

UNLEASHING THE PROMISE OF BIOTECHNOLOGY

Advancing American Innovation to Cure Disease and Save Lives

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A SUMMARY OF BIO'S 5-YEAR STRATEGIC PLAN: RE-ENGINEERING THE BIOTECH ECONOMIC MODEL & RE-INVENTING THE IDEA-TO-MARKET PATHWAY

A. RE-ENGINEERING THE ECONOMIC MODEL

Research and development in the biotechnology industry is a high-risk undertaking because of the substantial start-up costs, lengthy experimentation period, and possibility that the technology will not be viable commercially or otherwise. Congress has historically provided tax incentives to high-risk industries (such as oil and gas, alternative energy, and high-tech start-ups) as a means for encouraging investment in new endeavors. Additionally, the Administration and Congress have repeatedly stated the importance of supporting innovation in health, renewable energy, and green technologies. However, current tax law does not reflect a cohesive strategy to foster growth for health, green technology, or energy-focused biotechnology companies. Given the potential economic and societal benefits of ensuring a robust biotechnology industry in the United States, it is imperative that Congress and the Administration adopt policies that recognize the unique financial structure and needs of biotechnology companies.

The proposals described below are designed to incentivize investors, strengthen small business, and promote innovation in the United States. There are proposals for early-, mid-, and late-stage companies across the biotechnology spectrum, as well as for larger pharmaceutical, biofuels, and renewable energy companies.

SMALL BUSINESS INVESTOR INCENTIVES

Incentivizing Small Biotech Investment: Angel Investor Tax Credit

Modeled after numerous state programs, a federal Angel Investor Tax Credit would provide an incentive for high net worth individuals to invest in emerging biotech companies. To be eligible for this credit, investors would have to make an investment in a company with fewer than 500 employees performing qualifying research. The credit would be equal to 50% of their investment, thus providing an important tax incentive for investment in innovative research-intensive industries.

Stimulating Private Capital for Biotechnology: R&D Partnership Structures

Due to the drawn out nature of the drug development process, small biotechnology companies often have difficulty obtaining early-stage financing for their research and development. Given that these smaller biotech companies are not yet profitable, they are unable to immediately use their tax assets to offset income. New partnership structures wherein biotech companies would enter into a joint venture with high net worth investors and flow through certain tax assets (i.e., tax credits and losses) from the biotech company or its projects to the investors would provide more immediate benefits by allowing investors to offset their income with the company's tax assets, thus stimulating private investment.

Improving Capital Gains Treatment for Small Businesses: Section 1202 Reform

Section 1202 of the Internal Revenue Code, which provides for a reduced capital gains rate for qualified investments in certain small business stock, is not currently beneficial to small biotech companies. Due to the valuable intellectual property and successive rounds of financing inherent in innovative industries, biotech companies do not meet the definition of qualified small businesses under Section 1202. Thus, the Section does not provide investors an incentive to invest in small biotech companies. Among other changes, modifications to the small business definition in Section 1202 would encourage investment in research performed by capital-intensive small biotech companies.

Doubling Private Funding: Small Business Early-Stage Investment Program

A small business early-stage investment program would provide matching grants to venture capitalists that specialize in funding small innovative companies. The government grants would match investments in targeted small businesses, including emerging biotech companies, essentially doubling their financing. Such funding would give start-up biotech companies important seed financing, while also enabling them to leverage the funding to spur further investment. The Board previously supported this policy when passed last year by the U.S. House of Representatives.

SMALL BUSINESS TAX INCENTIVES

Removing Financing Restrictions: Section 382 NOL Reform

Section 382 of the Internal Revenue Code restricts the usage of net operating losses (NOLs) by companies which have undergone an “ownership change.” The law was enacted to prevent NOL trafficking, but small biotech companies are caught in its scope – their reliance on outside financing and deals triggers the ownership change restrictions. Reform of Section 382 would include two provisions: (1) exempting NOLs generated by qualifying research and development by a small business from Section 382; and (2) redefining “ownership change” to exclude certain qualified investments, like those in rounds of venture financing. If small biotech companies could retain their NOLs, they would be able to include them as tax attributes on the balance sheet, thus increasing their value when preparing for additional rounds of financing like mergers or initial public offerings.

INCENTIVES FOR NON-INVESTOR CAPITAL

Increasing R&D Investment: Repatriation

Many small biotechnology companies rely on collaborations with large multi-national corporations to fund their research and development. A repatriation tax holiday on funds brought back to the United States from abroad would incentivize these large companies to repatriate earnings they are holding overseas, and give them the ability to invest in and collaborate with small biotech companies conducting ground-breaking research.

Rewarding Innovative R&D Businesses: U.S. Innovation Box

Many Western European countries have implemented an innovation box that provides for a reduced corporate tax rate on income stemming from certain types of intellectual property, the

lifeblood of the biotechnology industry. Allowing for a reduced corporate rate on this type of income would make investment in U.S. biotechnology more attractive and provide innovative companies with a greater return on their R&D expenses, allowing them to undertake more research projects in the United States.

Supporting Industry Collaborations: Section 197 Amortization Reform

Tax incentives, such as accelerated amortization, can encourage large company investors contemplating acquisitions of specific intangible assets of small biotech companies to invest at an earlier stage in the company's research. Small biotech companies typically have intangible assets that are amortizable under Section 197 of the Internal Revenue Code; thus, reforming that Section to provide for faster cost recovery for intangible assets acquired by investors would stimulate early-stage investment in these companies.

POLICIES TO STIMULATE A BIO-BASED ECONOMY

The "Bio-based Economy" refers to economic activity and jobs generated by the use and conversion of agricultural feedstocks to higher value products, the use of microbes and industrial enzymes as transformation agents or for process changes, and the production of bio-based products and biofuels. The proposals below seek to elevate the concept and awareness of the bio-based economy and advance the policy priorities of the Industrial & Environmental Section (IES) working groups, highlighting the outstanding job creation and rural/rust belt economic development potential of industrial biotechnology and biorefinery commercialization.

Agriculture

Biomass Crop Assistance Program (BCAP) – Reauthorization and Enhancement

BCAP is the key program encouraging and facilitating farmers and landowners to produce new purpose grown energy crops (PGEs) for advanced biofuels and bio-based products. This proposal would reauthorize BCAP through December 2017, and enhance the program by: (1) ensuring funds are directed primarily to production of next-generation crops for biofuels and bioenergy; (2) establishing a dedicated funding mechanism for awarded contracts; (3) providing for eligibility of non-food Title I crops; and (4) clarifying eligibility of certain other PGEs.

Federal Crop Insurance for Purpose Grown Energy Crops

While the U.S. Department of Agriculture's (USDA) Risk Management Agency (RMA) is currently studying the feasibility of developing crop insurance programs for certain biofuels and bio-products feedstocks, there is no formal federal crop insurance program available to producers of new PGEs. This proposal would direct the RMA to finalize its research and work with stakeholders to establish by January 1, 2013, a formal crop insurance program that will cover PGEs, and would authorize such sums as are necessary from the Commodity Credit Corporation to carry out these crop insurance objectives.

Feedstock Sustainability Enhancement Grants

The continued development of domestic sources of energy, including for biofuels and renewable chemicals, depends upon the sustainable availability of consistent, high yield, good quality

feedstocks. This proposal would establish a grant program through USDA and the U.S. Department of Energy (DOE) to fund demonstration projects that utilize practices to enhance biofuels and bioenergy feedstock sustainability, and authorize \$50 million annually through 2017 for such purposes.

Farm Bill Energy Title Amendments for Renewable Chemicals

Many of the programs in the 2008 Farm Bill's Title IX renewable energy programs are not available to renewable chemicals and bio-based products, despite their profound potential benefits to rural America. This proposal would codify the definition of renewable chemicals; modify the Section 9003 Biorefinery Assistance Program and the Section 9007 Rural Energy for America Program to provide for eligibility of renewable chemicals projects; and expand the USDA BioPreferred program to increase program outreach and education.

Tax

Tax Credit for Production of Qualifying Renewable Chemicals

Renewable chemicals and bio-based plastics represent an important technology platform for reducing reliance on petroleum, creating green U.S. jobs, increasing energy security, and reducing greenhouse gas emissions. By providing a renewable chemicals tax credit, Congress can create jobs and other economic activity, and can help secure America's leadership in the important arena of green chemistry. This proposal would provide a federal income tax credit for domestically produced renewable chemicals. Like renewable electricity production credits in current law, these new credits would be general business credits available for a limited period per facility. Similar to the operation of Internal Revenue Code Section 48C, the Treasury Department and USDA would review taxpayers' applications in a competitive process to ensure conformance with legislative intent. Per calendar year, each taxpayer would be entitled to claim as much as \$25 million in renewable chemicals production tax credit associated with production of eligible renewable chemicals.

Advanced Biofuels Tax Reform

Current tax law on advanced biofuels does not provide an ordered pathway toward U.S. energy security. Congress should consider amendments to current law tax incentives that focus on bringing commercial volumes of affordable advanced biofuels to market in the near term. This proposal would implement several changes to the tax code towards this end: (1) extend the Cellulosic Biofuels Production Tax Credit through 2016 and add eligibility for algal biofuels; (2) allow advanced biofuels facility developers the option of electing to receive an investment tax credit; (3) provide for eligibility of biorefinery retrofit projects; (4) provide eligibility to the federal Section 1603 Grants in Lieu of Tax Credits program; and (5) extend and expand eligibility for cellulosic biofuels property accelerated depreciation.

Defense

Strategic Biorefinery Initiative and Offtake Authority

Substantial energy security benefits would accrue to the U.S. Department of Defense (DOD) from development of domestic sources of renewable biofuels and bio-based products. As a major potential customer and as a potential source of funding for biorefinery construction, DOD

is uniquely positioned to help accelerate deployment of these vital products. This proposal would establish and provide necessary funding for a DOD Strategic Biorefinery Deployment Program to finance construction of the first five commercial military advanced biofuels biorefineries. It directs DOD to identify existing funding authority for such projects, and to conduct by January 1, 2012, a biorefinery “fly-off” to identify and fund construction of the most promising projects. In addition, this proposal would provide DOD with the authority to enter into long-term (up to 15 years) offtake agreements for procurement of advanced biofuels for military use.

Energy

Repurpose and Retrofit Grant Program

It is widely recognized that repurposing or retrofitting existing idled or under-utilized U.S. manufacturing facilities to integrate next-generation processes capable of producing advanced biofuels and renewable chemicals and bio-products is one of the most time and cost effective ways to build out the advanced biofuels and renewable chemicals sector. This proposal would establish a federal matching grant program through DOE to fund projects to repurpose or retrofit existing idle or under-utilized manufacturing facilities for the production of advanced biofuels and/or renewable chemicals, up to 30 percent of eligible costs. It would authorize \$100 million annually through 2017.

Synthetic Biology for Enhanced Sustainability of Biofuels and Renewable Chemicals

The advancing field of synthetic biology has the potential to greatly enhance both the economic and environmental sustainability of fuels and chemicals manufacturing. This proposal would create a DOE Synthetic Biology Research and Development Grants Program to fund research and development in industrial biotechnology for the enhanced sustainability of biofuels and renewable chemicals produced through synthetic biology technology. This program would support work on biological catalysts and processes that enable the cost-effective sustainable production of advanced biofuels, renewable chemicals, and other technologies that reduce or minimize greenhouse gas emissions, including biological processes for removing carbon dioxide from the atmosphere. The proposal would authorize \$20 million annually for this program through 2017.

Industrial Bioprocess R&D Program

The use of industrial biotechnology for the production of renewable chemicals and bio-based products is enabling dramatic improvements in industrial energy efficiency, as well as a host of renewable alternatives to traditional petrochemical-based products. This proposal would create an Industrial Bioprocess Research & Development program through the DOE Office of Energy Efficiency and Renewable Energy’s Industrial Technologies Program, to fund projects in industrial biotechnology for renewable chemicals, bio-based products, and renewable specialty chemicals. It would authorize \$150 million annually for this program through 2017.

Environment

EPA R&D Program for Renewable Chemicals

Renewable chemicals can be engineered to provide innovative solutions that save energy, are environmentally preferred, and are a direct substitute or “drop-in” replacement for petrochemicals. Presently, there are no strong standardized metrics to quantify environmental benefits of these innovative products, and allow renewable chemical companies to demonstrate substantial cost, environmental, and efficiency benefits, further encouraging the development of sustainable products. This proposal would establish a new Research and Development grant program funded by the Environmental Protection Agency (EPA) that would provide grants to conduct environmental assessments for renewable chemicals and industrial products produced with industrial biotechnology. This program would (1) conduct assessments to provide quantitative data to demonstrate chemical safety and pollution prevention in industrial biotechnology processes; and (2) be followed up with educational and awareness programs for U.S. businesses for the purpose of providing education and data on the environmental and economic benefit of using green chemistry and biological processes in manufacturing. It would authorize \$30 million for this program annually through 2017.

B. RE-INVENTING THE IDEA-TO-MARKET PATHWAY

CREATING A 21ST CENTURY FDA

The proposals below are designed to ensure a clear and effective pathway for turning ideas into realities that will benefit patients and improve public health. The proposals are focused on creating a 21st century U.S. Food & Drug Administration (FDA), and creating more effective clinical research and development processes. With an increasingly aging population, it has never been more critical to support an industry that offers solutions to the most pressing health care needs of today and tomorrow. It is imperative that FDA be an agency that recognizes its national role in advancing innovation, maintains the ability to effectively review innovative products in a timely manner, and promotes a consistent and science-based decision making process that is reflective of patient needs. The proposals described below are designed to address each of these principles. They are organized under three main headings: Elevating FDA and Empowering Operational Excellence; Advancing Regulatory Science and Innovation; and Enabling Modernized Patient-Centric Clinical Development.

ELEVATING FDA AND EMPOWERING OPERATIONAL EXCELLENCE

Update the FDA Mission Statement

FDA needs a clear mandate to encourage the development of innovative products. In addition, FDA must have the capacity and commitment to incorporate the latest scientific advances into its decision making so that regulatory processes can keep pace with the tremendous potential of companies’ leading edge science. Congress can help by updating FDA’s statutory mission to underscore the need for FDA to advance medical innovation by incorporating modern scientific tools, standards, and approaches into the agency’s work, so that innovative products can be made available to those who need them and in a timely manner.

Establish a Fixed Term of Office for the Commissioner of Food and Drugs

The Commissioner of Food and Drugs is charged with leading a science-based, regulatory agency to advance the public health. As required by statute, the President appoints the Commissioner with the advice and consent of the U.S. Senate. However, a presumption of replacement with each new President has politicized the appointment and confirmation process. The Federal Food, Drug, and Cosmetic Act (FFDCA) should be amended to provide that the President appoint the Commissioner to a six-year term of office. Once confirmed, the Commissioner would be removable by the President only for pre-specified reasons – neglect of duty, malfeasance in office, or an inability to execute the agency’s mission. Encouraging consistent and stable leadership at FDA, with protection from political influence that typically occurs during a presidential administration transition, better equips the agency to fulfill its mission to protect and promote the public health.

Grant FDA Status as an Independent Agency

FDA regulates nearly a quarter of the consumer goods supplied to the American public. As such, the agency should have the same authorities to make budget, management and operational decisions as afforded other independent agencies such as the Environmental Protection Agency. This would empower the agency to work more effectively with the President and Congress to carry out its mission to promote and protect the public health. Creating an independent agency would also enhance the agency’s ability to obtain quality and consistent leadership.

Establish an External Management Review Board for FDA

FDA is a large, complex organization, and in order to fulfill its responsibilities effectively, it must be well organized and well managed. It is critical that the agency’s organization and management capabilities be periodically analyzed, and that the Commissioner of Food and Drugs be provided with fresh, visionary, and independent thinking on how to improve the ability of the agency and its centers to promote and protect the public health, as well as the support necessary to implement recommendations. An external advisory board composed of individuals with experience in organizational management could help the agency address operational challenges. Current law should be amended to establish a Management Review Board (MRB) to conduct periodic reviews of FDA’s management and organizational structure, and to provide recommendations to the Commissioner about ways to improve FDA operations.

ADVANCING REGULATORY SCIENCE & INNOVATION

Support Regulatory Science Public-Private Partnerships

Under the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress established the Reagan-Udall Foundation for the Food and Drug Administration, an independent non-profit organization intended to support public-private partnerships for the purpose of advancing the mission of FDA to “modernize medical [and other] product development, accelerate innovation, and enhance product safety.” The Foundation could, for example, form collaborations to advance the use of biomarkers, surrogate markers, and new trial designs to improve and speed clinical development. However, Congressional appropriations bills for the

agency have subsequently restricted FDA’s ability to transfer federal funding to the Foundation. These funding restrictions should be lifted so that the Reagan-Udall Foundation can fulfill its promise.

Create an FDA “Experimental Space,” led by a Chief Innovation Officer, to Pilot Promising New Scientific and Regulatory Approaches

FDA has developed several initiatives to advance regulatory science. These include the FDA/NIH Joint Leadership Council, the academic Centers of Excellence in Regulatory Science, and FDA’s Critical Path Initiative. However, FDA’s ability to incorporate modern science into its regulatory processes has been limited because there is no entity within the agency with unified responsibility for systematically analyzing the findings and recommendations from these groups, and with clear authority to pilot promising scientific and regulatory approaches. An FDA “Experimental Space,” led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new approaches are integrated into agency operations at all levels.

Enhance FDA’s Access to External Scientific and Medical Expertise

FDA is the preeminent federal agency charged with evaluating cutting-edge science as it is applied to the prevention, diagnosis, and treatment of human disease. FDA also has been perceived by many as the global standard bearer for regulatory review of drug and biologic applications. However, scientific and medical knowledge, techniques, and technology are advancing at a more rapid pace today than at any other time, and FDA’s capacity to access information about these advances has not kept pace. It is essential that FDA’s access to scientific and medical advice be enhanced by improving the operations of FDA Advisory Committees, establishing Chief Medical Policy Officers in the immediate offices of the Center Directors, and providing FDA staff with additional avenues for accessing external scientific and medical expertise.

