as 50 feet of surface soil. That entails transporting billions of tons of contaminated soil over hundreds of miles of highway. Those activities alone will provide wear on highways that in turn will require replacement of many roads. The traffic and noise associated with removal and replacement of soil is also undesirable for neighbors of the bases and highly undesirable for commuters heading to work and school every day.

But recent research is uncovering nanotech solutions to cleanups. By pumping water through contaminated soil it has been shown that over time most contaminants can be removed. The volume of water needed make that approach impractical if continuous supplies of new water are used. However, if that water can be cleaned inexpensively and used over and over at a toxic site, there can be a workable solution.

Nanopore membranes are one possible solution that can separate pure water and concentrate contaminants in a small collection unit. Nanoparticle agents that bind to specific contaminants and have some other property such as magnetic moments are also showing promise. Either or both of these approaches can be used to clean up sites. By using nanotech-based solutions it may be possible to reduce cost of each environmental cleanup by an order of magnitude or more.

That lower cost level would make cleanup viable in the near term. Sites that have been cleaned and returned to commercial uses generate jobs and taxes. At a lower cost level, using nanotech for cleanup, the benefit of those jobs and taxes can pay back the cost of cleanup in a short time period making cleanup a high-payback investment by government. With acceptable cost levels, cleanup could then be financed by state or municipal bond measures.

Recommendations Summary

Recommendations fall into two categories. Category A items are actions that governmental organizations, industry association and other non-business entities should perform. Category B items are specific nanotech application areas that should be addressed by Bay Area business and non-business entities to ensure benefits to the region.

Summary of Non-Business Actions and Activities

- Make California as business-friendly as possible for the application fields targeted
- Promote businesses that use or spin out from California universities and federally-funded research centers in the application fields targeted.
- Develop re-education programs for professionals who are unemployed and underemployed in the application fields targeted
- Enhance science education at the secondary school level to prepare students for the application fields targeted
- Focus on a modest number of targeted application fields of nanotechnology that fit the unique strengths of California, and avoid its weaknesses
- Enhance science education at the secondary school level using teachers with advanced science degrees and active interaction of secondary science students with industry
- Expand post-secondary education to fit the higher skill level needs of upcoming nanotech-related employment opportunities

The skill level issues will become a key factor in winning the leadership position in this nanotech century (the 21st century). Unlike former boom cycles, the fraction of jobs for semi-skilled and unskilled workers will be much lower.

There are numerous factors that impact the competitive position of geographical regions. The following tables summarize how California and Northern California compare to the rest of the US and the rest of the world. Following those tables is a chart that shows how nanotech product categories and market sectors intersect and the product opportunities that are enabled.

Summary of Specific Application Fields Targeted for California

Field	All CA/ Bay Area Fit	Stage	Action(s)	Semi-Skilled Workers	Skilled Workers
Nanotechnology to enhance biology					
Equipment and molecules for disease screening / diagnosis	Very good/ excellent	Equip. close/ molecules later	Commercialization funding plus university training incorporating biochem, physics and EE	Very limited	Large numbers needed for research, development and clinical trials
Devices for disease treatment and management	Very good/ excellent	Some prototypes near with many more to come	Commercialization funding plus university training incorporating biochem, physics and EE	Limited	Large numbers needed for research, development and clinical trials
Molecules and organisms to correct environmental problems	Excellent/ excellent	Early research	Commercialization funding plus university training combining molecular biology, chemistry and engineering	Potential for service workers to travel & perform cleanup at field sites worldwide	Large numbers needed for research, development and field trials
Targeted delivery of therapeutic agents	Excellent/ excellent	Many in development	Commercialization funding plus training in nursing type technician with molecular biology and interpersonal skills	Potential for nursing type skills to administer and monitor customized agents	Large numbers needed for research, development and clinical trials
New and customized therapeutic agents	Very good/ excellent	Many in development	Commercialization funding plus university training combining medicine, molecular biology	Limited	Large numbers needed
Enhanced devices using or applying NanoBio					
Specialized sensors with wireless for environmental monitoring	Excellent/ excellent	Some prototypes available and many in research	Commercialization funding plus university training incorporating biochem, physics and EE	Limited	Large numbers needed for research, development and field trials
Cost-effective solar energy systems	Excellent/ excellent	Components being researched but no systems	Commercialization funding plus university training incorporating chemistry, physics and EE	Potential for AA degreed workers for field installation	Moderate numbers for research, development and field trials
Medical Nanomaterials	Excellent/ excellent	Few suitable for trials and many over time	Commercialization funding plus university training combining medicine, molecular biology and mechanical engineering		Large numbers needed for research, development and clinical trials
Nano membranes for efficient environmental cleaning	Excellent/ very good	Lab research on membranes	Commercialization funding plus university training combining biology, physics and mechanical engineering	Potential for AA degreed workers for field application	Moderate numbers for research, development and field trials

Summary of Regional Issues for Competitive Employment

Need	Northern California	All California	Other US	Rest of World
Workforce with advanced degrees	**plentiful** but **re-education needed for > 10,000**	plentiful but re-education needed for >50,000	plentiful in some regions, limited in most regions, but re-education needed for ~ 1,000,000	limited for most countries except for few developed countries
Flexible workforce with bachelors degrees	**plentiful** but **re-education needed for > 200,000**	plentiful but re-education needed for >500,000	plentiful in numerous regions, but re-education needed for > 10,000,000	limited for most countries except for few developed countries without unions
Labor rates	**very high**	very high	High	low except very high in developed countries
Strong research institutions	**exceptionally strong**	exceptionally strong	strong overall and exceptionally strong in some regions	exceptionally strong in several locations, strong in numerous locations but weak in many regions
Experienced entrepreneurs	**exceptionally strong**	exceptionally strong around Bay Area and adequate around Orange County	exceptionally strong in few regions but weak overall	generally weak with very few exceptions
Capital	adequate for basic research but **funding needed to bridge valley of death**	adequate for basic research but funding needed to bridge valley of death	adequate for basic research but funding needed for all other categories	adequate for basic research in highly developed countries but funding needed for all other categories
Professional services	**exceptionally strong and offers deferred billing for startups**	very strong	strong in few metropolitan areas and modest or weak most locations	Generally lacking dedicated services for startups
Energy	larger supplies needed and **blackouts must be eliminated**	larger supplies needed and blackouts must be eliminated	needs more supply overall	needs much more supply overall
Water	larger supplies needed and rationing must be eliminated	larger supplies needed and rationing must be eliminated	needs more supply overall	needs much more supply overall
Taxation, restrictive regulations	**overly burdensome regulation for small businesses** with some cities severely restrictive	0verly burdensome for small businesses	generally burdensome for small businesses with some exceptions	extremely burdensome in some highly developed countries and unduly lax in some less developed countries
Political risk	limited except for **product liability litigation risk**	limited except for product liability litigation risk	limited except for product liability litigation risk	limited in most developed countries but high in many less developed countries
Facilities costs	**very high**	very high in major metropolitan areas	moderate except very high in select metropolitan areas	low except very high in select metropolitan areas
Global transportation access	more runway capacity needed and improved ground transport critical	more runway capacity needed	adequate in some regions but others need new airports	adequate in few regions and others need new airports

Legend: **Undesirable but no correction needed** **needs fix** **Very good**

Categories of Nanotechnology

The following chart illustrates the products and markets covered by nanotechnology.