Request for Information: Building a 21st Century Bioeconomy

QIAGEN Response

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Introduction:

QIAGEN respectfully submits this document in response to the Notice of Request for Information (RFI) by the Science and Technology Policy Office on October 11, 2011 as a means of providing input into the development of the National Bioeconomy Blueprint.

Note: The responses to the individual questions in the RFI are intentionally brief to ensure the most important points are captured. In addition, the responses are brief to maximize OSTP's ability to capture and synthesize the volume of input that is expected to be received in response to this RFI.

Corporate Information:

QIAGEN (www.qiagen.com) is the leading provider of sample and assay technologies. Sample technologies are used to isolate DNA, RNA, and proteins from any biological sample. Assay technologies are then used to make specific target biomolecules, such as the DNA of a specific virus, visible for subsequent analysis.

We have developed and market more than 500 consumable products and automated solutions. The company provides these products to molecular diagnostics laboratories, academic researchers, pharmaceutical and biotechnology companies, and applied testing customers for purposes such as forensics, animal or food testing and pharmaceutical process control. QIAGEN's assay technologies include one of the broadest panels of molecular diagnostic tests available worldwide. This panel includes the Digene HPV Test, which is regarded as a "gold standard" in testing for high-risk types of human papillomavirus (HPV), the primary cause of cervical cancer, as well as a broad suite of solutions for infectious disease testing and companion diagnostics.

QIAGEN employs more than 3,000 people in over 35 locations worldwide, with over 1000 employees in four sites and remote locations throughout the United States. Our sales exceed $1.0 billion globally.

Grand challenges:

OSTP question:

(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.

QIAGEN response –

Grand challenges for the bioeconomy include the development and expanded use of cost effective molecular based clinical diagnostics for:

- Disease Prevention - screening of non-symptomatic patients to detect risks for specific diseases such as cancer.
- Disease Profiling - testing of symptomatic patients to determine the type and severity of an infection.
- Personalized Healthcare – testing of pre-diagnosed patients to guide treatment decisions and use of medicines.
- Point of Need testing – testing in non-laboratory settings such as doctors' offices or field based sites.

Through early detection, appropriate profiling, personalized healthcare, and point of need testing, hundreds of thousands of lives can be saved and health care costs can be reduced significantly.

Concrete steps that can be taken to achieve these goals include:

- Effective and efficient federal regulatory processes that work in cooperation with academia and industry to appropriately balance the risk/benefit of a test or treatment.
- Enhanced and optimized funding programs spanning from basic research through discovery and translation to a commercially viable product with a focus on those disease states of greatest impact to the population. These funding programs should incentivize the research and industry community based on speed of development, utility, and impact of a given diagnostic or treatment.
- Enhanced public/private partnerships that foster innovation while appropriately protecting the Intellectual Property created as a result of these partnerships.
- Improved public and private cooperation in creating awareness of new molecular based diagnostics through the communication of best practices and clinical outcomes.

In addition to the expanded use of cost effective molecular based clinical diagnostics, grand challenges for the bioeconomy exist in the development and expanded use of cost effective molecular based tests in applied applications including:

- Forensics – increased use of genetic "fingerprinting" to help solve criminal investigations and better ensure the safety of the population.
- Food safety – quickly and accurately identifying food contamination from pathogens in all stages of the food cycle – from "farm to fork".
- Veterinary diagnostics - quickly and accurately preventing, profiling, and treating diseases within our nation's livestock.

Concrete steps that can be taken to achieve these goals include:

- Expanding upon the existing National Institute of Justice funding programs for state and federal crime laboratories to facilitate the acquisition of state of the art molecular based methods including automation; as well as persuade CODIS SSO to adopt a requirement that all patent covering STR Loci must be disclosed and/or made available for licensing.
- Streamlined and more efficient federal regulatory processes from FDA and USDA to quickly approve and create awareness about new technologies that provide greater sensitivity and specificity for detecting pathogens and disease while decreasing the overall cost of testing food or livestock.

Research and development:

OSTP question:

(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?