ENABLING MODERNIZED PATIENT-CENTRIC CLINICAL DEVELOPMENT

Increase Access to Innovative Treatments and Therapies through Progressive Approval

Patients, industry, Congress, and others are eager to find ways to deliver safe and effective new drugs and biologics to patients. Patients, particularly those with illnesses for which no adequate therapy exists, want access to promising new therapies earlier in the drug development process. Smaller biopharmaceutical companies that develop those therapies are sometimes unable to maintain operations through extensive phase III testing without revenue from the sale of products. Expanding and improving the accelerated approval pathway into a progressive approval mechanism would help provide patients more timely access to needed therapies. This pathway would be limited to innovative products for unmet medical needs, significant advances to standard of care, targeted therapies, and those that have been approved by the European Medicines Agency (EMA) or other mature regulatory agencies. This pathway also would ensure risk-benefit analysis that incorporates the safety and needs of patients in the real world.

Empower FDA to Utilize a Weight-of-Evidence Approach

FDA's current statutory authority requires that the agency approve applications for new drugs when they have been demonstrated to be safe and effective under the intended conditions of use. The law provides that effectiveness is established where FDA is satisfied that there is "substantial evidence" that the new drug has the intended effect that it is purported to have. FDA typically requires two "adequate and well controlled" studies under this standard. A weight-of-evidence approach to data analysis, however, would allow the decision-maker to look at all data and information, whatever its value, and give each appropriate consideration.

Leverage Electronic Health Records to Facilitate Clinical Research

Every new drug's sponsor spends years designing and conducting clinical trials to show the drug is safe and effective. Using health information technology (IT) such as electronic health records (EHRs) in clinical research will improve and speed up the drug development process, and decrease costs. However, there are significant barriers preventing wide-spread use of health IT in clinical research, including slow adoption by providers and lack of standards development. FDA can help remove those barriers. Congress should create a Clinical Informatics Coordinator in the Office of the Commissioner of Food and Drugs charged with developing processes to validate and encourage the use of health IT in clinical research, and establishing pilot projects to use health IT in clinical research.

Require FDA to Disclose to the Sponsor Reasons for Non-Approval

The Federal Food, Drug, and Cosmetic Act (FFDCA) implies that licensing or approval applications are a binary question – approve or deny – due to phased, investigational review of applications; however, there is in practice a third response. In this case, FDA neither approves nor officially denies the application (which would require FDA to give the sponsor specific procedural rights such as a hearing); rather it finds the application to be incomplete in some way that makes the application ineligible for approval. When FDA makes such a finding, it should communicate to sponsors in clear terms why risk was determined to outweigh benefits, and why other agency authorities such as Risk Mitigation and Evaluation Strategies (REMS) – which are designed to mitigate risk for approved products – are insufficient (in addition to indicating what must be done to address any deficiencies). Such an approach would help create a consistent and transparent evaluation of risk-benefit, and provide the sponsor with better information on what, if any, additional studies are required to achieve approval.

THE ROAD TO A BRIGHTER FUTURE FOR AGRICULTURAL BIOTECHNOLOGY

For the past two decades, the United States has played a leadership role in agricultural biotechnology innovation, contributing billions of dollars to the U.S. GDP. Unfortunately, the U.S. regulatory system for plant and animal biotechnology, which was designed in the mid-1980s to facilitate product development, is fast becoming an impediment to the development and commercialization of safe, beneficial products. Today, developers of agricultural biotechnology are less certain about the length and scope of federal regulatory approvals and the susceptibility of approvals to legal challenge. Greater certainty is needed to drive scientific innovation and reassure international trading partners, which is essential to U.S. producers of genetically-engineered products. While the underlying statutory authorities and regulatory framework for

agricultural biotechnology are sound, to improve the process it will be important for Congress to give necessary direction to the federal agencies responsible for implementing the governing statutes that most directly impact genetically-engineered plants and animals. BIO therefore will propose a series of appropriate directives for the Congress to enact.

ATTACHMENT I: CAPITAL FORMATION POLICIES

SMALL BUSINESS INVESTOR INCENTIVES

ANGEL INVESTOR TAX CREDIT

Background

There is no federal income tax credit for investments in small businesses by the “angel investors” that bridge the gap between friends-and-family financing and venture capital funds. This “early-stage” or “seed” capital is vital to fund the operations of start-up ventures, especially in capital intensive industries such as biotechnology. For biotechnology companies, the lengthy time period from research and development to commercialization requires “patient capital” – investors who have a longer term investment horizon to achieve their desired economic returns. This is because those companies do not generate profits to fund operations and have little access to debt financing. Such patient capital often comes from angel investors.

Many states have recognized that a state income tax credit is an effective incentive to increase investment by angel investors. Currently, more than 20 states have some form of an angel investor tax credit. In general, the credit amounts have ranged from 25% to 50% of the qualified investment (with one state, Hawaii, providing a 100% tax credit). These programs often have a cap on the amount of credit available per investor or per company. Also, many states curtail the cost of the credit by maintaining a cap on the total amount of credits that the state will give out. Such provisions limit the revenue cost of these incentive programs.

A federal angel investor income tax credit (“Angel Investor Tax Credit”) would provide a tax credit for individuals investing in certain qualified small companies, such as biotechnology start-ups. The tax credit could be used by the individual to offset other income tax liability, thus decreasing the angel investor’s overall tax liability and freeing up additional investment capital. Thus, the Angel Investor Tax Credit would incentivize high net worth individuals to invest in small biotechnology and other companies, providing these companies with critical funding.

Proposed Federal Angel Investor Tax Credit

The Angel Investor Tax Credit would be available to qualified angel investors making a qualified equity investment directly or through a qualified fund in an eligible small business. The credit would be nonrefundable and would not be subject to limits on its use for alternative minimum tax purposes.

Qualified Angel Investor

To take advantage of the Angel Investor Tax Credit, the qualified equity investment would have to be made by an individual that is an “accredited investor” for SEC purposes. Such accredited investors include a natural person who has an individual net worth, or joint net worth with their spouse, that exceeds \$1 million, and a natural person with income exceeding \$200,000 in each of the two most recent years or joint income with a spouse exceeding \$300,000 for those years and a reasonable expectation of the same income level in the current year. In addition, a qualified equity investment could be made by a “qualified fund”, which would be defined as (A) a pass-

through entity (*i.e.*, an S corporation, tax partnership, etc.) formed and operated for the purpose of making equity investments in an eligible small business and (B) of which all the shareholders, partners or members are individuals who are “accredited investors” for SEC purposes. A qualified angel investor would not include a person controlling (directly or indirectly) 50% or more of an eligible small business, or an employee of such business. For purposes of clarity, a person would not fail to be a qualified angel investor solely on account of serving as a director of the company or entering into a *bona fide*, arm’s-length consulting agreement.

Qualified Equity Investment

The taxpayer would generate an income tax credit with respect to each “qualified equity investment.” A qualified equity investment is the acquisition of any equity interest (whether stock, partnership interest, limited liability company membership interest, etc.) at original issuance (either directly or through an underwriter) in an eligible small business.

Eligible Small Business

The Angel Investor Tax Credit would be available to qualified angel investors investing in an eligible small business, which is a business entity that meets the following criteria:

1. Either (a) the average annual number of full-time equivalent employees employed by the company during either of the two preceding years was 500 or fewer under Section 41(b)(3)(D)(iii) or (b) a corporation or other company that would (if treated as a “C” corporation for federal tax purposes) meet the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company).
2. 50% of the company’s employees must perform substantially all of their work in the United States and the headquarters must be located in the United States.
3. Conducts a specified amount of research and development. The research and development criterion would be based on the existing Section 41 research credit. Thus, the company’s research and development activities would need to meet the “qualified research” definition under Section 41(d)(1)(B). Specifically, the project would need to focus on research activities undertaken for the purpose of discovering information—
 - which is technological in nature, and
 - the application of which is intended to be useful in the development of a new or improved business component of the taxpayer.¹
4. Has been in existence for 5-years or less at the time of the qualified equity investment.

¹ The research and development requirement would also incorporate the standards used by the IRS in determining whether there is “qualified research” under Section 41(d) (*e.g.*, uncertainty, related to development/improvement, etc.), with appropriate modifications for purposes of this provision.

Angel Investor Tax Credit Amount and Limitations

The amount of the Angel Investor Tax Credit would equal 50% of the qualified angel investor's qualified equity investment. The amount of the tax credit would be subject to limitations as follows:

- An individual/married couple would be capped as to the aggregate amount of the Angel Investor Tax Credit per eligible small business in a single taxable year.
- An individual/married couple would be capped at the total amount of Angel Investor Tax Credits in all eligible small businesses in a single taxable year.
- The aggregate amount of Angel Investor Tax Credits per eligible small business in a taxable year would be capped.
- The aggregate amount of Angel Investor Tax Credits per eligible small business would be capped at a maximum amount.

Other Rules

The Angel Investor Tax Credit would be part of the general business credit of Section 38 and treated as a specified credit for such purposes (*i.e.*, removing the AMT limitation otherwise applicable to general business credits). Controlled group rules would apply for purposes of determining whether commonly-owned business entities that were eligible small businesses on a stand-alone basis would qualify as such if aggregated. The credit would be subject to recapture as a result of certain recapture events, such as a sale or exchange of the qualified equity investment within three years of that investment. The qualified equity investor's tax basis in their equity interest that is a qualified equity investment would be reduced by the amount of the Angel Investor Tax Credit.

Benefits of Angel Investor Tax Credit Proposal

Incentive for High Net Worth Individuals to Increase Investment

The tax credit would decrease the risks associated with investing in a small research-intensive company because it would provide immediate tax benefits that would free up additional capital that can be invested in the high-tech businesses.

Incentive for Critical Early-Stage/Seed Investment

The proposal would motivate individual angel investors to increase their investments at the seed/early-stage level. This would help close the "capital gap" that start-up companies currently face. This capital gap is especially prevalent for companies with equity investment needs in the \$250,000 to \$5 million range. Below that level, entrepreneurs rely on credit cards, second mortgages, and friends-and-family investments. At higher levels of funding, venture capital funds may invest. But for smaller companies, the capital gap at this critical range is vital to the commencement and expansion of their business. The tax credit would provide funding to earlier stage companies that is not currently available through the traditional venture capital process because venture capital investors typically do not invest at such an early stage.

Promotion of Innovation in Multiple Industries

Individual investors and qualified funds will only receive the credit if they invest in small, American companies engaged in Section 41(d) research and development. Many of these types of companies are emerging biotechnology and life sciences companies. However, the proposal extends the tax incentive more broadly than biotech companies. Thus, the proposal is ideal for coalition building, as other innovative industries that qualify under Section 41(d) (high tech, green tech, etc.) would also benefit from more early-stage investment.

The Benefits of Angel Investing Reward Society

Studies show that research and development has historically been underfunded because social returns may exceed private returns. Thus, the enactment of the Angel Investor Tax Credit would effectively act as a public-private partnership, which would provide significant positive externalities to society and not just benefit the angel investors.

R&D PARTNERSHIP STRUCTURES

PART 1: TAX INCENTIVES FOR SMALL BIOTECHNOLOGY INVESTMENTS

Background

Congress has historically provided tax incentives to high-risk industries (such as oil and gas, alternative energy, and high-tech start-ups) as a means for encouraging investment in new endeavors. The oil and gas industry is a primary example, where it is often necessary to invest significant amounts of capital to determine whether a particular well will be successful. Tax incentives have been provided to mitigate the geologic risk and the uncertain cash flows from oil and gas projects by enhancing the after-tax returns from the projects. In certain cases, Congress has restricted the tax incentives in a manner that provides the tax benefits to smaller producers that are less able to diversify the economic risks that inhere in oil and gas exploration.

The challenges faced by smaller producers in the oil and gas industry in finding and developing new resources and diversifying risk is analogous to the challenges faced by small life sciences companies. Small life sciences companies expend substantial financial resources on research and development of technology before successful FDA approval. In many cases, the projects may be the technological equivalent of a “dry well” and may not prove technologically or commercially viable.

There exist generally available tax incentives in the Code that can benefit companies in the biotechnology industry. For example, Section 41 provides a research tax credit for increases in qualifying research activities and Section 174 provides an immediate deduction for qualifying research and experimental expenditures.² These tax incentives are not specifically targeted to small biotechnology start-ups and generally are of little use to such companies organized as “C” corporations or as pass-through entities owned by individuals. “C” corporation start-ups often incur large net operating losses and do not generate the taxable income necessary to utilize losses and credits. Instead, the “C” corporation carries the tax attributes forward as deferred tax assets

² All “Section” or “§” references are to sections of the Internal Revenue Code of 1986, as amended, or the Treasury Regulations promulgated there under.

that may be used at some (distant) point in the future, provided that they are not in the interim subjected to limitation (*e.g.*, Section 382, which can severely restrict the value of loss carry-forwards). For individual owners of start-ups organized as pass-through entities, the passive activity loss rules of Section 469 impose restrictions on the ability to offset unrelated income with losses.

Even where start-up biotech companies are “C” corporations with taxable income or where individual owners of pass-through entities have the ability to take advantage of these incentives, the general tax credit and deduction provisions contain limitations that make them less effective as an incentive. Section 41 provides a credit only for incremental increases in research under a formula. For individuals, Section 174 expenditures are not fully deductible against the alternative minimum tax. The passive activity loss rules also defer the use of losses and tax credits generated. More recently, Congress enacted a credit more specific to the biotechnology industry, albeit narrowly drafted. The Code provided a credit for qualified investments in qualifying therapeutic discovery projects in Section 48D. However, the provision had a sunset date at the end of 2010.

Tax incentives for the biotechnology industry still can be useful where the start-ups are organized as “C” corporations with taxable income or are organized as pass-through entities (*e.g.*, tax partnerships) and the individual owners are able to use losses and credits, taking into account restrictions under the passive activity loss rules and other restrictions. Tax incentives are also useful for “C” corporation investors that can or do invest in biotech start-ups organized as pass-through entities because such investors that have taxable income can use the tax losses and credits generated by the start-up.

The present proposal would provide further incentives for start-up “C” corporation biotechnology companies and investors in pass-through biotechnology start-ups by providing tax benefits modeled after those available in the oil and gas industry. The types of tax incentives available to the oil and gas industry would be equally beneficial to (and are adaptable to) the life sciences industry, because the incentives would increase investment and attract new investment to this important activity.

Existing Tax Incentives for the Oil and Gas Industry

Tax incentives that apply to the oil and gas industry include the following:

1. **Deduction of Intangible Drilling Costs**: Oil and gas investors can immediately deduct intangible drilling costs (“IDCs”), which include many of the costs necessary for drilling the well (other than tangible equipment costs). Section 263(c). These expenses generally constitute a significant portion of the pre-production costs of drilling a well.
2. **Depletion**: Oil and gas investors can choose (subject to various restrictions) their method for recovering the costs of an oil and gas project. The two available methods are “percentage depletion” and “cost depletion.” Section 611 *et seq.* The taxpayer may use whichever method provides for a higher deduction, providing the ability to accelerate deductions.

3. Passive Activity Loss Exception: The passive activity loss rules are an anti-tax shelter measure intended to curtail abusive transactions involving passive investments by individuals and certain other taxpayers. Congress provided an exception in these rules for working interests in oil and gas projects, which exception enables an investor to deduct losses from working interests even if the taxpayer does not “materially participate” in the activity. Section 469(c)(3). The ability of individual investors to offset these losses against other forms of income enhances their after-tax returns.
4. Geological and Geophysical Costs: These costs are amortizable over a 24-month period (7-years for major integrated oil companies). Section 167(h).
5. AMT Relief: There is favorable alternative minimum tax treatment of IDCs and depletion for independent producers. Section 57(a)(1).
6. Tax Credits: Tax credits are available for production of oil and gas from marginal wells and for various oil recovery methods. Sections 45I and 43.
7. Deduction for Qualified Tertiary Injectant Expenses: Certain types of injectant expenses are deductible, subject to limitations. Section 193.
8. Publicly-Traded Partnerships: Partnerships and limited liability companies that are publicly-traded are generally taxed as “C” corporations, which are not “flow-through” entities for tax purposes. There is an exception to these rules for entities that have sufficient amount of income from certain types of investments, including income from oil and gas sources. Section 7704(d).

Proposal for Biotechnology Incentives

Targeted tax incentives in the oil and gas industry increase the after-tax returns of investors by providing, *e.g.*, accelerated deductions, tax credits and special alternative minimum tax treatment. These types of tax incentives could similarly be applied in the biotechnology industry.

The proposal would follow the model of the taxation of the oil and gas industry and provide targeted tax incentives for biotechnology sector investments. The tax incentives would be available to projects that meet the definition of a small biotechnology business.

Small Biotechnology Business Definition

Under the proposal, a taxpayer that invests in a company that qualifies as a specially-defined “small biotechnology business” would be eligible for targeted tax incentives. A small biotechnology business would be defined as: (1) any flow-through entity if the annual average number of employees employed by such person during either of the 2 preceding calendar years was 500 or fewer under Section 41(b)(3)(D)(iii) or (2) a company that, if treated as a “C” corporation for federal tax purposes, meets the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company). Controlled group rules would apply to ensure that the tax incentives were being generated by small biotechnology businesses.

Qualified Biotechnology Research and Development

In order to be eligible under this proposal, the small biotechnology business must conduct “qualified biotechnology research and development” in an amount that meets a minimum threshold amount.

The research and development prong would build off of the existing Section 41 research credit. Thus, the company's activities would need to meet the "qualified research" definition under Section 41(d)(1)(B). Specifically, the project would need to focus on research activities undertaken for the purpose of discovering information—

- which is technological in nature, and
- the application of which is intended to be useful in the development of a new or improved business component of the taxpayer.

This prong would also incorporate the standards used by the IRS in determining whether there is "qualified research" under Section 41(d) (*e.g.*, uncertainty, related to development/improvement, etc.), with appropriate modifications for purposes of this provision.

The biotechnology portion of the test would provide that the research and development conducted by the company must be in a recognized biotechnological field. This would be defined as a project designed to:

- Treat or prevent diseases or conditions by conducting pre-clinical activities, clinical trials, and clinical studies, or carrying out research protocols, for the purpose of securing FDA approval of a product under section 505(b) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act.
- Diagnose diseases or conditions or to determine molecular factors related to diseases or conditions by developing molecular diagnostics to guide therapeutic decisions.
- Develop a product, process, or technology to further the delivery or administration of therapeutics.
- Develop other projects in the biotechnology industry.

