

- 1) Identify one or more grand challenges for the bioeconomy in areas such as health, energy, the environment, and agriculture, and suggest concrete steps that would need to be taken by the Federal government, companies, non-profit organizations, foundations, and other stakeholders to achieve this goal.

[Reply to 1\)](#)

The best grand challenge that I can think of is 4) which you have listed below – a dedicated effort to determine the function of genes. Please see my reply to 4).

Research and development: R&D investments, particularly in platform technologies, can support advances in health, energy, the environment, and agriculture, and accelerate the pace of discovery in fundamental life sciences research.

- 2) Constrained Federal budgets require a focus on high-impact research and innovation opportunities. With this in mind, what should be the Federal funding priorities in research, technologies, and infrastructure to provide the foundation for the bioeconomy?

[Reply to 2\)](#)

This is not really an issue of constrained budgets. Federal funding should always look to fund high-impact research and innovation. However, innovation often comes from small projects. The research budget is better spent when it also reserves sufficient funding for more researchers to seed many projects. In the past decade, there is a trend to fund larger research proposals often with multiple investigators. Overall, it is better to fund more single investigator projects, which are more carefully conceived and where the responsibility for success lies directly on that investigator.

- 3) What are the critical technical challenges that prevent high throughput approaches from accelerating bioeconomy-related research? What specific research priorities could address those challenges? Are there particular goals that the research community and industry could rally behind (e.g., NIH \$1,000 genome initiative¹¹)?
- 4) The speed of DNA sequencing has outstripped advances in the ability to extract information from genomes given the large number of genes of unknown function in genomes; as many as 70% of genes in a genome have poorly or unknown functions. All areas of scientific inquiry that utilize genome information could benefit from advances in this area. What new multidisciplinary funding efforts could revolutionize predictions of protein function for genes?

[Reply to 4\)](#)

Yes, you are exactly correct in identifying this issue as a key bottleneck in biology R&D. In fact, two core technologies already exist for tackling the problem. So the hurdle here is not that we need to invent new technology. We mostly need to fund projects to utilize the technology that we have. In doing so, the developers and sellers of the technology, such as

our company Biolog, Inc., will be able to reduce the cost and improve the technology, just as the cost of DNA sequencing has plummeted as the speed and accuracy has improved after the government provided funding for large scale sequencing projects. Prioritizing and funding an appropriate number of large scale and high profile gene function projects (for example within Core Facilities) will also have the beneficial effect of making these technologies available to more labs at lower cost.

One technology that I am referring to is high throughput (HTP) image processing. Gene engineering technology allows construction of cells with green fluorescent protein (GFP) fused to protein-coding genes of interest. HTP image processing can then be used to determine if and where the protein localizes within the cell. The location of the protein provides insight into and validation of the protein function.

The second HTP technology, which was developed by our company more than 10 years ago with SBIR funding, is Phenotype MicroArray (PM) technology. This technology employs a redox dye to precisely measure cell energy production in thousands of microwells, with each well measuring the activity of a different cell pathway or phenotype. With this technology one can directly compare two cells, one with a knockout or other alteration of a gene of interest. It provides a direct assay for gene function as it measures the biologic consequences to the cell of altering a specific gene. The technology can be used with bacterial, fungal, and even human cells and has already been proven to work in hundreds of scientific publications. It can be termed a metabolic and physiologic or a chemical biology approach to determination of gene function and it is quite different from and complementary to the image processing technology.

The potential benefits of funding the adoption and use of these pre-existing technologies are enormous, ranging from treatment of disease and drug discovery to improving the engineering of microorganisms for more efficient energy and biofuel production by microorganisms. I would be happy to provide much more detail in support of these contentions described above.

Moving life sciences breakthroughs from lab to market: It is a challenge to commercialize advances in the life sciences because of the risk, expense, and need for many years of sustained investment. The Administration is interested in steps that it can take directly, but is also interested in encouraging experimentation with new private-sector-led models for funding commercialization of life sciences research.

- 5) What are the barriers preventing biological research discoveries from moving from the lab to commercial markets? What specific steps can Federal agencies take to address these shortcomings? Please specify whether these changes apply to academic labs, government labs, or both.