QIAGEN response:

From our routine analysis and according to publically available Health and Human Resources information (http://report.nih.gov/rcdc/categories/), there are 229 research/disease areas that receive funding. The top ten funding priorities are:

- Clinical Research
- Genetics
- Prevention
- Cancer
- Biotechnology
- Neurosciences
- Infectious Diseases
- Brain Disorders
- Women's Health
- Behavioral and Social Science

These ten areas receive approximately 43% of current funding. QIAGEN generally supports the current prioritization of funding given that these areas are pragmatic in nature and provide for clear utilization of emerging genetic based analysis leading to appropriate treatment of disease. As mentioned earlier in the corporate information, QIAGEN has been focused on providing state of the art clinical diagnostics, including the digene HPV Test, which is regarded as a "gold standard" in testing for high-risk types of human papillomavirus (HPV), the primary cause of cervical cancer, as well as a broad suite of solutions for infectious disease testing and companion diagnostics. In addition, QIAGEN plays a key role in providing the tools (instruments and reagents) for collection and analysis of nucleic acids from all sample types that are required in all areas of research currently prioritized by HHS.

QIAGEN would suggest a continuing shift in research funding to the area of companion diagnostics or personalized health care. FDA has already identified more than 30 different diagnostic target markers in the context of approved drug labels. As this number increases new molecular technologies will and must be developed to more accurately gauge the efficacy and safety of drugs in individual patients.

OSTP question:

(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 initiative)?

QIAGEN Response:

There are many challenges to high throughput research both technically and pragmatically. The researcher must balance high throughput with flexibility. Flexibility is needed based on sample type and source. Researchers must be provided access to next generation platforms that must take many types of biological samples (such as blood, tissue, or saliva) isolate and purify target molecules in a specific sequence and analyze these materials reliably and efficiently to provide useful results. It's clear that a balanced approach towards funding both high throughput and low/medium throughput platforms with flexibility areas is needed. QIAGEN has clearly recognized and validated this need for flexibility within the research community and as a result has developed and launched the fully automated QIAsymphony RGQ, which allows customers to use their own tests, as well as QIAGEN developed tests, to conduct basic or applied research as well as clinical diagnostics.

To specify a particular rallying point within the research community and industry is quite difficult and potentially limiting to the necessary creativity and innovativeness that is a hallmark of the existing US Bioeconomy. As mentioned previously within this document, personalized medicine has clear long term implications to healthcare outcomes and overall costs.

OSTP question:

(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?

QIAGEN response:

Recent developments in high throughput sequencing techniques has generated a wealth of new information on gene sequences whose functions are yet to be determined. Further analysis of those DNA sequences will likely be based on two major efforts: One route will consist of the comparative study of genomes and

structural genome information of other organisms mainly based on the same discovery technologies such as high throughput sequencing. A second approach will address the functional analysis of those gene sequences by means of investigating the regulatory network in which those genes may be involved as well as protein expression of gene sequences from cDNA libraries and using a variety of tools for protein analysis. This second approach will rely on the development of robust yet cost-effective tools that allow higher throughput analysis of expression levels of RNAs and proteins as well as their cellular localization and interaction with other regulatory proteins or nucleic acids in the context of the genome organization. Different technological approaches require highly standardized sample preparation techniques to reliably isolate and analyze RNAs and proteins or e.g. regulatory proteins bound to genomic sequences for which QIAGEN has developed a variety of highly standardized robust sample preparation technologies that can be also automated for higher throughput. Another core activity at QIAGEN focuses on validation of such regulatory gene networks with real-time PCR based array products for sensitive, reproducible and robust detection of gene expression levels or gene mutations within its biological context. QIAGEN believes that multidisciplinary projects and technology developments should be funded that focus on the elucidation of genome structure and its regulation as well as effects attributed to mutations or regulatory molecules such as miRNA or proteins bound to DNA regulatory regions and their modifications along with the development of software tools that can be employed to statistically evaluate the significance of gene functions and -interactions.

Moving life sciences breakthroughs from lab to market:

OSTP question:

(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.