The minimum threshold amount of qualified biotechnology research and development would require that substantially all of the business activity of the company would consist of conducting research and development in the biotechnology field. "Substantially all" would be determined based on appropriate measures that are suitable for research and development small businesses, such as a specified ratio of research and development expenditures to product revenues.

Small Biotechnology Business Tax Incentive Proposals

First, there would be a tax credit for expenditures in biotechnology projects that would either be modeled after the qualified therapeutic discovery project credit as a stand-alone provision or incorporated within the framework of the Section 41 research credit. The amount of the credit would be based on 50% of the qualifying expenditures in the project, as determined under specified conditions, and it would not be an incremental credit as presently applies under Section 41.

Second, to the extent that biotechnology companies are presently required to capitalize costs and depreciate or amortize those costs over a lengthy recovery period, small biotechnology businesses would be permitted to accelerate the depreciation and amortization deductions. This provision would be similar to, but broader than, the deduction currently permitted under Section

174 for research and experimental expenditures. This tax incentive would be modeled after the IDC deduction currently permitted to oil and gas producers and would be intended to similarly incentivize investors in biotechnology projects.

Third, the proposal would enact, for individuals, an exception to the alternative minimum tax rules for specified biotechnology research and experimental expenditures.

Each of these amendments would be available to, and encourage investment in the biotechnology sector by, individuals who are able to use such tax benefits taking into account the passive activity loss rules and “C” corporation biotechnology start-ups that have taxable income. Other investors (for example, “C” corporations who invest in a pass-through small biotechnology business, but do not cause the company to fail to qualify as a small biotechnology business) could also take advantage of these tax incentives.

Other Considerations

The statutory amendments and relevant legislative history would provide that tax benefits from investments in these small biotechnology businesses would not be disallowed under the economic substance doctrine of Section 7701(o) and case law or Section 183 (the hobby loss rules) solely as a result of start-up losses incurred by such businesses. The proposal would also contain aggregation rules based on existing Code provisions that treat separate entities as being under “common control” in order to ensure that taxpayers do not inappropriately set up separate research and development companies intended to qualify as small biotechnology businesses.

R&D PARTNERSHIP STRUCTURES

PART 2: PASSIVE ACTIVITY LOSS EXCEPTION

Background

Research and development in the biotechnology industry is a high-risk undertaking because of the substantial start-up costs, lengthy experimentation period, and possibility that the technology will not be viable commercially or otherwise. This industry shares many similarities to the oil and gas industry, where exploration, development, and commercialization of new petroleum-based resources has comparable risks. These risks are compounded for smaller biotechnological companies, just as they are for smaller oil and gas companies, because of the inability to spread the risk of failure across a broad number of projects.

Tax incentives in the oil and gas industry include favorable depreciation and amortization regimes (*e.g.*, deduction of intangible drilling costs, depletion, geological and geophysical cost amortization), tax credits for certain types of production, exceptions from the publicly traded partnership rules for oil and gas investments, alternative minimum tax relief associated with certain tax incentives, and, the subject of this proposal, an exception from the passive activity loss rules for certain oil and gas investments.

The passive activity loss rules were designed to thwart tax shelters that had developed by the mid-1980s for marketing to individuals. Congress enacted provisions that allowed losses from passive investment activities to only offset passive income (other than portfolio income from

investment-type activities). This limitation applies to individuals (including those investing through flow-through entities) and closely-held “C” corporations, but does not apply to broadly held corporations, such as publicly-traded corporations.

The passive activity loss provisions were relaxed in the case of some oil and gas industry investments. There is an exception to the passive activity loss rules for taxpayers otherwise subject to this onerous limitation if the taxpayer acquires a working interest in an oil and gas property. The use of such tax losses, which are prevalent in the start-up phase of many projects, provides a higher after-tax return to the investor. This working interest exception is limited in scope, however, and precludes the use of a limited partnership or limited liability company taxed as a “flow-through” entity. This limitation acts as a *disincentive* to investment to project financing by individuals.

The same generally applicable passive activity loss rules apply to ventures in the biotechnology field. This is one of the major factors in the organization of numerous life sciences projects as “C” corporations, which are taxed at the entity level, rather than tax partnerships or other types of flow-through entities. The passive activity loss rules defer the utilization of tax losses and tax credits for individuals investing through flow-through entities unless the individuals otherwise have passive income. As a result, existing tax incentives such as the Section 41³ research credit or the Section 174 research and experimental expenditure deduction can be ineffective for individual life sciences investors that do not otherwise have passive income. This imposes a tax drag on returns from start-up investment in the life sciences industry. In contrast to tax partnerships and other flow-through entities, “C” corporations do not flow through losses or credits to the stockholders of the corporation at all. As a result, if the entity does not become profitable or if it is acquired in certain transactions, the tax losses and tax credits may end up expiring unused or otherwise being limited.

There may be non-tax reasons for the use of “C” corporations in the life sciences industry, but the application of the passive activity loss rules (and resultant inability to immediately take advantage of tax benefits at the investor level) is a significant tax reason. A major impact of the enactment of this provision was the move away from the use of research and development limited partnerships (“R&D LPs”) that once financed biotechnology investment and played a significant role in the 1980s and 1990s to fund critical research and development projects of some of today’s successful biotech companies. Since the introduction of the passive activity loss rules in 1986, R&D LPs were forced to rely more heavily on including other benefits (product royalties and warrants of the biotech company) to provide a more attractive return for investors. This in turn altered the economic sharing of the potential gains and losses from these deals.

This proposal would amend the federal income tax laws to remove or modify tax law restrictions on the use of tax losses and tax credits by investors in flow-through entities that invest in life sciences projects in a manner that encourages investment without reinvigorating tax shelters. A

³ All “Section” or “§” references are to sections of the Internal Revenue Code of 1986, as amended, unless specified otherwise.

separate proposal would provide tax incentives similar to those available to the oil and gas industry to incentivize investment in the life sciences industry.

Description of Proposal

This proposal would enact amendments that would promote investments by individual taxpayers in the biotechnology industry through non-corporate joint ventures, limited liability companies, limited partnerships, or “S” corporations that conduct biotechnology research. Specifically, the proposal would enact amendments to the Code that would permit a life sciences company’s tax benefits (deductions related to research and experimental expenditures, losses from the research and development of a project, and research tax credits) to “flow through” to the individual investor without limitation under the passive activity loss rules. This would result in immediate tax benefits to individual investors and thus attract more investment in small life sciences companies. The exception to the passive activity loss rules would be modeled after the existing exception for working interests in oil and gas properties.

Small Biotechnology Business Definition

Under the proposal, a taxpayer that invests in a flow-through entity that qualifies as a specially-defined “small biotechnology business” would be eligible for an exception to the application of the passive activity loss rules. Such a small biotechnology business would be based on existing Code provisions that are similarly targeted towards small businesses. A small biotechnology business would be defined as: (1) any flow-through entity if the annual average number of employees employed by such person during either of the 2 preceding calendar years was 500 or fewer under Section 41(b)(3)(D)(iii) or (2) any flow-through entity that, if treated as a “C” corporation for federal tax purposes, meets the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company). Controlled group rules would apply to ensure that the persons availing themselves of this passive activity loss exception are truly a small biotechnology business.

Qualified Biotechnology Research and Development

In order to be eligible under this proposal, the small biotechnology business must conduct sufficient “qualified biotechnology research and development” to meet a minimum threshold amount.

The research and development prong would build off of the existing Section 41 research credit. Thus, the company’s activities would need to meet the “qualified research” definition under Section 41(d)(1)(B). Specifically, the project would need to focus on research activities undertaken for the purpose of discovering information—

- which is technological in nature, and
- the application of which is intended to be useful in the development of a new or improved business component of the taxpayer.

This prong would also incorporate the standards used by the IRS in determining whether there is “qualified research” under Section 41(d) (*e.g.*, uncertainty, related to development/improvement, etc.), with appropriate modifications for purposes of this provision.

The biotechnology portion of the test would provide that the research and development conducted by the company must be in a recognized biotechnological field. This would be defined as a project designed to:

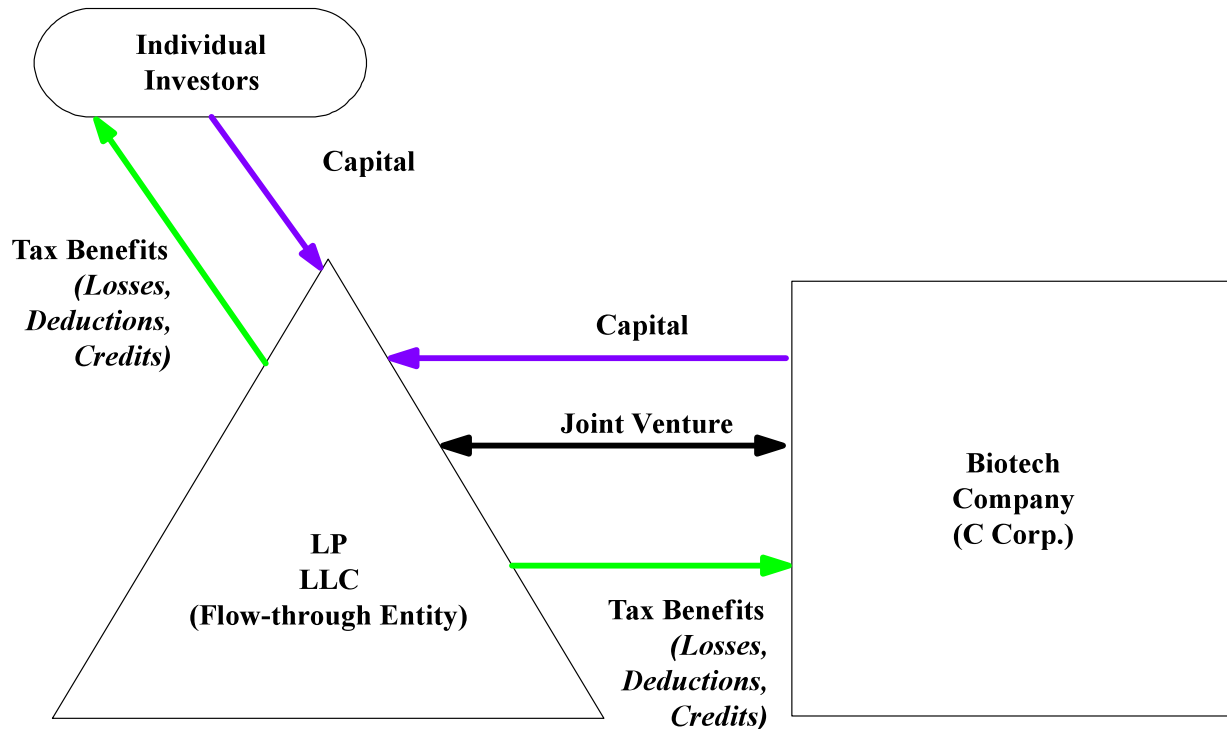
- Treat or prevent diseases or conditions by conducting pre-clinical activities, clinical trials, and clinical studies, or carrying out research protocols, for the purpose of securing FDA approval of a product under section 505(b) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act.
- Diagnose diseases or conditions or to determine molecular factors related to diseases or conditions by developing molecular diagnostics to guide therapeutic decisions.
- Develop a product, process, or technology to further the delivery or administration of therapeutics.
- Develop other projects in the biotechnology industry.

The minimum threshold amount of qualified biotechnology research and development would require that substantially all of the business activity of the company would consist of conducting research and development in the biotechnology field. “Substantially all” would be determined based on appropriate measures that are suitable for research and development small businesses, such as a specified ration of research and development expenditures to product revenues.

Other Considerations

The statutory amendments and relevant legislative history would provide that tax benefits from investments in such projects would not be disallowed under the economic substance doctrine of Section 7701(o) and case law or Section 183 (the hobby loss rules) solely as a result of start-up losses incurred by such businesses. The proposal would also contain aggregation rules based on existing Code provisions that treat separate entities as being under “common control” in order to ensure that taxpayers do not inappropriately set up separate research and development flow-through entities intended to qualify as small biotechnology businesses.

Project Structure Using Flow-through Entity for Biotechnology Investment



SECTION 1202 CAPITAL GAINS REFORM

Present Law

Section 1202 provides a small business investment tax incentive that Congress enacted in 1993.⁴ Under Section 1202, non-corporate taxpayers generally may exclude 50% (temporarily increased) of their gain from the sale or exchange of qualified small business (“QSB”) stock that has been held for more than 5 years. Special exclusion rates apply to certain empowerment zone businesses.

Section 1202 currently has had a greater theoretical than practical impact on small business investment, including the biotechnology sector. Tax law changes dating back to the mid-1980s have caused many biotech start-ups to organize as “C” corporations. In 1986, Congress enacted the passive activity loss rules of Section 469, which limits individuals and closely-held corporations from offsetting active income (such as wage income) and investment income with losses from passive activities. This change made the use of so-called “R&D limited

⁴ All “Section” or “§” references are to sections of the Internal Revenue Code of 1986, as amended, or the Treasury Regulations promulgated there under.

partnerships” and other pass-through entities less attractive to individual investors, who could no longer immediately use the tax losses generated by these projects.

For “C” corporation biotech firms, individual investors are potential candidates for the Section 1202 exclusion. Despite the seemingly favorable tax benefits provided by Section 1202, in practice the provision has never lived up to expectations. This has been due to the complexity of the rules, its limited scope, subsequent changes in tax rates, and the alternative minimum tax (“AMT”).

This proposal would simplify Section 1202 in some respects to make it more user-friendly. This is an important consideration given anecdotal reports of high IRS audit rates for taxpayers claiming the exclusion. The QSB stock rules would also be modified to provide an actual tax benefit to investors and expanded to apply to start-up ventures not organized in corporate form (such as limited partnerships and limited liability companies), reflecting the evolution of business entity choice since the enactment of Section 1202.

Qualified Small Business Eligibility

The Section 1202 exclusion applies to QSB stock, which is stock:

- issued by a “C” corporation after August 10, 1993,
- issued by a corporation that is a QSB as of the date of issuance,
- acquired by the taxpayer at original issue, including through an underwriter, in exchange for money or property other than stock or for services (excluding underwriting services),
- the issuer of which is an eligible corporation that meets an active business requirement during substantially all of the taxpayer’s holding period for such stock, and
- that is not disqualified as QSB stock on account of specified types of redemptions.

There are multiple requirements for a business to be treated as a QSB under the current rules:

- **“C” Corporation.** A QSB must be a domestic “C” corporation.
- **Active Business Requirement.** In order to meet the active business requirement, at least 80% of the corporation’s assets (based on value) must be used in the active conduct of one or more “qualified trades or businesses.” Qualified trades or businesses are any trades or businesses other than specified business engaged in providing services (*e.g.*, health, law and those relying on the reputation or skill of employees), finance, farming, certain natural resource production or extraction, or a lodging or restaurant business. The active trade or business test takes into account assets held by subsidiaries, portfolio investments, working capital, real estate holdings, and computer software royalties. Taxpayers engaged in Section 195 start-up activities, Section 174 research and experimental activities, or Section 41 in-house research activities are treated as using their assets in the active conduct of a qualified trade or business. The active business requirement takes into account factors such as working capital, investment assets and investments in subsidiaries for purposes of the 80% test.
- **Gross Assets Test.** The issuer’s gross assets must be \$50 million or less both before and immediately after the stock is issued. Although stock can continue to be QSB if the issuer’s assets exceed \$50 million after the issuance of the stock, once the \$50 million

threshold has been exceeded, the corporation will not be permitted to again issue stock that will qualify as QSB stock. The determination of gross assets is generally determined by reference to the amount of cash and the adjusted tax basis of other property. In the case of contributed property, gross assets are determined based on FMV. Modified controlled group rules apply to aggregate parent-subsiary corporations.

Per-Issuer Limitation

Taxpayers can only exclude a specified amount of gain with respect to the QSB stock of a single issuer. The gain limitation is the greater of:

- (1) 10 times the taxpayer's aggregate adjusted tax basis in the QSB stock of that issuer disposed by the taxpayer during the taxable year, or
- (2) \$10 million (reduced by the aggregate amount of the gain taken into account by the taxpayer under Section 1202 with respect to that issuer in any prior year).

5-Year Holding Period

In order to qualify for the exclusion, the QSB stock must have been held for more than 5 years.

Redemption Rules

Certain redemptions can preclude a purchase of stock from qualifying as a purchase of QSB stock. The rules are more restrictive if there is a "significant redemption" of more than 5% of the QSB's stock (by value) during a specified period.

Miscellaneous Rules

Section 1202 also contains rules addressing stock acquired through the conversion feature of convertible QSB stock, QSB stock held by pass-through entities, certain tax-free and other transfers, basis rules, and short position rules.

Increased Exclusion for QSB Stock Issued in 2009, 2010 and 2011

The American Recovery and Reinvestment Act of 2009 temporarily raised the Section 1202 exclusion from 50% to 75% for QSB stock acquired after February 17, 2009, and before January 1, 2011 (amended as indicated below).

The Small Business Jobs Act of 2010 and the Tax Relief, Unemployment Insurance Reauthorization, and Job Creation Act of 2010 temporarily have provided a 100% exclusion for QSB stock acquired after September 27, 2010, and before January 1, 2012. In addition, the preference item treatment under the AMT for such stock was temporarily eliminated.

Problems with Existing Section 1202

Impact of the Reduction in Capital Gains Tax Rates

At the time of enactment of Section 1202 in 1993, capital gains tax rates were higher. The application of the QSB stock exclusion was (and remains) linked to a 28% tax rate that results in little benefit for sellers of QSB stock (a 14% effective tax rate on the gain). The maximum long-term capital gain rate has since been reduced to 15% (expiring December 31, 2012). As a result, the effective tax rate for QSB after application of the exclusion remains 14%, so there is a mere

1% difference from otherwise applicable long-term capital gain tax rates. This 1% difference hardly acts as an incentive for a taxpayer to hold QSB stock for 5 years, when a 15% long-term capital gains tax rate is otherwise available after one year.

Impact of the Alternative Minimum Tax

The AMT reduces the benefit of the Section 1202 exclusion because a portion of the QSB gain is treated as a preference item. The add-back of this preference item (7% of the excluded gain) can result in the taxpayer paying a higher effective tax rate, although this tax preference has temporarily been eliminated for certain investments.⁵ Another issue that arises under the AMT is that Section 1202 is mandatory, so if the taxpayer is not benefitted under this provision on account of the AMT, then the taxpayer must deliberately fail to qualify for the provision.