Reply to 5)

Our company has encountered regulatory barriers from the FDA. See my Reply to 13) and 14) below. If our product had been cleared years ago, we would have a lot more sales and would have substantially increased our hiring.

- 6) What specific changes to Federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs [2] would help accelerate commercialization of federally-funded bioeconomy-related research?

Reply to 6)

I and my company Biolog Inc., have benefited greatly for more than 20 years from the SBIR Program. It is very well run and very well administered. The main problem that I have noticed more and more each year is the deterioration of the quality of scientific reviews of SBIR proposals. The reasons for this are clear. They cannot recruit top scientists for these panels because they are already over-committed. It is a lot of work to serve on these review panels and it is somewhat of a thankless job. There has been and continues to be a deterioration of the quality of scientists serving on these panels and/or the time and thought that these scientists are able to donate in reviewing proposals. I have three suggestions on this. One is to use older and retired scientists with greater knowledge and broader experience in these review panels. Another is to pay scientists for their time spent in reviewing proposals. A third idea is to have a system for grant submitters to rate the quality and accuracy of the reviews that they receive so that unskilled and unqualified reviewers get filtered out of the review process.

- 7) What high-value data might the government release in the spirit of its open government agenda that could spur the development of new products and services in the bioeconomy?
- 8) What are the challenges associated with existing private-sector models (e.g. venture funding) for financing entrepreneurial bioeconomy firms and what specific steps can agencies take to address those challenges?

Reply to 8)

See reply to 13 below.

Workforce development: Investment in education and training is essential to creating a technically-skilled 21st century American bioeconomy workforce.

- 9) The majority of doctorate recipients will accept jobs outside of academia. What modifications should be made to professional training programs to better prepare scientists and engineers for private-sector bioeconomy jobs?

Reply to 9)

Our biotech company has no problem finding skilled scientists that want to do experimental work, but we have great difficulty finding skilled scientists that want to work in sales, marketing,

and manufacturing. Programs should be established or modified to train or retrain scientists to work in these alternative but equally-important areas.

- 10) What roles should community colleges play in training the bioeconomy workforce of the future?
- 11) What role should the private sector play in training future bioeconomy scientists and engineers?
- 12) What role might government, industry, and academia play in encouraging successful entrepreneurship by faculty, graduate students, and postdocs?

Reducing regulatory barriers to the bioeconomy: As President Obama has stated, our regulatory system must “identify and use the best, most innovative, and least burdensome tools for achieving regulatory ends” and “protect public health, welfare, safety, and our environment while promoting economic growth, innovation, competitiveness, and job creation.”

- 13) What specific regulations are unnecessarily slowing or preventing bioinnovation? Please cite evidence that the identified regulation(s) are a) slowing innovation, and b) could be reformed or streamlined while protecting public health, safety, and the environment.

Reply to 13)

The government should update the laws to make it easier for small companies to go public - in particular they should change investment banking regulations and Sarbannes/Oxley.

The USA has been the envy of the world for innovation and startup high tech companies. We are rapidly losing that enormous advantage. Because of Enron and other misguided businesses, which had nothing to do with high technology, the Congress over-reacted as it often does, and changed the laws making it much more expensive and difficult for companies to go public and gain access to crucial public funding. They essentially threw out the baby with the bath water.

What really needed to be reformed was the investment banking field, their conflicts of interest, and their stranglehold as gate keepers of public money. The internet is a great thing, but the internet bubble demonstrates the unreliability and greed of much of the investment banking community.

Currently there are 2 major sources of capital for developing high technology and products: (1) venture capital, and (2) government funding, especially the SBIR Program. Venture capital works for certain situations. In our case our company received most of its money from SBIR. We have been a profitable company for most of our 25 years in business, we employ about 40 people, mostly in California, and we sell 60% outside of the USA. We have an innovative and totally unique biotechnology product portfolio and our products support many other companies in developing and producing better products of their own.