QIAGEN response:

Barriers preventing the commercialization of biological discoveries include:

- Total available market – uncertainty in the final free market revenue contribution of a given discovery.
- Market accessibility – uncertainty in the inherent "pull" from the market versus the "push" required to generate revenue from a given technology.
- "Valley of death" - uncertainty in the ability of a technology to navigate over the period where academic funding stops and commercial funding starts
- Development costs – inherently expensive clinical trial costs required to validate sensitivity, specificity, efficacy, and utility.

- Regulatory complexity – navigating the complicated and at times unclear regulatory pathway
- Commercialization costs – extensive sales and marketing resources necessary to create awareness and uptake of a new technology.
- Intellectual property – inherent risks in rights of ownership of a given discovery

Specific steps that can be taken to address these barriers include:

- Stronger public/private partnerships with shared risk to market for a given discovery.
- Additional funding for translational research that bridges the current "valley of death".
- Federally guaranteed markets such as that created for biodefense vaccines.
- Streamlined regulatory processes.

OSTP question:

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

QIAGEN response:

QIAGEN does not participate in SBIR or STTR programs. Enhancement of these programs to facilitate small business to larger business programs would be helpful. These programs may include risk mitigation approaches to better entice the larger entities to engage with small business.

OSTP question:

(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?

No QIAGEN response:

OSTP question:

(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?

QIAGEN response:

Challenges and responses are the same as those identified in OSTP Question (5).

OSTP Question:

Workforce development:

QIAGEN Summary Statement:

In order to create a technically-skilled workforce, education about bioeconomy (still quite a new topic/term) should start early and a foundation should be laid in High School. Potential employees need to learn very early on about career opportunities in bioeconomy. Additionally, education needs to be affordable for everyone who wants to pursue a college degree/academia education to ensure a high number of potential candidates for the bioeconomy workforce.

OSTP question:

(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?

QIAGEN response:

- Redesign programs to better meet current and future science and technologies needs in close cooperation with the private sector
- Universities might need to adapt their approach by including current business trends, development/technologies and more real life examples into their programs

OSTP question:

(10) What roles should community colleges play in training the bioeconomy workforce of the future?

QIAGEN response:

Community colleges are vital resources for manufacturing and technical associate positions within the biotechnology industry. By utilizing a model similar to the auto and aviation industry we can ensure the community colleges are producing students that have the right set of skills and training.

- Auto & aviation industries have provided engine schematics and blueprints to community colleges and trade schools for years so that students are learning how to build and repair actual engines. We can mimic this by providing our manufacturing and production procedures to professors so that

they can create curriculum that trains students in relevant procedures and methods

- Create a relationship with local community college professors and industry managers that ensure the curriculum develops broad skills necessary for entry-level work.
- By working with QIAGEN, BioReliance, and Human Genome Sciences, Montgomery County Community College in Maryland has developed curriculum that trains students using actual FDA regulated documentation and manufacturing procedures. The Biotechnology coursework includes learning procedures that are certified cGMP and cGDP by the FDA and is being reviewed every year to ensure the curriculum adapts to the needs of the industry.

OSTP question:

(11) What role should the private sector play in training future bioeconomy scientists and engineers?

QIAGEN response:

- Learn from educational standards/programs in other countries and how the private sector cooperates with academia, i.e. on the job training which is support by educational programs at college
- The private sector should influence and guide what their (potential) employees should learn by working closing with academia, influence their programs and sponsor education to develop a workforce according to their business needs

OSTP question:

(12) What role might government, industry, and academia play in encouraging successful entrepreneurship by faculty, graduate students, and postdocs?

QIAGEN response:

Several types of programs can be expanded or created to ensure this relationship.

- Capstone Programs – Industry problems or projects are given to a group of students (bachelors or graduate level) and are tasked with creating a solution to the problem. Monthly collaborative meetings are scheduled between the students and an industry Capstone Program Leader to ensure the team is working in the right direction for a solution. Final presentation is made at the end of a semester to the company and awards or scholarships can be awarded to students for their work.