Valuation and Measurement Issues.

The qualified trade or business requirement necessitates both valuations and monitoring for compliance/record-keeping in connection with the “substantially all” requirement throughout the 5 year holding period. For example, the QSB must monitor its “reasonably expected” research and experimental expenditures and working capital needs in connection with holding investment assets for compliance with the substantially all test. Similarly, the gross assets test can require difficult valuation issues and record-keeping issues that can be especially problematic with intellectual property and follow-on investments.

Cap on Excluded Gains of a Single Issuer.

The per-issuer cap can work counter to the stated purpose of incentivizing investment in small businesses. Many taxpayers invest in numerous projects, a large portion of which do not pan out. Large gains from a successful project or projects are hoped to offset losses from other small business projects, plus provide a significant return (the “home run” scenario). The cap on the amount of gain able to be excluded undermines the benefits of having a large gain from a winning investment.

Holding Period for QSB.

The 5-year holding period can be problematic because it is lengthy, especially given the historically minimal benefit of Section 1202. Moreover, it can be problematic for follow-on financings, because later-stage investors may not be able to satisfy the holding period requirement by the time of a liquidity event.

C Corporation Requirement for QSB.

The “C” corporation requirement excludes “S” corporations and pass-through entities (such as partnerships and limited liability companies that have not elected to be taxed as “C” corporations).

Non-corporate Investor Requirement.

⁵ Other examples of where AMT rules were eliminated temporarily or permanently include the specified credit rules of Section 38(c)(4) for specified credits, such as the Section 45 refined coal credit and Section 40 alcohol fuels credit.

Corporate taxpayers, which do not enjoy preferential long-term capital gains tax rates, cannot benefit from the Section 1202 exclusion.

Miscellaneous Provisions

The testing period for assets held for investment that are reasonably expected to be needed in the next two years for research and experimental expenditures or increased working capital limits the amount of investment assets that the QSB can hold and imposes a monitoring requirement on taxpayers.

The “significant redemption” rules may cause some equity investments in the QSB to not be eligible for QSB stock treatment, even if such redemption had a business purpose and was not intended to avoid the rules of Section 1202.

Description of Proposal

Congress’s original intent in enacting Section 1202 was to encourage and reward individuals for taking risks by investing in new ventures and small businesses. This laudable policy goal continues to thrive today. Along the same lines, the Obama Administration’s 2012 budget proposal included a permanent extension of the 100% exclusion of gains on QSB stock. While the congressional intent of Section 1202 and the Administration’s proposal are intended to spur job creation and economic growth through new investments in small businesses stocks, the current Section 1202 requirements unfortunately are overly complex and do not provide adequate incentives to invest in small companies.

The application of the QSB exclusion to many small companies is hindered by the complexity, administrative cost, uncertainty, and out-dated parameters of the current rules. The simplification of existing Section 1202 and expansion of its exclusion to adapt it to current business entity choice practices would provide the platform to carry out the congressional intent to increase investment in small companies.

Proposed Amendments to Section 1202

1. Implementation of a graduated series of exclusions for QSB stock (or, as described below, equity interests in other types of entities) based on the taxpayer’s holding period for the stock. The exclusions would be:
 - 50% for QSB stock held for more than one year but not more than three years.
 - 75% for QSB stock held for at least three years, but not more than 5 years.
 - 100% for QSB stock held for more than 5 years.
2. Repeal the AMT preference.
3. Increase the aggregate gross asset test for a “qualified small business” from \$50 million to \$150 million, indexed to inflation, and simplify the active business requirement to apply based on a Section 162 trade or business standard.
 - Also, other helpful revisions would include allowing increased assets from follow-on rounds of financings to not automatically be included for purposes of the gross assets test and excluding intellectual property/intangibles from the gross assets test.
4. Eliminate the per-issuer limitation or increase it to \$20 million per QSB.
5. Permit “S” corporations and non-corporate entities to qualify as QSBs, subject to appropriate limitations such as controlled group rules.

6. Allow corporations (and not just individuals) to take advantage of the gain exclusion for QSB stock.
7. Modify the significant redemption rules that apply to determine whether stock is QSB stock by providing that a purchase with a business purpose shall be disregarded if one of the principal purposes was not the avoidance of limitations in Section 1202.
8. Modify the rules for determining when working capital is taken into account for purposes of the active business test by treating investment assets reasonably expected to be used within 5 years to finance research and experimental activities in a qualified trade or business or increases in working capital needs of a qualified trade or business.
9. Delink the Section 1202 exclusion from the 28% tax rate that currently applies
10. Clarify that biotech is a qualified trade or business.

Comparison of Existing Law and Section 1202 Proposal

In its current form, Section 1202 is too complex and has failed to track recent developments in both the tax laws and in entity choice for small businesses. Thus, Section 1202 is little-used by small business investors. In order for Section 1202 to achieve its stated goals of encouraging investment in small businesses, a number of revisions are needed. The impact of such changes would be increased investment by venture capitalists and other investors in the biotechnology industry, among other sectors of the economy. Below is a side-by-side comparison of existing law and the proposed revisions to Section 1202, along with supporting reasons for each of the amendments.

	Current Law	Proposed Modification/Rationale
Gain Exclusion and Holding Period	<p>Taxpayers generally may exclude up to 50% of the gain from the sale of QSB stock held for more than 5 years.</p> <p>Under ARRA, the exclusion was temporarily increased to 75% for stock acquired after 2/17/09 and before 1/1/11 (modified by subsequent legislation)</p> <p>Under the Small Business Jobs Act of 2010 and the Tax Relief, Unemployment Insurance Reauthorization, and Job Creation Act of 2010, the exclusion was temporarily increased to 100% for stock acquired after 9/27/10 and before 1/1/12.</p>	<p>Support graduated exclusion rates based on the taxpayer's holding period for the QSB stock.</p> <p><u>*Rationale</u>-While a 50% exclusion of gain from the sale of QSB stock can incentivize investors, such exclusion should be available to investors not holding QSB for substantial period of time. A 75% ex-clusion (3-5 year holding period) and a 100% exclusion (5 year + holding period) would likely increase the inflow of investment, particularly to higher-risk innovative small business such as biotech, clean tech, and high tech.</p>
AMT Preference	A percentage of the excluded gain is a preference under the AMT,	Support the permanent elimination of the AMT preference item for

	Current Law	Proposed Modification/Rationale
	subject to the temporary elimination of this rule.	gain excluded. * <u>Rationale</u> -The AMT preference reduces the existing Section 1202 tax benefits. By eliminating the AMT preference, investors would be able to fully benefit from Section 1202.
Aggregate Gross Assets Test and Active Trade or Business	The issuer of stock must meet a \$50 million gross assets test and apply complicated rules to determine whether there is an active trade or business.	Support raising the gross asset test to \$150M in gross assets and exclude intellectual property/intangibles for purposes of the test. Related changes would permit maintenance of QSB stock status for newly-issued stock in follow-on rounds of investments. * <u>Rationale</u> -The use of a gross assets test to define “small businesses” that qualify for Section 1202 limits innovative small businesses that become ineligible for the QSB exclusion for later investors due to their continuous need for private financing coupled with high value intellectual property. Thus, innovative small businesses, while small in terms of operations (<i>i.e.</i> , employee size, product revenue) are penalized for their intellectual property and ability to raise much-needed scarce private capital. Simplify the active trade or business test by applying a Section 162 standard. * <u>Rationale</u> -Eliminating the complex active trade or business test would simplify compliance and avoid difficult valuation and monitoring issues.
Per-Issuer Limitation	The maximum amount of gain eligible for the exclusion by a taxpayer for any corporation	Support elimination of the per issuer limitation or an increase in the limitation to \$20 million.

	Current Law	Proposed Modification/Rationale
	during any year is the greater of: (1) 10X the taxpayer's basis in stock issued by the corporation and disposed of during the year, or (2) \$10M reduced by gain excluded in prior years on dispositions of the corporation's stock.	<u>*Rationale</u> -Given the long lead time and substantial financing needed to bring a therapy to market, a cap on the exclusion that an investor can receive from an emerging biotech company deters investment of further additional private capital into the company. Thus, by eliminating the per-issuer limitation/cap, an investor will have all of their gains be eligible for the exclusion, which will likely spur additional rounds of financing by existing investors.
C Corporations	A QSB must be a corporate entity.	Support expanding the QSB rules to non-corporate entities. <u>Rationale</u> -Many more businesses organize today as non-corporate entities. The amendment would attract greater investment to small businesses.
Non-corporate Investors	Only non-corporate investors can use the Section 1202 exclusion.	Support expanding Section 1202 to corporate investors. <u>Rationale</u> -This would attract greater investment to small businesses by larger companies who are in the same industry and work on a collaborative manner.
Redemptions	Significant redemptions are taken into account for purposes of determining whether stock issued is QSB stock.	Support disregarding any purchase that has a business purpose provided that one of the principal purposes was not the avoidance of limitations in Section 1202. <u>Rationale</u> -Redemptions that meet such a test do not present an abusive situation and will promote increased investment in QSB's because potential investors will now not be trapped by an unfair technical rule that would otherwise apply.
Working Capital	Investment assets may only be	Support permitting companies to

	Current Law	Proposed Modification/Rationale
	taken into account for purposes of the active business test if such assets are reasonably expected to be used within two years for research and experimental purposes or increased working capital needs.	take investment assets into account if reasonably expected to be used within 5 years for research and experimental purposes or increased working capital needs. <u>Rationale</u> -This will provide greater flexibility for QSB's to use funds in their business without running afoul of the active business test and permit QSB's to expend such funds in due course without the threat of failing to qualify as a QSB.
28% Rate Subject to Exclusion	The Section 1202 exclusion (ranging from 50% to 100%) applies to a base 28% tax rate, resulting in an effective tax rate ranging from 14% to 0%.	Delink the Section 1202 exclusion from the base 28% rate and apply it to the long-term capital gains tax rate. <u>Rationale</u> -At the time of enactment, there were higher capital gains rates and the 28% base rate provided an incentive for the Section 1202 exclusion as compared to the long-term capital gains rate. Lower capital gains tax rates have reduced the spread between the Section 1202 exclusion (apart from the recent tax acts providing for a 100% exclusion) and long-term capital gains tax rates. By applying the Section 1202 exclusion to the long-term capital gains tax rate, investors in QSB's will have a true incentive to qualify for this tax benefit, which will promote investment in such entities.
Qualified Trade or Business	Certain businesses are excluded from the definition of a qualified trade or business, including those in the field of health where the principal asset is the reputation or skill of one or more of the	Support clarification that biotech is not excluded from the definition if a qualified trade or business, even if the reputation or skill of an employee is a principal asset at the outset of the business.

	Current Law	Proposed Modification/Rationale
	employees.	<u>Rationale</u> -This clarifies that life sciences are not the type of trade or business intended to be excluded.

SMALL BUSINESS EARLY-STAGE INVESTMENT PROGRAM

Background

Bringing groundbreaking therapeutics from bench to bedside is a long and arduous road, and small biotechnology companies are at the forefront of the effort. It takes an estimated 8 to 12 years for one of these breakthrough companies to bring a new therapy from discovery through Phase I, Phase II, and Phase III clinical trials and on to FDA approval of a product. The entire endeavor costs between \$800 million and \$1.2 billion. However, the current economic climate has made private investment dollars extremely elusive.

As U.S. biotech companies face financial uncertainty, other countries are increasing their investments and considering intellectual property protections to encourage domestic biotech growth. As part of its efforts to develop a world class biotech industry, the Chinese government is implementing a 5-year plan (2006-2010) in which it promotes agricultural biotechnology, builds demonstration projects for the commercial production of vaccines and gene-modified medicines, and enhances the capabilities for new medicine development and production. India is in the process of laying out its National Biotechnology Regulatory Authority. Among the initiative’s goals is to encourage early-stage innovation, technology transfer, and startup formation. Up to 30% of the government’s biotech budget will be invested in public-private partnership programs designed to promote innovation, pre-proof-of-concept research, accelerated technology, and product development.

While grant programs such as SBIR have proven helpful to the industry, more needs to be done to ensure the U.S. biotech industry’s prosperity for years to come. In 2010, venture capital fundraising endured its fourth straight year of decline and its worst since 2003. Biotechnology received just \$2 billion in venture funds, a 27 percent drop from its share in 2009. Even worse, the biggest fall was seen in initial venture rounds, which are the most critical for early-stage companies. Series A deals last year brought in just over half of what they did in 2009. Incorporating an early-stage venture capital matching program would provide a capital infusion for the beginning stages of therapeutic projects.

Proposal

The “Small Business Early-Stage Investment Program” would provide \$1 billion in grants for venture capital investments in certain industries, including life sciences. Under the program, the SBA’s investments would be treated the same as investments by other limited partners in an investment fund, except that the SBA would not receive any control or voting rights with respect to the early-stage small business. Importantly, the new program protects the interest of the taxpayer by specifying that grants could only be awarded to investment companies that had

already raised an equivalent amount of capital from private-sector sources. Ideally, over time, the SBA's investment program will become self-sustaining as funds from successful small businesses are repaid into a revolving fund.

Investment Company Criteria:

- In order to participate, an investment company (incorporated body, LLC, or limited partnership) must submit a business plan describing its investment strategy in early-stage and small business concerns in targeted industries or other business sectors, information about the expertise of the management team, and as the likelihood of success and profitability.
- Targeted businesses include the following: agriculture technology; energy technology; environmental technology; life sciences; information technology; digital media; clean technology; defense technology; and photonics technology.
- A participating investment company must make all of its investments in small business concerns, 50% of which must be early-stage small businesses. The definition of an early-stage small business requires that it is a U.S. small business concern and has less than \$15 million in gross annual sales revenues for the previous 3 years.

Investment Company Application Process:

- The SBA must make conditional approvals or disapprovals of applications within 90 days of receiving the application. If an investment company has met all of SBA conditions final approval will be given 30 days after the date SBA has determined all conditions have been met.
- If there are areas that need to be addressed in order to receive final approval the investment company will have a year to satisfy conditions for final approval. Final approval of the applications will be made within 90 days after the date the applicant has met all approval conditions. If conditions are not met within the time period the application will not be able to participate in the program.

Equity Financing:

- The SBA will commit equity financing to an investment firm that can be drawn upon to make new investments for 5 years from the date of the first draw, and make follow-on investments and management fees for 10 years from the date of the first draw.
- The SBA will not provide equity financing that is greater than the amount of non-federal capital (on or before date when equity financing is used) and no single investment company can receive more than \$100 million.

Investment Shares & Equity Financing Interest:

- Each investment made by the investment company shall be treated as comprised of capital from equity financings under the program according to the ratio that capital from the program bears to all capital available to the investment company for investment.

- Equity financing interest conveyed to the SBA has the same rights of other investors (receives distributions in the same time and in the same amount as other investors) in regards to interests but does not denote control or voting rights to the SBA.
- The SBA is entitled to a pro rata portion of any distributions made equal to the percentage of capital in the investment company the equity financing comprises.
- Manager profits interest cannot exceed 20 percent of the profits (exclusive of any profits that may accrue as a result of capital contributions of managers). No manager profits interest (other than a tax distribution) shall be paid prior to the repayment to investors and the SBA.

SMALL BUSINESS TAX INCENTIVES

SECTION 382 NOL REFORM

Present Law

General

A “C” corporation may generally carry forward its unused net operating losses (“NOLs”) to future years and use these NOLs to offset its future taxable income. Section 382 was enacted to limit tax-motivated acquisitions of corporations with NOLs, built-in losses, and other tax attributes eligible to be carried forward (referred to as a “loss corporation”).⁶ Section 383 similarly applies to loss corporations with tax credits, capital loss carry-forwards, and other tax attributes.

Section 382 plays a significant role in limiting the use of tax attributes in the high tech industry. Many high tech start-up companies (including biotech start-ups) are organized as “C” corporations for a variety of reasons (including an individual investor’s inability to use losses flowing through a tax partnership or “S” corporation on account of the passive activity loss rules, desire to issue stock options, non-tax preferences for more well-developed corporate law, etc.). These high tech companies are involved in capital intensive research and development that involves a significant lag time (up to a decade or more) for the commercialization of their products. On account of their expenditures being deductible (including immediately under Section 174, unless 5-year or greater amortization is elected), depreciable or amortizable, these “C” corporations can generate significant losses in their early years. The financing of these early-stage ventures is typically through multiple stage equity financings, as the companies grow and can attract the attention of angel investors and then venture capitalists. This multi-stage equity financing can and does result in significant restrictions on the ability of these companies to use their tax losses. This is because increases in the ownership of the company on account of, e.g., new investors purchasing stock, may cause an “ownership change” for purposes of Section

⁶ All “Section” or “§” references are to sections of the Internal Revenue Code of 1986, as amended, or the Treasury Regulations promulgated there under.

382. This ownership change may limit a high tech company's ability to use its losses to offset income that is ultimately generated from the commercialization of the research and development.

Operation of Section 382

In general, Section 382 operates by limiting the amount of taxable income that a loss corporation may offset with NOLs, built-in losses, and other tax attributes that arise before an "ownership change." Such limitation is determined by multiplying the value of the stock of the loss corporation immediately before the ownership change by a specified interest rate.

Ownership Change

For purposes of Section 382, an ownership change occurs when there is an increase of more than 50 percentage points in stock ownership of a loss corporation by one or more "5-percent shareholders" during the testing period (generally, a 3-year period ending on the date on which a transaction is tested for an ownership change). The determination of whether an ownership change has occurred is made after any owner shift involving a 5-percent shareholder or any equity structure shift (generally, tax-free reorganizations or mergers).

5-percent Shareholder

A 5-percent shareholder generally includes any individual who directly or indirectly owns 5-percent or more of the loss corporation during the testing period, and public groups of individuals, entities or other persons, each of whom directly or constructively owns less than 5-percent of the loss corporation, but whose ownership is aggregated together as a 5-percent shareholder.