However, our business is still relatively small. I would like to expand our business, but it would mean taking private investment which always comes with many strings attached. Private investors demand preferred stock which means that if the company stumbles, the current owners can lose their entire share. These private investors will also usually demand faster return on their investment and, in doing so, force small companies to sacrifice longer term stability and growth for earlier, shorter term returns. Therefore we chose to not take private investment money and to grow slowly, as our limited capital resources permit. What we would really like to do is to go public, raise public capital, and grow the business in partnership with our public investors. However there are two major hurdles: (1) investment bankers demand a heavy toll, and (2) Sarbanes/Oxley makes it very expensive for a smaller company to comply. The company Google showed a better approach to going public, using a public Dutch auction instead of buckling under to investment bankers. This should be a model to replace the current stranglehold of investment bankers. Set up a process for complete public disclosure and make it simple and inexpensive for companies to go public via a supervised internet auction.

As CEO and CSO for Biolog I try my best to always look at the future and serve as company visionary. High tech companies often need to be led by visionaries. Steve Jobs showed that very clearly in his start-up and his turnaround of Apple. Simply stated, smart government policy would encourage visionaries by keeping down the barriers to starting new companies and the barriers that prevent them from gaining access to public funding.

- 14) What specific steps can Federal agencies take to improve the predictability and transparency of the regulatory system? (Please specify the relevant agency.)

Reply to 14)

In our case, we have had issues with the FDA in trying to get our bacterial identification products approved for sale to clinical laboratories. We feel that the rules that the FDA has established are too vague, too arbitrary, and have been applied more stringently against our company (a small US company) compared to our two main competitors (a large French and a large German company). I would be more than happy to discuss the details privately.

- 15) What specific improvements in the regulatory processes for drugs, diagnostics, medical devices, and agricultural biotechnology should federal agencies implement? What challenges do new or emerging technologies pose to the existing regulatory structure and what can agencies do to address those challenges?

Reply to 15)

The FDA, the drug companies, and the overall drug approval and drug liability process are a huge problem that needs a massive reform.

Let me start with the drug companies. They are both the cause of problems and also victims. To promote innovation, the largest pharma companies should be broken up. The US government made a huge mistake by allowing so many mergers. The industry was much

healthier and much more productive when there were 30 pharma companies instead of 5. When the companies are smaller there is a much greater diversity of ideas and research projects. There is also greater competition. When the companies are too large, they have to find drugs with multi-billion dollar potential, so they focus in a few areas and ignore important diseases that are not as common. They also become very fearful of making mistakes and getting sued.

The FDA has no incentive to streamline the approval process. Hospitals and clinical trials have become much too slow and expensive. This kills innovation and slows the discovery and release of important new drugs.

Lawyers are an enormous and unproductive leach on the entire process. If a drug clears all of the FDA hurdles and reviews, it should be immune from law suits. Pharma companies should be relieved of this huge non-productive burden. Instead, more money should be spent to monitor for problems after the drug is on the market. This is a good and valid use of money. If a drug proves safety and efficacy to the current state of science, but later turns out to have an unforeseen detrimental effect, then its use for certain patients should be curtailed or it should be taken off the market. Pharma companies should not be shaken down by law suits. When people chose to take new drugs, they are clearly taking some risk. Life has risks and people must make choices. When lawyers and injured parties win in the current law suits, many other people lose because the money is not used in the development of newer and better drugs and devices.

FDA regulation of diagnostics should also be reformed. See my Reply to 14). In this case, I think that regulations defining what is needed to market a device for identification of bacteria in hospitals should be determined not by FDA staff but by an independent qualified committee of scientists with detailed knowledge of this field. The committee should meet every year to decide if and how the regulations should be modified. The same should be done with regulations defining what is needed to market a device of determining antibiotic susceptibility. The current regulations are inappropriate, unnecessarily expensive, and stifle innovation.

Public-private partnerships: The Administration is interested in serving as a catalyst for public-private partnerships that build the bioeconomy and address important unmet needs in areas such as health, energy, agriculture, and environment.

16) What are the highest impact opportunities for public-private partnerships related to the bioeconomy? What shared goals would these partnerships pursue, which stakeholders might participate, and what mutually reinforcing commitments might they make to support the partnership?

17) What are the highest impact opportunities for pre-competitive collaboration in the life sciences, and what role should the government play in developing them? What can be learned from existing models for pre-competitive collaboration both inside and outside the life-sciences sector? What are the barriers to such collaborations and how might they be removed or overcome?