- Beyond the Bench – Business skills are not generally included in Biological Sciences curriculum. Industry hosted online seminars or on-site presentations at places like the NIH or colleges and universities should be more prevalent to ensure students are knowledgeable about what is needed to start their own company, patent an idea or product, or pursue innovative new business concepts within biotechnology.
- Internships/Co-op Programs – Industry must provide more opportunities for students to work at companies while still in school. Internship programs can help reduce cost-per-hire, reduce required training time for entry-level employees, and provide the industry with a pipeline of young talent that is eager to learn. QIAGEN has successfully hosted 70+ students in the past 2 years and has been able to fill 8 full-time openings with "graduates" of our Internship Program. Of those students, 100% responded in surveys that they were better trained and more knowledgeable about careers within the industry, and 98% were better equipped with the tools and training it would take to land a position within the industry.

Reducing regulatory barriers to the bioeconomy:

OSTP question:

(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.

QIAGEN Response:

In vitro Diagnostic (IVD) Tests are currently treated by the FDA in the same way as other more invasive devices. Many diagnostics are even classified as Class III and require premarket approval, due to the lack of predicate devices. This in turn puts them under the same level of criticality and scrutiny as invasive devices like catheters, many of which are Class II devices. This is a direct impediment to innovation especially when compared to Europe.

The EU, under the IVDD directives, allows most diagnostic tests to be "self-declared". While it would be legislatively difficult for FDA to move to self-declaration, they could re-classify IVD assays to Class I and if need be issue special controls to insure the assays are developed under design controls as well as specific assay requirements. In this way the approval process would be closer to par with the EU but still maintain FDA oversight and audit authority.

OSTP question:

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

QIAGEN Response:

See (13)

OSTP Question:

(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?

As stated in (13) many new In vitro Diagnostics are slow to be implemented or adopted due to the hurdle created by the FDA Pre-Market Approval process. On the other hand independent testing labs are able to develop these same tests under CLIA without this regulatory burden but also without the same scientific rigor required for manufacturers. A potential solution would be to allow manufacturers to partner and supply these labs with well characterized component "sets" that are not characterized sufficiently to meet the hurdle for PMA "kit" approval but could be manufactured under full FDA cGMP controls. This could provide the laboratory with a much more rigorous and reliable product while accelerating a new assay technology to the market.

Public-private partnerships:

OSTP question:

(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?

QIAGEN response:

Public-private partnerships are essential to the efficient and effective commercialization of biological discoveries. As stated earlier in this document, a stronger and more defined sharing of risk/reward is needed to span the gap from the end of academic funding to the start of private funding. This could take the form of clear responsibilities and deliverables on each side of this translational research cooperation. Greater public contribution to offset risk could be rewarded by defined funding payments to the public institution should the commercialization of the biological discovery reach certain points. Clarity of intellectual property ownership

has also been a downfall of many public-private partnerships. Again, a more balanced approach towards risk/reward may be beneficial here as well.

OSTP question:

(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?

QIAGEN response:

The following barriers make pre-competitive collaboration difficult:

- Intellectual property ownership issues
- Lack of control
- Uncertain return and risk
- Commercialization uncertainty – sales and marketing channel management

The overriding issue is related to the risk/reward balance. Typically companies prefer to work within their own sphere of control. Having said this though, the companion diagnostic space may be an area where clear pre-competitive collaboration has been successful. There are numerous examples, including many within QIAGEN, where strong partnerships have developed across the pharma/diagnostic spectrum. These relationships are based on mutual need and benefit with enough clarity of intellectual property and commercialization approaches to make the relationship successful. Government has the opportunity to foster these kinds of relationships early since many of these markers are identified in academia and HHS could consider a provision for clear pre-competitive collaboration and appropriate milestones as a requirement in awarded grants.

In addition, meetings similar to the Annual PHEMCE Stakeholders Workshop and BARDA Industry Day (http://www.federalregister.gov/articles/2010/10/15/2010-26047/5th-annual-phemce-stakeholders-workshop-and-barda-industry-day) held in early 2011 are also a very positive in helping to build pre-competitive knowledge and linkages between the public and private sectors.