Owner Shift Involving a 5-percent Shareholder

An owner shift involving a 5-percent shareholder is any change in the respective ownership of stock of a corporation that affects the percentage of stock held by any person who is a 5-percent shareholder before or after such change. An owner shift involving a 5-percent shareholder includes, but is not limited to, the following types of transactions:

- (1) A taxable purchase of loss corporation stock by a person who is a 5-percent shareholder before the purchase;
- (2) A disposition of stock by a person who is a 5-percent shareholder either before or after the disposition;
- (3) A taxable purchase of loss corporation stock by a person who becomes a 5-percent shareholder as a result of the purchase;
- (4) An exchange of property for stock in a Section 351 transaction that affects the percentage of stock ownership of a loss corporation by one or more 5-percent shareholders;
- (5) A redemption or recapitalization that affects the percentage of stock ownership of a loss corporation by one or more 5-percent shareholders; and
- (6) An issuance of loss corporation stock that affects the percentage of stock ownership of a loss corporation by one or more 5-percent shareholders.

Equity Structure Shift

An equity structure shift is generally includes tax-free reorganizations under Section 368 (with a few exceptions for special types of tax-free reorganizations, including those involving bankrupt corporations), public offerings and taxable mergers.

Example. An acquiring corporation and a target loss corporation without any overlapping ownership combine in a taxable merger in which the target's shareholders receive mostly cash and some acquiring corporation stock. The acquiring corporation is the survivor of the merger. Following this equity structure shift, an ownership change would occur if the shareholders of the target loss corporation do not own at least 50% of the stock of the acquiring corporation immediately after the merger. If the shareholders of the target loss corporation receive less than 50% of the acquiring corporation's stock, the original shareholders of the acquiring corporation would have increased their ownership interest in the target loss corporation by more than 50 percentage points (*i.e.*, 0% ownership immediately before the transaction and more than 50% ownership interest immediately after).

Proposals

Congress's original intent in enacting Section 382 was to prevent the trafficking of NOLs and other tax attributes - *e.g.* profitable companies buying loss corporations in order to acquire their NOLs to offset taxable income. Unfortunately, the law as written is overly broad and fails to recognize that certain corporations, such as high tech start-up companies, often rely on raising equity through successive financing rounds to successfully negotiate a long product development process. The following proposals are limited exceptions that maintain the underlying rationale for Section 382 – preventing abusive trafficking of NOLs and other tax attributes – while providing high tech corporations with the ability to raise needed capital through multiple stock issuances and to combine the research and development operations of multiple high tech corporations, without incurring an unnecessary tax penalty. These proposals are set forth as alternatives below.

Description of First Proposal: Section 174 Expenditures

Under the first proposal, in the event of a Section 382 ownership change, the portion of any net operating loss or net unrealized built in loss attributable to research and experimental expenditures under Section 174 paid or incurred when the corporation was a “qualified small business corporation” and the portion of that corporation's federal income tax credits generated by research and development under Section 41 would not be subject to limitation under Section 382 or Section 383, respectively.

Qualified Small Business Corporation

Corporations eligible for this provision would include any domestic corporation that is not in bankruptcy and that meets the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company).

COBE

The continuity of business enterprise or “COBE” test of Section 382(c) would apply. Under the COBE test, the qualified small business corporation must continue its business enterprise at all times during the two year period following the ownership change.

Description of Second Proposal: Qualified Investments

Under the second proposal, a Section 382 ownership change would not be triggered by: (1) a qualified investment in a qualified start-up corporation or (2) such other transactions involving mergers and acquisitions involving qualified start-up corporations as provided in Treasury Regulations. It would be expected that the Treasury Regulations would provide that the merger of two loss qualified start-up corporations would be eligible for this Section 382 exception.

Qualified Investment

A qualified investment in stock of certain loss corporations that results in an owner shift involving a 5-percent shareholder would be treated as occurring outside of the three-year testing period under the following circumstances.

- The loss corporation must be a qualified start-up corporation.
- The stock must be acquired at its original issuance (directly or through an underwriter).
- The stock must be acquired solely for cash.
- The 5-percent shareholder must not own (directly, indirectly or constructively after the acquisition) 50% or more of the loss qualified start-up corporation.

For purposes of this rule, stock issued in exchange for convertible debt would be treated as stock acquired by the debt holder at its original issuance for cash if the debt was acquired at its original issuance and solely in exchange for cash.

Qualified Transaction

A qualified transaction means any merger or acquisition involving two qualified start-up corporations that results in an owner shift or an equity shift to the extent provided in Treasury Regulations.

Qualified Start-Up Corporation

A qualified start-up corporation is a corporation that (A) has an average annual number of employees during either of the two preceding years that was 500 or fewer under Section 41(b)(3)(D)(iii) or (B) meets the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company). A qualified start-up corporation must meet the COBE test and an expenditure test.

COBE Test

The qualified start-up corporation must meet the COBE test described above.

Expenditure Test

Under the expenditure test, the qualified start-up corporation must have at least 35% of its expenditures in a taxable year (taking into account redemption payments) be for research and development expenditures described in Section 41(b) and/or research and experimental expenditures described in Section 174. The expenditure test would apply for a measuring period that includes the taxable year in which the closing of the stock issuance occurs and the two preceding taxable years.

Redemptions, Qualified Investment Groups, and Other Rules

There would be rules similar to those applied to redemptions under the Section 1202 qualified small business stock provision for redemptions of stock in a qualified start-up corporation for purposes of determining whether an investment is a qualified investment.

Unless specified in regulations to be published by the Treasury Department addressing customary transactions in the high technology industry, transactions occurring between a qualified start-up corporation and a member of its “qualified investment group” may disqualify what would otherwise be a qualified investment. A presumption against a qualified investment would apply if the qualified start-up corporation received, in a transaction taking place during the two year period beginning one year before any qualified investment, any consideration other than cash. A qualified investment group with respect to a qualified investment means one or more persons who receive stock in exchange for the qualified investment and persons related thereto applying Section 267(b) or Section 707(b).

Treasury regulations would also be authorized to address abusive transactions and the application of similar rules to this provision for Section 383 (concerning similar limitation on tax credits and other tax attributes) and Section 384 (concerning use of pre-acquisition losses to offset built in gains of acquiring corporations).

Other necessary rules and regulations (*e.g.*, exemption from the separate return limitation year rules that can be applicable to consolidated group members) would also be provided for transactions under Treasury Regulations to be issued.

AMT

The alternative minimum tax net operating loss rules would be revised for qualified start-up corporations to remove the current AMT NOL restrictions.

INCENTIVES FOR NON-INVESTOR CAPITAL

REPATRIATION

Present Law

Overseas earnings of U.S. companies are currently taxed at 35 percent when they are repatriated back to the United States. In 2004, Congress passed the American Jobs Creation Act in an effort to create jobs and boost the economy. This legislation contained a repatriation provision granting U.S. multinational corporations a one-time tax break on money earned in foreign countries.

The tax break allowed foreign earnings to be taxed at a rate of 5.25%, which is significantly lower than the corporate tax rate of 35%. Previously, much of the earnings derived from foreign countries were not transferred back to the U.S. because multinationals can defer paying taxes on foreign earnings until such earnings are repatriated to the U.S. in the form of a dividend.

Ultimately, Congress's rationale was that the tax break would act as a strong incentive for American multinationals to send their foreign earnings back to the U.S. and then use the earnings to create more American jobs and/or expand operations in the U.S.

Critics of repatriation believe that because the companies were not required to use the repatriated earnings for the sole purpose of American job creation, there was no guarantee that the tax break would increase job creation. Companies were, however, barred from using the money for executive compensation, dividends, and stock investments. Furthermore, the tax break was seen by critics as a reward for companies that deferred regular repatriation of foreign earnings and a punishment for companies that regularly send money back. Critics worried that the act would set a bad precedent, as U.S. multinationals could view the tax break as an incentive to withhold future foreign earnings in the hope that another repatriated tax break would occur.

Description of Proposal

This proposal would allow a taxpayer to return foreign earnings at a tax rate of 5.25%, provided that the returned funds are used in the United States to advance activities as they relate to IRC Section 41(d). Examples may include but are not limited to:

- 1) Hiring scientists, researchers, and comparable personnel engaged in research and development.
- 2) Making new investments in research and development projects or facilities.
- 3) Conducting research related to a new or improved function, performance, reliability, or quality.

The returned funds would be required to be kept in a separate account from the rest of the taxpayer's finances, and could only be withdrawn for permitted activities. Companies would have to invest in U.S. research and development in the same tax year that they file for the reduced rate.

The taxpayer would have the burden of proving to the Internal Revenue Service (IRS) that its returned funds were used solely and specifically for activities associated with Section 41(d). The election to return certain foreign earnings for qualified use is limited to the first 2 years following enactment.

Analysis

The proposal could make the U.S. more competitive with other countries that have lower corporate tax rates.

This proposal directly incentivizes U.S. research and development by tagging activity to Section 41(d). One of the critiques of other repatriation proposals is that companies would bring funds

back to the U.S. to enjoy the tax break, but would be unwilling to expend the funds into the U.S. economy during a recession. This proposal requires that taxpayers invest the money immediately into the economy to take advantage of the reduced rate. Additionally, the proposal would bring some additional revenues to the U.S. Treasury because there would be some tax paid on it which is not being paid today. The proposal would make the U.S. competitive with other countries that have lower tax rates. Supporters of similar repatriation proposals cite international tax laws — as well as the U.S.'s extremely high corporate tax rate — as making the U.S. less competitive and hindering economic growth and job creation. Supporters of repatriation proposals credit the 2004 repatriation law for helping to return roughly \$300 billion in overseas income.

Lawmakers in both parties are looking for fiscal remedies, and this proposal aims to bring funds that would otherwise remain abroad back to be reinvested into the U.S. economy.

Politically, the return of Republican control in the House and persistently high unemployment have tech leaders and coalitions hopeful that lawmakers will see a repatriation proposal as a worthwhile fiscal remedy, even amid split party control of Washington. Also, there appears to be some bipartisan support as long as funds returned are immediately invested into the U.S. economy.

Given the current deficit, repatriation could have significant costs.

The Joint Committee on Taxation (JCT) would score the proposal as a tax cut, meaning that it would have a significant cost associated with it.

Repatriation without conditions could be viewed as only beneficial to large multinational corporations. Bipartisan support could exist for a repatriation proposal with conditions, but the types of conditions that will attract support remain unclear.

Politically, repatriation is seen by its detractors as a tax cut for profitable multinational companies that does little to spur growth for smaller companies. With the Senate still controlled by Democrats, it will be unlikely to pass a repatriation bill with no strings attached. It is unclear whether this proposal's requirement of direct investment into the economy will be enough to pass the Senate. Additionally, there is a call from both sides of the aisle to simplify the tax code in upcoming tax reform legislation. With the creation of a special account and the burden to prove to the IRS investment into R&D, it could be argued that this proposal would further complicate the tax code, albeit for a limited amount of time.

Outstanding Issues

1. A repatriation bill limited to the life sciences industry is anticipated to be introduced by Senator Casey and Congresswomen Schwartz. It is a bill that will have a cap of \$150M and a 5 year window for the repatriated funds to be used. These conditions would be helpful to mid-size companies rather than large pharmas, which do more collaborations with small biotechs. Is eliminating the cap on the amount of funds that could be brought back, widening the available uses of the funds, and shortening the time horizon to reinvest money a worthwhile approach?
2. The requirement that repatriated funds be used for R&D may be viewed as too strict.

3. Since the repatriation proposal would tag to the current R&D credit, the limitations on contract research may significantly reduce the amount of repatriated funds that a pharma would use in collaborations with small biotechs.

U.S. INNOVATION BOX

Present Law

Currently, the top corporate tax rate in the United States is 35%. In the absence of other tax credits, deductions, etc., this rate is applicable to the entirety of a corporation's taxable income, including capital gains.

Innovation box (or patent box) regimes have been implemented in various forms during the last decade by several countries in Western Europe. These countries, which include Ireland, Luxembourg, Belgium, Spain, France, and the United Kingdom, were attempting to stimulate innovation and job growth within their borders. However, European Union laws regarding freedom of labor movement prevent these countries from requiring that companies participating in the innovation box actually conduct research and create jobs in the country implementing the rate. The U.S. does not face similar restrictions; thus, a U.S. innovation box would more clearly have an employment impact.

Proposed Innovation Box Regime

An innovation box regime would reduce the corporate tax rate on income derived from certain qualifying intellectual property (IP). Any income stemming from the qualifying IP would be taxed at the lower innovation box tax rate, while the remainder of a corporation's income would be taxed at the regular corporate rate of 35%.

The purpose of an innovation box is to attract the employment and economic activity associated with the development and commercialization of certain types of IP, thus fostering innovation and creating jobs through research and development (R&D).

Qualifying IP

Under this proposal, "qualifying" IP would be defined as a patent registered with the U.S. Patent Office. Additionally:

1. All research and development must be conducted in the United States. This includes the original research that leads to the patent application, development between patent application and receiving patent certification from the Patent Office, and further development between certification and the final product.
2. The research must meet the standards of "qualified research" as defined by Section 41(d) of the Internal Revenue Code.

Manufacturing

If the income stemming from the qualifying patent derives from the sale of a product, the manufacturing of that product must take place in the United States for the income to be eligible for the reduced tax rate.

Self-developed vs. acquired IP

Companies would be able to receive a reduced rate for self-developed or acquired IP. For example, if a large pharmaceutical company acquires the rights to a patent in a collaboration with a small biotech company, the income derived from that patent would be eligible for the reduced rate, providing that the acquired IP was developed in accordance with Section 41(d).

The income that the small biotech company gains from the collaboration (upfront payment, milestone payments, etc.) would also be eligible.

If a company markets its self-developed patent on its own, that income would also be eligible.

New vs. existing IP

The reduced tax rate would apply to patents applied for after the date of enactment of an innovation box regime.

Innovation box tax rate

Income derived from qualifying IP would be taxed at a rate of 10%. This rate would remain constant for all income derived from all qualifying patents.

This rate is similar to other western nations that have enacted an innovation box regime. Most recently, the United Kingdom, which has an innovation environment similar to that of the United States, proposed an innovation box with a 10% rate.

Note: This rate represents a negotiable starting point. Other proposed rates in this range would have a similar effect on innovation, research & development, and job creation.

Compatibility with other tax incentives

Participation in the innovation box regime would be elective. If a company elected to take the innovation box rate on the income derived from a given patent, it would not be eligible for any other deductions or credits for the activities that led to that patent or the income stemming from it. However, if a company elected the innovation box rate for one patent and not for another, it would be able to claim credits/deductions for which the latter patent's activities were eligible.

Innovation box election would have to be made in the tax year that R&D began on a project.

Companies could choose not to participate in the innovation box regime and would therefore remain eligible for the current array of other tax incentives.

Cap on eligible income

There would be no cap on the amount of income eligible for the reduced rate. Any income stemming from qualifying IP would be taxed at 10%.

Note: Capping eligible income would be a way to reduce the cost of the regime while retaining the general incentive structure. This cap could be a certain dollar amount or could be a multiple of the cost of developing the patent. In Europe, some countries with a sliding rate scale have implemented a cap on the amount of income eligible for the lowest tax rate (often 0%).

Analysis

A U.S. innovation box regime would incentivize increased R&D and manufacturing jobs in the U.S. and potentially foster collaborations between pharma and small biotechs.

An innovation box regime would have a direct positive effect on R&D jobs in the United States. The possibility of increased profits would incentivize increased investment in R&D, thus creating jobs in both research and manufacturing. Additionally, companies making larger profits would have more funds available to reinvest in new R&D.

Though the confines of Section 41(d) are broader than just biopharmaceuticals, it would incentivize investment in that sector and lead to more innovation and research into potential cures.

The provision allowing the reduced rate even on acquired IP would incentivize collaborations between large pharmaceutical companies looking for preferred tax treatment and small biotech companies conducting qualifying research. A lower tax rate on income related to the collaboration should make the economics of the collaboration more attractive to both parties.

A U.S. innovation box regime would make America competitive as other countries implement new innovation box regimes to boost their research-intensive economies.

The reduced corporate rate would make the United States more competitive on the global stage as companies decide where to locate their research and manufacturing. In the United Kingdom, GlaxoSmithKline recently announced several new domestic projects as a result of the new innovation box regime.

Under a U.S. innovation box, pharma would receive the most immediate benefits since small companies are years away from revenues.

The potential benefits for small companies (i.e. increased collaborations with large pharmaceuticals) are indirect, while the benefits for large companies would be more immediate.

Outstanding Issues

1. Should “qualified research” be defined as Section 41(d) or Section 41? Specifically, many biotech companies use CROs to conduct multi-country clinical trials. Would these activities abroad be considered “qualified research” given that an innovation box is designed to increase domestic R&D? Under IRC Section 41(d)(4)(F), “any research conducted outside the United States, the Commonwealth of Puerto Rico, or any possession of the United States” does not qualify for the R&D tax credit. Is there a way we can allow these sorts of trials – perhaps by citing a different section of the code which is focused on research but allows for

activities done abroad? Another option is to have a new definition for “qualified research” to allow for research that has to be done abroad (i.e., patient population not in existence in U.S.) while putting a limit on the amount of research done out of the U.S. (i.e., less than 50% of activities are done abroad).

2. If applying the innovation box to only new IP, molecules/drugs/products already in the development process would not be eligible. The purpose of the innovation box is to stimulate *new* R&D, innovation, and jobs; it does not make sense to make the reduced rate retroactive. However, one option would be to apply the reduced tax rate to only patents applied for after a certain date (e.g., January 1, 2000) in order to take into account the long development period for biotech. What would be the appropriate date in that scenario? Should there be a phase in for drugs retroactively? A phase in could be very complicated to administer.
3. Would a company’s revenues generated outside the U.S. be taxed at the lower innovation box rate?

SECTION 197 AMORTIZATION REFORM

Background

Earlier stage high tech and other research-intensive companies may receive investments from strategic acquirers – venture capital firms established by companies primarily involved in businesses other than investing – that are interested in a commercial relationship with the high tech company. These strategic investors typically have a complementary business that can benefit from license, supplier or service provider arrangements with the high tech company. Strategic investors can also offer assistance in the growth of the high tech company by providing advice and referrals. Investors may also desire to directly acquire the business of the high tech company for commercial reasons. For example, smaller high tech companies often conduct cutting edge research and experimentation that can ultimately benefit more established industry players. Such strategic acquisitions are very important in the biotechnology industry in particular.

Business acquirers often prefer to purchase the assets of a company, for both non-tax and tax reasons. Non-tax reasons include that an asset purchase permits the acquirer to pick and choose the liabilities that are assumed. There are also tax reasons for the purchase of assets, including a step-up in the tax basis of appreciated assets that can then be depreciated or amortized for tax purposes. In an asset purchase or in a transaction that is deemed to be an asset purchase for tax purposes (such as a Section 338(h)(10) transaction), the acquirer may amortize certain purchased intangibles under Section 197 provided that the acquirer holds those intangibles in connection with the conduct of a trade or business or in an activity for the production of income.⁷ Section 197 was enacted in 1993 to implement a more uniform approach to the amortization of intangibles.

⁷ All “Section” or “§” references are to sections of the Internal Revenue Code of 1986, as amended (“*Code*”).

For intangibles that are subject to Section 197, the amortization of the tax basis is taken over a 15-year period on a straight line basis. This amortization period is established by statute and may result in cost recovery over a longer period than the expected or actual useful life of the intangible. Section 197 also imposes restrictions on taxpayer's ability to take a loss or worthlessness deduction for Section 197 intangibles that are disposed of if that intangible was acquired along with other intangibles in a transaction or series of related transactions until the taxpayer no longer retains any intangibles acquired in the relevant transaction(s).

For small high tech companies, attracting funding from investors as early as possible in the life-cycle of the company is of critical importance. This is especially true in the biotechnology industry where there is typically a significant time lag between commencement of research and FDA approval of a product (if such approval ever can be obtained). Earlier stage acquisitions of such companies by better-financed acquirers can mean the difference between making significant technological advances and an unsuccessful business. Properly targeted tax incentives can spur such earlier stage acquisitions.

Tax incentives can encourage investors contemplating acquisitions of the trade or business assets of high tech biotechnology businesses to purchase the business at an earlier stage in the company's developmental cycle. These companies typically have intangible assets that are amortizable under Section 197. Under the proposal, Section 197 would be amended to provide for faster cost recovery for intangible assets acquired by investors purchasing the trade or business of a qualified small high biotechnology company. The amendment is further proposed to provide that acquirers of such trade or business assets not be as restricted in their ability to take loss/worthlessness deductions for acquired Section 197 intangibles by amending the onerous limitation that currently exists.

Current Law

Section 197(a) permits taxpayers to amortize an "amortizable Section 197 intangible" ratably over a fifteen year period. An amortizable Section 197 intangible generally includes any "Section 197 intangible" that is acquired after August 10, 1993 and that is held in connection with the conduct of a trade or business or in an activity for the production of income. Section 197 intangibles include, without limitation, goodwill (Section 197(d)(1)(A)), going concern value (Section 197(d)(1)(B)), workforce in place (Section 197(d)(1)(C)(i)), business books and records, operating systems, or any other information base (Section 197(d)(1)(C)(ii)), and patents and know-how (Section 197(d)(1)(C)(iii)). Certain self-created intangibles, including goodwill and going concern value, are not treated as amortizable Section 197 intangibles unless they are created in a transaction or series of transactions involving the acquisition of assets constituting a trade or business.⁸ The costs of these intangible may be deductible currently by the creator if

⁸ A "trade or business" for purposes of Section 197 is defined by reference to Section 1060, which addresses the allocation of purchase price among the assets in an "applicable asset acquisition." An applicable asset acquisition is defined as the purchase of assets to which goodwill or going concern value can attach. For purposes of Section 197, a trade or business is similarly defined as assets to which goodwill or going concern value can attach. Treas. Reg. § 1.197-2(e)(1).

self-created, but must be amortized over 15 years under Section 197 if purchased as part of a trade or business.

There are exceptions to the applicability to Section 197, including for certain intangibles that were “acquired separately.” Patents, copyrights, and any rights to receive tangible property or services under a contract are among the intangibles that are not Section 197 intangibles if they are not acquired in an acquisition of assets constituting a “trade or business” or a substantial portion thereof. Section 197(d)(4). Separately-acquired intangibles would be subject to depreciation/amortization under Code provisions other than Section 197.

Section 197(f) provides that a taxpayer cannot recognize a loss upon the disposition of a Section 197 intangible acquired in a transaction or series of related transactions in which the taxpayer acquired other Section 197 intangibles, if the other intangibles are retained by the taxpayer. In lieu of the loss, the taxpayer must increase the basis in the intangibles that it retains on a pro rata basis by the amount of the disallowed loss. Section 197(f)(1)(A); Treas. Reg. § 1.197-2(g). For purposes of these rules, the worthlessness of a Section 197 intangible is treated as a disposition. Section 197(f)(1)(A).

Proposed Changes:

Amortization

Amortizable Section 197 intangibles are amortized on a straight line basis over 15 years. This method of amortization contrasts with the faster depreciation that may apply to certain separately acquired intangibles and to many tangible assets, which often can be amortized/depreciated over a shorter period on an accelerated (*i.e.*, not straight line) basis. The proposal would shorten the recovery period for the costs of amortizable Section 197 intangibles acquired in connection with the acquisition of the trade or business assets (or a deemed purchase of the trade or business assets) of high tech and other research-intensive companies that are “qualified small high tech companies.” The amortization period for such acquired intangibles would be reduced to 5-years and purchasers would be permitted to amortize their basis using the “double declining balance method” that is available for tangible assets. The double declining balance method of cost recovery is commonly used for depreciable property under the Code and would permit the faster recovery of the cost of such purchased intangibles.

Dispositions and Worthlessness

In some cases, amortizable Section 197 intangibles are sold or become worthless before the end of the 15-year amortization period. Section 197 prohibits a loss deduction or worthlessness deduction so long as other intangibles acquired in the same or related transactions are still held by the taxpayer. This rule is intended to prevent taxpayers from reducing the effective recovery period for intangibles from the 15-year amortization period by taking earlier write-offs. The proposal would permit acquirers of intangibles of qualified small biotechnology technology companies to deduct their adjusted basis in the disposed of/worthless intangibles at the later of three years or the time of the disposition/worthlessness rather than having to continue the amortization of those intangibles over the remaining amortization period of the retained intangibles. Due to the proposed shorter amortization period (5 years) and accelerated cost

recovery method, the restriction on loss/worthlessness dispositions is less relevant for policing the possibility of taxpayers significantly shortening their cost recovery periods from 15-years.

Trade or Business of a Qualified Small High Technology Business

The proposal would only apply to purchasers of trade or business assets from a qualified small biotechnology business. Thus, the separately acquired intangibles currently excluded from treatment as Section 197 intangibles would continue to be excepted from the application of Section 197. The proposal would apply to purchased goodwill, going concern value, customer and supplier-based intangibles, and would apply to patents, copyrights, and rights to goods or services under a contract that were acquired in an acquisition of a trade or business.

A qualified small biotechnology company would first have to meet a size restriction, and would be defined as: (1) any entity if the annual average number of employees employed by such person during either of the 2 preceding calendar years was 500 or fewer under Section 41(b)(3)(D)(iii) or (2) any entity that, if treated as a “C” corporation for federal tax purposes, meets the definition of a qualified small business under Section 1202(d), substituting a \$150 million gross asset test (with special rules for taking into account intangible assets of the company). Controlled group rules would apply to ensure that the acquired companies for which this accelerated amortization and loss/worthlessness deductions would apply are appropriately limited to those that are in fact small businesses. Second, a qualified small high biotechnology company would have to meet a “biotechnology business” requirement. This would require the conduct of sufficient “qualified biotechnology research and development” to meet a minimum threshold amount.

The research and development prong would build off of the existing Section 41 research credit. Thus, the company’s activities would need to meet the “qualified research” definition under Section 41(d)(1)(B). Specifically, the project would need to focus on research activities undertaken for the purpose of discovering information—

- which is technological in nature, and
- the application of which is intended to be useful in the development of a new or improved business component of the taxpayer.

This prong would also incorporate the standards used by the IRS in determining whether there is “qualified research” under Section 41(d) (*e.g.*, uncertainty, related to development/improvement, etc.), with appropriate modifications for purposes of this provision.

The biotechnology portion of the test would provide that the research and development conducted by the company must be in a recognized biotechnological field. This would be defined as a project designed to:

- Treat or prevent diseases or conditions by conducting pre-clinical activities, clinical trials, and clinical studies, or carrying out research protocols, for the purpose of securing FDA approval of a product under section 505(b) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act.

- Diagnose diseases or conditions or to determine molecular factors related to diseases or conditions by developing molecular diagnostics to guide therapeutic decisions.
- Develop a product, process, or technology to further the delivery or administration of therapeutics.
- Develop other projects in the biotechnology industry.

The minimum threshold amount of qualified biotechnology research and development would require that substantially all of the business activity of the company would consist of conducting research and development in the biotechnology field. “Substantially all” would be determined based on appropriate measures that are suitable for research and development small businesses, such as a specified ratio of research and development expenditures to product revenues.

ATTACHMENT II: INDUSTRIAL & ENVIRONMENTAL PROPOSALS

THE BIO-BASED ECONOMY JOBS AND DEVELOPMENT ACT

Background

The “Bio-based Economy” refers to economic activity and jobs generated by the use and conversion of agricultural feedstocks to higher value products, the use of microbes and industrial enzymes as transformation agents or for process changes, and the production of bio-based products and biofuels. This proposal seeks to elevate the concept and awareness of the bio-based economy and advance the policy priorities of the IES working groups, highlighting the outstanding job creation and rural/rust belt economic development potential of industrial biotechnology and biorefinery commercialization.

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TITLE I: AGRICULTURE

BIOMASS CROP ASSISTANCE PROGRAM – REAUTHORIZATION AND ENHANCEMENT

Background

An available, continuous and consistent supply of biomass for energy (“purpose grown energy crops” or “PGECs”) is essential to the continued development of the domestic biofuels and bio-products industries. However, the development of such a supply is challenging for many reasons, including hesitation by farmers and landowners to produce PGECs on high-yielding farmland where traditional crop rotations exist, as well as concern about lack of a mature market. Congress has recognized the need for PGECs and has enacted several pieces of legislation in recent years to address these challenges.

One of the most important and effective programs to this end is the Biomass Crop Assistance Program (BCAP), established under the Food, Conservation, and Energy Act of 2008 (P.L. 110-246, 2008 Farm Bill). BCAP is set to expire on December 31, 2012. Assuming spending authority for BCAP will be reauthorized in a 2012 Farm Bill, USDA predicts that over the next ten years BCAP will create 70,000 jobs and will generate \$80 billion in economic activity.

BCAP is designed to incentivize and facilitate development of a sustainable supply of biomass from energy by (1) supporting the establishment and production of eligible crops for conversion to bioenergy in selected areas, and (2) assisting agricultural and forest land owners and operators with collection, harvest, storage, and transportation of eligible material for use in a biomass conversion facility.

Although BCAP was established in the 2008 Farm Bill, USDA did not publish its final rule implementing the program until October 22, 2010. The rule is designed to promote production of PGECs on approximately 17 million acres of traditional farmland and 34 million acres of pastureland. Since the rule was published, the USDA has been working diligently to disseminate BCAP funds to eligible parties, including farmers. However, BCAP must continue to be fully funded and reauthorized so its full potential to spur production of the requisite supply of PGECs for the growth of the biofuels and bio-products industries may be realized.

Proposal

This section reauthorizes the BCAP program through December, 2017, with funding through the Commodity Credit Corporation at such sums as necessary. In addition, this section provides for several clarifying amendments to (1) ensure funds are directed primarily to production of next generation crops for biofuels and bioenergy; (2) establish a dedicated funding mechanism for awarded contracts; (3) provide for eligibility of non-food Title I crops; and (4) clarify eligibility of certain other PGECs.

FEDERAL CROP INSURANCE FOR PURPOSE GROWN ENERGY CROPS

Background

Recent laws and Congressional proposals have sought to promote the development and commercialization of domestic sources of energy, including biofuels. One way to accomplish this goal is to increase domestic production and growth of dedicated crops to be used solely for energy (purpose grown energy crops, or PGECs). In order to increase the yields of such crops, U.S. farmers must decide to grow them. One deciding factor is the availability of crop insurance that will cover these new PGECs because, generally, banks and investors require crop insurance as collateral to approve operating loans for farmers that would cover the cost of the seed.

The 2008 Farm Bill directed the U.S. Department of Agriculture's (USDA) Risk Management Agency (RMA) to study the feasibility of developing crop insurance programs for biofuels feedstocks. While RMA is currently studying the feasibility of providing insurance for six specific PGECs, no formal program has been created to date. One must be established in the near term to keep up with the momentum and demand for the development of greater domestic sources of energy.

Proposal

Direct the USDA Risk Management Agency to (1) finalize research on the feasibility of providing crop insurance to producers of corn stover, straw and woody biomass, as well as energy cane, switchgrass and camelina, and (2) utilize that research to work with stakeholders, including industry and policymakers, to establish by January 1, 2013, a formal crop insurance program that will cover those six PGECs. Direct the RMA to also address a broader range of PGECs to be covered by crop insurance.

Authorize and provide such sums as necessary from the Commodity Credit Corporation to carry out the crop insurance objectives described above. In addition, authorize and provide \$25 million annually from the CCC for the RMA to carry out a PGEC insurance education/outreach campaign for growers.

FEEDSTOCK SUSTAINABILITY ENHANCEMENT GRANTS

Background

The continued development of domestic sources of energy, including for biofuels and renewable chemicals, depends upon the sustainable availability of consistent, high yield, good quality feedstocks. At the core of producing sustainable feedstocks is carefully selecting crops that can meet this nation's bioenergy needs, while remaining both good for the environment and for the farmers that produce them.

The Department of Energy's Offices of Biomass and Science, along with the U.S. Department of Agriculture (USDA) have done important research to help identify sustainable dedicated energy crops, and to help enhance the sustainability of currently available feedstocks. For example, there is increasing evidence that winter cover crops could provide a significant supply of

sustainable feedstocks for energy, while simultaneously offering great environmental benefits and financial potential for farmers.

Proposal

Establish a grant program through the U.S. Departments of Agriculture and Energy to fund demonstration projects, including cover crops, that will utilize and show various practices that could enhance biofuels and bioenergy feedstock sustainability. Authorized at \$50 million annually through 2017.

FARM BILL ENERGY TITLE AMENDMENTS FOR RENEWABLE CHEMICALS

Background:

Title IX of the 2008 Farm Bill contains several programs to accelerate commercialization of renewable energy technologies to reduce dependence on imported oil, revitalize rural economies, and enhance energy security. But many of the programs are not available to renewable chemicals and bio-based products, which offer the same benefits to rural America. In developing commercial scale biorefineries, renewable chemicals and biofuels should receive incentive parity. Farm Bill Energy Title programs should be opened to renewable chemicals and bio-based product projects.

Proposal:

BIO proposes modifying the 2008 Farm Bill by: a) adding a definition for “renewable chemicals” under Section 9001, in order to codify precisely what is meant by the term, so that law makers and industry participants are able to reference a legal authority and establish a standard for renewable chemicals in the biotechnology industry; b) amending section 9002 by implementing market awareness and acceptance of the renewable chemicals and bio-based products in the procurement program of the BioPreferred™ Program and increasing the mandatory funding to \$10 million, annually through 2017, and additional discretionary funding to \$10 million, annually through 2017; c) amending section 9003, USDA’s Biorefinery Assistance Program by adding renewable chemicals at each reference to advanced biofuels, and increasing the maximum amount of loan guarantee to \$500MM through 2017; d) amending section 9007, Rural Energy for America Program (REAP) by adding renewable energy technologies that also include energy efficient renewable chemicals and advanced biofuels manufacturing processes; e) amending section 9008 by adding the definition of renewable chemicals at each reference of bio-based products.

TITLE II: TAX

Tax Credit for Production of Qualifying Renewable Chemicals

Background:

Renewable chemicals and bio-based plastics represent an important technology platform for reducing reliance on petroleum, creating green U.S. jobs, increasing energy security, and reducing greenhouse gas emissions. By providing a renewable chemicals tax credit, Congress can create jobs and other economic activity, and can help secure America's leadership in the important arena of green chemistry. Most chemicals and plastics used today are made from petroleum. Advances in industrial biotechnology have led to renewable chemicals and bioplastics from renewable feedstocks that are providing innovative new products. Currently, bioplastics are used in everything from cups to carpets to cars, green airplane deicing compounds and cosmetics. Most of these products are competing in markets presently dominated by petroleum based products, and renewable chemicals still make up only a small percentage of total chemicals and plastics sales. The US has the potential to become the world leader in renewable chemicals, as we are currently home of the most advanced in renewable chemicals technology and intellectual property, and have access to a wide range of renewable feedstocks that can be sustainably produced. Renewable chemicals represent a historic opportunity to revitalize the U.S. chemicals and plastics industry, which has seen hundreds of thousands of jobs move overseas in the past decade. While U.S. policy has appropriately encouraged and supported the development of the biofuels sector to the benefit of rural economies, the environment, and national security, federal tax policy has largely failed to recognize and foster the substantial benefits provided by non-fuel renewable chemicals.

Proposal:

BIO proposes a federal income tax credit for renewable chemicals: a) that are domestically produced from renewable biomass; and like current law renewable electricity production credits, the credits would be general business credits available for a limited period per facility; b) similar to the operation of IRC section 48C, the Treasury Department and USDA would review taxpayers' applications in a competitive process to ensure conformance with legislative intent; c) producers found eligible to participate in the program will receive an allocation from a pool of credits based upon qualified production performed after date of enactment; and no credits will be allocated for production before date of enactment; d) which are composed of no less than 25% bio-based content will be eligible for production credits; e) per calendar year, each taxpayer would be entitled to claim as much as \$25MM in renewable chemicals production tax credit associated with production of eligible renewable chemicals.

ADVANCED BIOFUELS TAX REFORM

Background:

Current tax law on advanced biofuels does not provide an ordered pathway toward U.S. energy security. Congress must consider amendments to the current law tax incentives that focus on:

- Displacing foreign oil and gas
- Bringing commercial volumes of affordable advanced biofuels to market in the near term
- Lowering our greenhouse gas footprint
- Increasing our environmental sustainability of feedstocks
- Technology-Neutral incentive mechanisms
- Calculating incentive value on a performance-basis

Proposal:

The Cellulosic Biofuel Production Tax Credit expires on 31 December 2012, before commercial facilities can be placed in service. Congress should extend the credit through 2016. Additionally, the credit should be renamed the “Next Generation Biofuel” credit, and algal biofuels should be made eligible for the PTC. A special rule should allow bio-crude producers to obtain the PTC.

The Code should be amended to allow advanced biofuel facility developers the option of electing to receive an investment tax credit. Eligibility would be limited to advanced biofuels that meet federal GHG reduction standards of Section 211(o) of the Clean Air Act, and which are not currently produced on commercial scale.

A special rule in the Investment Tax Credit should clarify the eligibility of projects that convert traditional biofuel plants to advanced biofuels. The objective of the rule would be to encourage the rapid deployment of the first billion gallons of capacity of advanced biofuels.

Just like wind, solar and geothermal facilities, advanced biofuel facilities can be expected to encounter severe difficulty in monetizing the new federal ITC. For this reason, advanced biofuels ITCs should be made eligible for the federal Section 1603 Grants in Lieu of Tax Credits program.

Current law allows for 50% bonus depreciation for cellulosic biofuel production property. Congress should modify Section 168(l) to extend the program through 2016 and to harmonize the definition of eligible property to match that encompassed by “Next Generation Biofuel Property.”

TITLE III: DEFENSE

STRATEGIC BIOREFINERY INITIATIVE AND OFFTAKE AUTHORITY

Background

The Department of Defense (DOD) is a significant consumer of fuel and other petroleum-based products, representing close to 2 percent of annual U.S. petroleum use. The military is therefore at the mercy of the market – both in terms of stability of supplies and fluctuations in price. Substantial energy security benefits would accrue to the Department of Defense from development of domestic sources of renewable biofuels and bio-based products. The DOD and individual branches of the U.S. military have recognized the importance of diversifying their fuel supply. The DOD’s objective is to acquire 50 percent of its domestic jet fuel from alternative fuel blends by 2016. The U.S. Navy has set a target to fuel half of all of its energy needs with non-fossil fuel sources by 2020. In March, President Obama directed the Navy, DOE and USDA to work with the private sector to accelerate deployment of advanced biofuels for military use.

Advanced biofuels for military use are rapidly approaching commercialization, with demonstration projects online. For example, Solazyme delivered to the Navy the largest amount of advanced biofuel (20,000 gallons of jet and diesel) ever produced, and has a contract to deliver over seven times more fuel in 2011 – 150,000 gallons.

The greatest barrier to large-scale commercial production of military biofuels remains access to capital for construction of first-of-a-kind next generation biorefineries. As a major potential customer and as a potential source of funding for biorefinery construction, the DOD is uniquely positioned to help accelerate deployment of advanced biofuels. The DOD should fund construction of the first five commercial military advanced biofuel biorefineries to rapidly accelerate deployment. Congress should also provide DOD with long-term offtake authority for advanced biofuels to assist subsequent project developers in attracting private capital for biorefinery construction.

Proposal

A strategic biorefinery initiative is needed to accelerate deployment of advanced biofuels for military use. This section establishes and provides necessary funding for a DOD Strategic Biorefinery Deployment Program to finance construction of the first 5 commercial military advanced biofuel biorefineries. It directs DOD to identify existing funding authority for such projects, and to conduct by January 1, 2012, a biorefinery “fly-off” to identify and fund construction of the most promising projects. Evaluation criteria should include (1) commercial viability; (2) strategic / tactical value; and (3) compliance with EISA Sec. 526 greenhouse gas requirements.

In addition, this section provides DOD with the authority to enter into long-term (up to 15 years) offtake agreements for procurement of advanced biofuels for military use. Adopt language from H.R. 1847 of the current Congress.

TITLE IV: ENERGY

REPURPOSE AND RETROFIT GRANT PROGRAM

Background

Availability of supportive infrastructure is one of the greatest practical and economic challenges that will determine the growth and success of the advanced biofuels industry. As this industry matures, so does the pressing need for facilities and equipment to support its development from inception to market. At the same time, this country and the momentum of the advanced biofuels industry cannot afford the time and cost of building all new infrastructure. The great news is that many companies have and are developing advanced biofuels and renewable chemical technologies that can be used with existing idled or underutilized U.S. manufacturing facilities.

It is widely recognized that repurposing or retrofitting those facilities to integrate next generation processes capable of producing advanced biofuels and renewable chemicals and bio-products is one of the most time and cost effective ways to build out the advanced biofuels and renewable chemicals sector. It is also the fastest way to advanced biofuels commercialization that will lead to fulfillment of alternative fuel usage requirements under the federal Renewable Fuel Standard (RFS).

Depending on the advanced process and technology involved, industry efforts are underway to repurpose or retrofit several types of idled or underutilized manufacturing facilities, including first generation ethanol facilities, biodiesel refineries and pulp and paper mills. For example, Gevo, Inc., is retrofitting existing ethanol plants to produce isobutanol and hydrocarbons. Cetene Energy is integrating hydroprocessing capacity into an existing biodiesel refinery. And, Cobalt Technologies is working on retrofitting outdated pulp and paper mills to use existing feedstocks from those mills to make advanced biofuels.

Repurposing or retrofitting existing manufacturing facilities is not only the most efficient way to facilitate the development and commercialization of advanced biofuels and renewable chemicals to help increase U.S. energy independence and security, but it offers a wide variety of additional benefits to the nation. It reenergizes local economies by repurposing existing industrial assets, and retaining and creating jobs.

Proposal

Establish a federal matching grant program through the U.S. Department of Energy to fund projects to repurpose or retrofit existing idle or underutilized manufacturing facilities for the production of advanced biofuels and/or renewable chemicals. Grants would be eligible for up to 30 percent of eligible costs. Authorized at \$100 million annually through 2017.

Private companies will be able to leverage this support to attract greater private investment in retrofit projects that will enable faster commercialization of advanced biofuels and renewable chemicals.

SYNTHETIC BIOLOGY FOR ENHANCED SUSTAINABILITY OF BIOFUELS AND RENEWABLE CHEMICALS

Background:

The advancing field of synthetic biology has the potential to transform the U.S. economy by fundamentally changing the way we make and use chemicals and materials. By rapidly testing prototype biological systems with a speed and complexity not previously feasible or cost effective, synthetic biology can be applied to help resolve important challenges in synthesizing new products, whole cell systems, and other biologic processes in ways that can enhance both the economic and environmental sustainability of fuels and chemicals manufacturing. In the chemicals sector, the production of chemicals using engineered microorganisms and enzymes could generate global revenues of \$1 trillion and create 1.2 million direct jobs. Additional revenue and job creation will occur as synthetic biology delivers advanced biofuels and pharmaceutical intermediates for the healthcare industry.

As with most product development, innovation and competitiveness can often be tied to the ability to rapidly and predictably obtain optimum performance outcomes. Synthetic biology offers this promise to academic research groups, government technology institutes, and to public and private corporations seeking to develop biological solutions to today's challenging needs in fields such as advanced biofuels and renewable chemicals.

Proposal:

BIO proposes the establishment of a DOE Synthetic Biology Research and Development (R&D) Grants Program to fund research and development in industrial biotechnology for the enhanced sustainability of biofuels and renewable chemicals produced through synthetic biology technology. This program would work towards breakthroughs, yield new knowledge, and lead to the design of biological catalysts and processes that would enable the cost-effective sustainable production of: (a) advanced biofuels and renewable chemicals from renewable biomass (as defined in 2008 farm bill); and (b) other technologies that reduce or minimize greenhouse gas emissions, including biological processes for removing carbon dioxide from the atmosphere. BIO proposes \$20M be authorized annually for this program through 2017.

INDUSTRIAL BIOPROCESS R&D PROGRAM

Background:

The use of industrial biotechnology for the production of renewable chemicals and bio-based products is enabling dramatic improvements in industrial energy efficiency as well as a host of renewable alternatives to traditional petrochemical-based products. These technologies have the potential to create high-value domestic green jobs, reduce the United States' trade balance, reduce greenhouse gas (GHG) emissions, and enhance energy security by reducing dependence on imported oil. To date, however, federal investment in research and development for industrial biotechnology for non-fuel applications has been minimal. The U.S has the potential to become the world leader in the renewable chemicals and bio-based products markets, as we are currently home to the most advanced renewable chemicals technology and intellectual property and have

access to a wide range of renewable feedstocks that can be sustainably produced. Renewable chemicals based products represent a historic opportunity to revitalize the U.S. chemicals and plastics industry, which has seen hundreds of thousands of jobs move overseas in the past decade. The renewable chemicals industry has created or saved 40,000 jobs thus far, and achieving the industry's full potential could create tens of thousands of additional high-paying green jobs in the US over the next few years.

Proposal:

BIO proposes the establishment of an Industrial Bioprocess Research & Development (R&D) program through the Department of Energy (DOE), Office of Energy Efficiency and Renewable Energy (EERE), Industrial Technologies Program (ITP), to fund projects in industrial biotechnology for renewable chemicals, bio-based products, and renewable specialty chemicals.

Given industrial biotechnology's unique ability to improve both the efficiency and sustainability of chemical manufacturing, the EERE Office of Industrial Technologies Program (ITP) would be a natural home for such funding. This program would provide grants for the demonstration of advancements in energy efficiency and the reduction of greenhouse gases (GHG) through: a) process improvements showing increases in energy efficiency of existing process systems and/or reduction of lifecycle GHG emissions from the development of new biocatalysts (enzymes or microorganisms); b) basic research leading to process development that involves either biological or chemical conversion of sustainable feedstocks into renewable chemicals and show an increase in energy efficiency and/or reduction of lifecycle GHG emissions; c) research and development of new processes to utilize sustainable feedstocks (or pure sugar as feed) for manufacturing renewable chemicals that show an increase in energy efficiency against an existing industrial petrochemical manufacturing standard; d) basic research leading to development of processes to utilize sustainable feedstocks (or pure sugar as feed) for manufacturing renewable chemicals that show an increase in energy efficiency against an existing industrial petrochemical manufacturing standard. BIO proposes authorizing \$150M annually through 2017.

Title V: Environment

EPA R&D PROGRAM FOR RENEWABLE CHEMICALS

Background:

Though most chemicals and plastics used today are petroleum-based, rapid advancements in industrial biotechnology are providing petrochemical alternatives by utilizing renewable feedstocks. These renewable chemicals and bioplastics are used in a growing number of everyday products such as cups and carpets, deicers, detergents, personal care products, food and flavoring ingredients, pharmaceutical intermediates, composites, adhesives, sealants, coatings, additives, lubricants, and insulating materials.

Renewable chemicals can be engineered to provide innovative solutions that save energy, are environmentally preferred, and are a direct substitute or “drop-in” replacement for petrochemicals. Domestically produced high-volume drop-in replacement renewable chemicals would show how industrial biotechnology is reducing consumption of petroleum resources, reducing waste, and improving sustainability. Presently, there are no strong standardized metrics. If the EPA had energy data or generated such data for benchmarking petrochemical processes, life cycle analysis (LCAs) models could be produced. These LCAs would allow renewable chemical companies to demonstrate substantial cost, environmental, and efficiency benefits which could be added to partnering and investment brochures that would assist in further encouraging the development of sustainable products in the U.S.

Proposal:

BIO seeks to establish a new Research and Development (R&D) program funded by the Environmental Protection Agency (EPA) that would provide grants to conduct environmental assessments for renewable chemicals and industrial products produced with industrial biotechnology processes. This program would (1) conduct assessments to provide quantitative data to demonstrate chemical safety and pollution prevention in industrial biotechnology processes; and (2) be followed up with educational and awareness programs for U.S. businesses for the purpose of providing education and data on the environmental and economic benefit of using green chemistry and biological processes in manufacturing. BIO is requesting \$30M to be authorized annually through 2017.

ATTACHMENT III: FDA REGULATORY ENVIRONMENT PROPOSALS

CREATING A 21ST CENTURY FDA

ELEVATING FDA AND EMPOWERING OPERATIONAL EXCELLENCE

UPDATE THE FDA MISSION STATEMENT

Executive Summary

The Food and Drug Administration (FDA) needs a clear mandate to encourage the development of innovative products. In addition, FDA must have the capacity and commitment to incorporate the latest scientific advances into its decision making so that regulatory processes can keep pace with the tremendous potential of companies' leading edge science. Congress can help by updating FDA's statutory mission to underscore the need for FDA to advance medical innovation by incorporating modern scientific tools, standards, and approaches, so that innovative products can be made available to those who need them.

Background

FDA's mission, as set forth in section 1003 of the Federal Food, Drug, and Cosmetic Act (FFDCA), is to promote and protect the public health. FDA is charged with promoting the public health by "promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner." FDA also is charged with protecting the public health by ensuring the safety, and where appropriate, effectiveness of FDA-regulated products and protecting the public from electronic product radiation. However, the FDA mission statement fails to mention the agency's critical role in incorporating modern scientific advances into review practices to ensure that innovative treatments and therapies are made available to the patients that need them.

FDA should continually strive to remain on the cutting edge of science. Developments in modern science, such as personalized medicine, have the potential to yield innovative, safe, and effective new therapies by better targeting medicines to patients that need them. FDA's mission should reflect the importance of a modern agency that is equipped to respond to advances in science that can benefit the public health. Amending the FFDCA to update FDA's mission will keep FDA focused on, and accountable to, this important principle.

Proposal

To subparagraph (b) of section 1003 of the FFDCA:

(b) MISSION. — The Administration shall —

(1) promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;

(2) with respect to such products, protect the public health by ensuring that —

(A) foods are safe, wholesome, sanitary, and properly labeled;

(B) human and veterinary drugs are safe and effective;

(C) there is reasonable assurance of the safety and effectiveness of devices intended for human use;

(D) cosmetics are safe and properly labeled; and

(E) public health and safety are protected from electronic product radiation;

(3) advance medical innovation, and strive to make novel products available to those who need them, by incorporating modern scientific tools, standards, and approaches to ensure the timely and effective review, and approval as appropriate, of innovative treatments, therapies, devices and other regulated products;

~~(3)~~ **(4)** participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements; and

~~(4)~~ **(5)** as determined to be appropriate by the Secretary, carry out paragraphs (1) through ~~(3)~~ **(4)** in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.

ESTABLISH A FIXED TERM OF OFFICE FOR THE COMMISSIONER OF FOOD AND DRUGS

Executive Summary

The Commissioner of Food and Drugs is charged with leading a science-based, regulatory agency to advance the public health. As required by statute, the President appoints the Commissioner with the advice and consent of the Senate. However, a presumption of replacement with each new President has politicized the appointment and confirmation process. The Federal Food, Drug, and Cosmetic Act (FFDCA) should be amended to provide that the President appoint the Commissioner to a six- year term of office. Once confirmed, the Commissioner would be removable by the President only for pre-specified reasons — neglect of

duty, malfeasance in office, or an inability to execute the mission of the Food and Drug Administration (FDA). Encouraging consistent and stable leadership at FDA, with protection from political influence that typically occurs during a presidential administration transition, better equips the agency to fulfill its mission to protect and promote the public health.

Background

FDA is a large, complex regulatory agency and requires stable leadership to effectively promote and protect public health. The Commissioner plays a critical role in setting direction for the agency, by encouraging empirically-based, scientifically sound decisions that allow FDA to achieve its public health mission.

Over the last 35 years, however, FDA has had ten Commissioners (including current Commissioner Hamburg) and nine acting Commissioners. The short tenure of the previous Commissioners and acting Commissioners has hampered the ability of the agency to advance policy initiatives or implement any sustained or long-lasting change. Further, significant turnover has subjected the agency to accusations of undue political influence and provided the opportunity for the politicization of approval decisions.

The FFDCFA requires that the President appoint the Commissioner with the advice and consent of the Senate. However, it fails to provide a term of office for the Commissioner position. Appointing the Commissioner for a fixed term that is out of sync with, and longer than, the Presidential term should lessen turnover in this position, and it could lead to more stability in other leadership positions at the agency that are typically filled by each incoming President. Although FDA would remain part of the Executive Branch and within the Department of Health and Human Services, a six-year term of office for the agency's head — while the Administration is subject to a four-year term — would inherently insulate the office from the political process itself. It should also help to ensure continuity in agency initiatives and stability of agency priorities even when the Administration changes. Finally, the fact that a Commissioner under consideration would likely serve well into the term of the next President could help to ensure that the selection and confirmation process prioritizes scientific and managerial credentials over political ideology.

The President appoints individuals to other department and agency positions for a fixed term. For example, the Director of the Federal Bureau of Investigation is appointed for a ten-year term, the Commissioner of the Social Security Administration for a six year term, the Director of the National Science Foundation for a six year term, and the Commissioners of the Federal Communications Commission for five year terms.

Proposal

To subsection (1) of subparagraph (d) of section 1003 of the FFDCFA:

(d) COMMISSIONER. —

(1) APPOINTMENT. — There shall be in the Administration a Commissioner of Food and Drugs (hereinafter in this section

referred to as the “Commissioner”) who shall be appointed by the President by and with the advice and consent of the Senate. **The Commissioner shall be appointed for one term of six years, subject to removal by the President only for neglect of duty, malfeasance in office, or an inability to execute the mission of the agency.**

GRANT FDA STATUS AS AN INDEPENDENT AGENCY

Executive Summary

The FDA regulates nearly a quarter of the consumer goods supplied to the American public. As such, the agency should have the same authorities to make budget, management and operational decisions as afforded other independent agencies such as the Environmental Protection Agency. This would empower the agency to work more effectively with the President and Congress to carry out its mission to promote and protect the public health. Creating an independent agency would also enhance the agency’s ability to obtain quality and consistent leadership.

Background

In its hundred year history, the FDA has been housed within a federal department, starting with the Department of Agriculture and then the Department of Health and Human Services (HHS) and its precursors. As a result, the agency has always been subject to the management, budgetary restrictions, and oversight of its parent department. In the meantime, several other high-impact regulatory agencies with powers to supervise certain sectors of the economy have been granted status as an independent agency, including the Environmental Protection Agency (EPA), the Social Security Administration (SSA), the Consumer Product Safety Commission (CPSC), the Federal Communications Commission (FCC), the Federal Trade Commission (FTC), and the Commodity Futures Trading Commission (CFTC). In 1987, Senator Al Gore (D-TN) pursued legislation that would have made FDA a virtually independent Agency within HHS, but that proposal was not approved. In 1990, the Edwards Commission also proposed either elevating FDA within HHS or making it an independent agency separate from the department or the Public Health Service.

If the FDA were to become an independent agency, it would increase the agency’s position and profile within the Executive Branch and correspondingly increase the profile of the Commissioner of Food and Drugs, which may also enhance FDA’s ability to supervise its sector. In addition, the FDA would have more freedom in its budget request since it would no longer be required to go through the department budget process, which often requires agencies to curtail their overall budget requests. It is critical that if FDA were to become an independent agency, it continue to coordinate appropriately with other HHS operating divisions such as the National Institutes of Health, the Centers for Disease Control, the Centers for Medicare and Medicaid Services, and the Agency for Healthcare Research and Quality.

Establishing a new independent federal agency would require an act of Congress.

Proposal

Establish FDA as a free-standing, independent agency outside of the departments of the executive branch, as defined under §104, Title 5 of the United States Code.

ESTABLISH AN EXTERNAL MANAGEMENT REVIEW BOARD FOR FDA

Executive Summary

The Food and Drug Administration (FDA) is a large, complex organization responsible for regulating nearly a quarter of the consumer goods supplied to the American public. To fulfill its responsibilities effectively, FDA must be well organized and well managed. It is critical that the agency's organization and management capabilities are periodically analyzed and that the Commissioner of Food and Drugs be provided with fresh, visionary, and independent thinking on how to improve the ability of the agency and its centers to promote and protect the public health, as well as the support necessary to implement recommendations. An external advisory board composed of individuals with experience in organizational management could help the agency address operational challenges. The Federal Food, Drug, and Cosmetic Act (FFDCA) should be amended to establish a Management Review Board (MRB) to conduct periodic reviews of FDA's management and organizational structure and provide recommendations to the Commissioner about ways to improve FDA operations.

Background

The substantial size of FDA presents a challenge to agency leadership. FDA consists of six product centers, one research center, and two offices. It employs over 11,500 full time equivalent (FTE) staff across the world. FDA has employees posted in China (Beijing, Shanghai, and Guangzhou), India (New Delhi and Mumbai), Costa Rica (San Jose), Chile (Santiago), Mexico (Mexico City), and Belgium (Brussels). The agency is responsible for regulating more than \$2 trillion in food, drugs, medical devices, cosmetics, dietary supplements, and other consumer goods—nearly a quarter of the U.S. consumer goods supply.

Since the passage of the 1906 Food, Drug, and Cosmetic Act, new statutory requirements have significantly expanded FDA responsibilities. Beginning in the 1950s and through the 1970s, Congress required FDA to review and approve, prior to marketing, the safety and effectiveness of human new drugs, animal new drugs, human biological products, medical devices for human use, and infant formula products as well as review and approve the safety of human food additives, color additives, and animal feed additives.

In the 1980s through the 1990s, Congress required FDA to establish a pathway for approval of generic drugs, implement a framework to identify and designate products as promising treatments for rare and neglected diseases (orphan drug program), approve disease prevention and nutrient descriptor claims for food products, and develop a program providing expanded access to investigational drugs. Congress also required FDA to review new dietary supplement ingredients prior to marketing and authorized the agency to establish good manufacturing practice regulations for dietary supplements.

More recently, the Food and Drug Administration Amendments Act of 2007 imposed substantial new requirements on FDA in a range of areas, including medical product safety, advisory committee membership and recruitment, and clinical trial registries. In June 2009, FDA was granted authority to regulate tobacco products. The Patient Protection and Affordable Care Act enacted in March of 2010 requires FDA, among other things, to establish a pathway for approval of biosimilar biological products. Most recently, in January 2011, the FDA Food Safety and Modernization Act (FSMA) provided FDA with tools to improve the agency's ability to prevent contamination in the food supply.

The globalization of the medical product and food industries also challenges FDA. The agency estimates that 80% of the active pharmaceutical ingredients (API) in drugs and approximately 40% of the finished products are imported. FDA estimates that the agency regulates \$49 billion worth of imported foods. High profile recalls involving substances that originated overseas, such as the contamination of the API used in heparin, a blood thinning drug, and the contamination of pet food with melamine, underscore the challenges FDA faces in this area.

The size and complexity of the FDA, increasing statutory responsibilities, and globalization of FDA-regulated industries have placed significant demands on FDA and may have hampered its ability to develop forward-thinking strategies. For example, FDA does not have a comprehensive information technology (IT) infrastructure that allows it to track information. To the extent IT systems exist, they often do not readily interact with each other. Data must be analyzed manually at times. Without an efficient means to accurately collect and analyze information, FDA cannot make data-driven decisions, or build upon past experience to systematically plan future activities to best advance the public health. Limited resources exacerbate these management and organizational shortcomings, and hamper FDA's ability to achieve its public health mission.

The establishment of an external management review board could help identify deficiencies in FDA's management and organizational structures that threaten the agency's ability to meet its numerous regulatory responsibilities. The creation of review board to advise an agency on management and organizational issues is not unprecedented. For example, the National Institutes of Health (NIH) Reform Act of 2006 established a Scientific Management Review Board (SMRB) to advise the NIH Director and other appropriate officials on the use of certain statutory authorities to reorganize NIH to carry out its activities more efficiently. The NIH SMRB helps to ensure that NIH's structure is optimal for supporting the advancement of science.

Proposal

To help FDA strategically manage its operations, FFDCA should be amended to create an external Management Review Board (MRB) to undertake a formal regulatory process review and improvement initiative, and make recommendations to the Commissioner on needed improvements to FDA's management structure and organization. The MRB would be governed by the Federal Advisory Committee Act (FACA), which sets forth the rules under which all federal advisory committees operate. Meetings of the MRB would be noticed in advance, and would generally be open to the public, except in the limited situations where proprietary information, classified information, or personal privacy interests were implicated. Further, members of the public could provide comments to the MRB, and records from the MRB

meetings would be available to the public for inspection. The success of the MRB will be highly dependent on the personal and committed involvement of FDA senior leadership, including the Commissioner of Food and Drugs, in recruiting highly qualified, visionary and independent thinkers to serve on the MRB; alternatively, an outside body might be charged with recruiting members and/or convening the board.

To Chapter 7, Subchapter A of the FFDCA:

Sec. 714. Management Review Board.

(a) IN GENERAL. — Not later than 60 days after the passage of this act, the Secretary shall establish an advisory committee with the Food and Drug Administration to be known as the Management Review Board (referred to in this section as the “Board”).

(b) DUTIES. —

(1) REPORTS ON MANAGEMENT ISSUES.— The Board shall provide advice to the Commissioner regarding the management and organization of the Food and Drug Administration. Not less frequently than once each 6 years, the Board shall —

(A) determine whether and to what extent changes should be made to the management and organization of FDA; and

(B) issue a report providing the recommendations of the Board regarding the changes to management and organization and the reasons underlying the recommendations.

(2) TOPICS.—

(A) The Commissioner may submit requests about management or organizational issues to the Board for assessment.

(B) The Board shall seek input from the public on management and organizational issues it would be helpful to assess.

(c) COMPOSITION OF BOARD.—

(1) The Board shall consist of the Commissioner, who shall be a permanent nonvoting member on an ex officio basis, and an odd number of additional members, not to exceed 21, all of whom shall be voting members. The voting members of the Board shall be the following—

(A) Not fewer than 9 officials who are directors of the product centers, directors of FDA divisions, or members of the FDA Science Board. The Secretary shall designate such officials for membership.

(B) Members appointed by the Secretary from among individuals who are not officers or employees of the United States for a three-year term, which could be renewed once. Such members shall include—

- (i) individuals representing the interests of public or private institutions of higher education;
- (ii) individuals representing the interests of the industry; and
- (iii) individuals with broad expertise regarding how FDA functions and experience successfully managing large scientific organizations (exclusive of private entities to which clause (i) applies).

(d) CHAIR.— The Chair of the Board shall be selected by the Secretary from among the members of the Board appointed under subsection (c)(1). The term of office of the Chair shall be 2 years.

(e) MEETINGS.—

(1) In general. — The Board shall meet at the call of the Chair or upon the request of the Commissioner, but not fewer than 5 times with respect to issuing any particular report under subsection (b)(1). The location of the meetings of the Board is subject to the approval of the Commissioner.

(f) REPORTS.—

(1) Each report under subsection (b)(1) shall be submitted to—

(A) the Committee on Energy and Commerce and the Committee on Appropriations of the House of Representatives;

(B) the Committee on Health, Education, Labor, and Pensions and the Committee on Appropriations of the Senate; and the Secretary.

(2) AVAILABILITY TO THE PUBLIC.— The Commissioner shall post each report under subsection (b)(1) on the Internet site of the Food and Drug Administration for public comment.

(3) IMPLEMENTATION. Within 100 days, FDA shall begin to implement the recommendations set forth in each report under subsection (b)(1), and the recommendations shall be fully implemented within 3 years, except when the Commissioner objects to any recommendation or if Congress passes a joint resolution overriding the recommendation.

ADVANCING REGULATORY SCIENCE & INNOVATION

SUPPORT REGULATORY SCIENCE PUBLIC-PRIVATE PARTNERSHIPS

Executive Summary

Under the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress established the Reagan-Udall Foundation for the Food and Drug Administration, an independent nonprofit organization intended to support public-private partnerships for the purpose of

advancing the mission of the Food and Drug Administration (FDA) to “modernize medical [and other] product development, accelerate innovation, and enhance product safety.”⁹ The Foundation could, for example, form collaborations to advance the use of biomarkers, surrogate markers, and new trial designs to improve and speed clinical development. However, Appropriations bills have subsequently restricted FDA’s ability to transfer federal funding to the Foundation. These funding restrictions should be lifted so that the Reagan-Udall Foundation can fulfill its promise.

Background

The FDAAA legislative history indicates that Congress envisioned the Foundation as helping to foster the development of new research tools to aid in the evaluation of the safety and effectiveness of drugs, biologics, and medical devices.¹⁰ Congress viewed the Foundation’s use of public-private partnerships and other research collaborations as “a way to develop [new research] tools – not so they can help just one researcher or one company, but so they can help the entire research enterprise.”¹¹ FDAAA provides detailed information on the composition and activities of the Foundation, including its duties, Board membership, governance, funding, and requirements for assuring accountability.¹²

The duties of the Foundation include the identification of unmet needs for the development, manufacture, and evaluation of drugs, biologics, and devices (including diagnostics), and establishing goals and priorities to meet these needs. They also include providing “objective clinical and scientific information to the [FDA] and, upon request, to other Federal agencies to assist in agency determinations of how to ensure that regulatory policy accommodates scientific advances and meets” the Agency’s public health mission.

Unfortunately, the Foundation has yet to receive any congressional appropriations. This is in large part due to concerns regarding accountability, including allegations that industry would have too much influence over the Foundation’s activities. However, FDAAA required the Foundation to establish policies on conflicts of interest (and many other) standards. The Foundation’s Board of Directors¹³ has adopted bylaws¹⁴ which were published for comment and which include several provisions that meet not only the FDAAA requirements but put in place further protections to protect the integrity of the Foundation’s work. The bylaws provide for significant transparency around conflicts of interest issues, acceptance of donations and grants;

⁹ 21 U.S.C. § 379dd.

¹⁰ Statement of Senator Kennedy (D-MA), 153 Cong. Rec. S11937 (Sept. 21, 2007).

¹¹ Statement of Senator Kennedy (D-MA), 153 Cong. Rec. S5759, S5764 (May 9, 2007).

¹² These requirements and other information are found in 21 U.S.C. § 379dd, unless specified otherwise.

¹³ On November 16, 2007, FDA issued a press release announcing the names of the initial 14 appointed voting members of the Board. FDA News Release, “FDA Announces Board Members of Reagan-Udall Foundation,” *available at* <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm109029.htm>.

¹⁴ 74 Fed. Reg. 68,028 (Dec. 22, 2009).

and review of gifts.^{15,16} The bylaws also set forth a separate, detailed policy in Appendix A, titled “Ethical Guidelines for Identifying and Managing Conflicts of Interest.”¹⁷ This policy requires, among other things, that the Foundation post on its website various information related to its conflicts of interest policies and decision-making. Moreover, the law requires that the Foundation and FDA conduct annual reviews of the Foundation’s activities and submit reports to Congress, allowing for multiple levels of oversight. With these statutory protections, the Foundation’s activities will remain objective and free of undue influence by any particular group.

Despite these efforts and protections Congress continues to block funding for the Foundation. The FY 2011 appropriation for FDA contained a prohibition against implementing the statutory provision that is the funding mechanism.¹⁸ The Foundation has reportedly received some funds from private sources to work on a few projects.¹⁹ Nonetheless, without the federal funds (and support) necessary to build an infrastructure, the Foundation will never become an operational organization. At present, the Foundation does not have a website, and a recent review of online sources did not permit identification of even basic information, such as a current list of the Board’s voting members.

Notably, while Reagan-Udall’s implementation continues to be stalled, European governments are lending strong support to the use of public-private partnerships to advance regulatory science. In 2007 (the same year Congress created the Foundation), the European Union and the European pharmaceutical industry association (EFPIA) established the Innovative Medicines Initiative (IMI), which is described as “Europe’s largest public-private initiative aiming to speed up the development of better and safer medicines for patients . . . [which] supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe.”²⁰ A March 2011 press release indicates that the IMI has recently launched a second wave of research projects (focusing on areas including cancer, infectious disorders and electronic health), with a total of 23 current research projects and over €450 million (approximately USD \$658 million at the time of publishing) committed by the European Commission and the EFPIA.²¹

¹⁵ *Id.* at 68,031.

¹⁶ *Id.* at 68,034.

¹⁷ *Id.* at 68,033-34.

¹⁸ Alliance for a Stronger FDA Website, Funding for the Reagan-Udall Foundation (May 23, 2011), available at <http://strengthenfda.org/2011/05/23/funding-for-the-reagan-udall-foundation/>.

¹⁹ For example, in March 2011 the Foundation received a grant from the Bill & Melinda Gates Foundation for the purpose of “accelerate[ing] the development of new TB drug regimens by testing drug candidates in combination before they are individually approved.” Gates Foundation Website, available at <http://www.gatesfoundation.org/Grants-2011/Pages/Reagan-Udall-Foundation-OPP1027026.aspx>.

²⁰ Innovative Medicines Initiative (IMI) Website, available at <http://www.imi.europa.eu/>.

²¹ On March 8, 2011, IMI issued a press release announcing new projects. IMI Press Release, “IMI announces a new total of 23 unique projects to boost drug innovation”, available at <http://www.imi.europa.eu/sites/default/files/uploads/documents/PRESS%20RELEASE%20IMI%20Press%20Briefing%208%20March%202011.pdf>.

Two sister agencies of FDA, the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC), do have active Foundations to facilitate public-private partnerships. NIH has the Foundation for the NIH (FNIH), established by Congress in 1990. FNIH raises private funds and creates public-private partnerships to support the mission of NIH by combining the expertise and resources of NIH with those of industry, the public and philanthropic communities.²² CDC has the CDC Foundation, which has provided \$300 million since 1995 to help CDC pursue innovative ideas that need support from outside partners, launching more than 500 programs around the world and building a network of individuals and organizations committed to supporting CDC and public health. CDC Foundation partnerships help CDC launch new programs, expand existing programs that show promise, or establish a proof of concept through a pilot project before scaling it up.²³

Proposal

Restore Funding for the Reagan-Udall Foundation: The Food and Drug Administration Amendments Act of 2007 (FDAAA) provides that FDA must transfer annually between \$500K and \$1.25 million to the Foundation for operations/administrative expenses. Congress should remove restrictions on FDA's ability to transfer federal funding to the Foundation as allowed by statute.

CREATE AN FDA "EXPERIMENTAL SPACE," LED BY A CHIEF INNOVATION OFFICER, TO PILOT PROMISING NEW SCIENTIFIC AND REGULATORY APPROACHES

Executive Summary

The Food and Drug Administration (FDA) has developed several initiatives to advance regulatory science. These include the FDA/NIH Joint Leadership Council²⁴, the academic Centers of Excellence in Regulatory Science, and FDA's Critical Path Initiative. However, FDA's ability to incorporate modern science into its regulatory processes has been limited because there is no entity within the agency with unified responsibility for systematically analyzing the findings and recommendations from these groups, and clear authority to pilot promising scientific and regulatory approaches. An FDA "Experimental Space," led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new scientific and regulatory approaches are integrated into agency operations at all levels.

Background

Currently, FDA's Office of the Chief Scientist is charged with coordinating internal and external outreach to identify critical regulatory science and innovation needs and developing a strategic plan for science at the FDA. The FDA has also established a high-level advisory board, the

²² Foundation for the NIH Website, available at <http://www.fnih.org/>.

²³ CDC Foundation Website, available at <http://www.cdcfoundation.org/who/story>.

²⁴ FDA-NIH News Release, available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2010/ucm201706.htm>.

Science and Innovation Strategic Advisory Council, comprised of the Chief Scientist and representatives from the Office of the Commissioner, the various Centers, and the FDA Office of Regulatory Affairs. The Advisory Council meets twice a year to identify and communicate key scientific priorities from each center, to set and discuss major cross-cutting scientific priorities for the agency, and to propose and evaluate major programs and partnerships. The FDA also has an FDA Science Board that provides advice to the Commissioner, the Chief Scientist and the centers on complex scientific and technical issues within the agency, industry, and academia. The Board reviews the Science and Innovation Strategic Advisory Council's scientific plan and regulatory science priorities.

Within the Office of the Chief Scientific Officer is the Office of Science Innovation, which provides strategic leadership, coordination, infrastructure and support for innovation in FDA science that is intended to advance the Agency's ability to meet its mission to protect and promote public health. The Office of Science Innovation is theoretically charged with, among other things, supporting core scientific capacity and infrastructure within FDA, and fostering development and use of innovative technologies in product development and evaluation. This Office, however, lacks the statutory mandate to respond to external and internal recommendations by establishing specific pilot programs, and to implement successful programs into FDA's everyday regulatory decision making process.

Proposal

The Federal Food, Drug and Cosmetic Act (FFDCA) should be amended to establish an FDA "Experimental Space", led by a new Chief Innovation Officer, with the responsibility and authority to identify promising new scientific and regulatory approaches, with input from stakeholders inside and outside the agency, and ensure that these approaches are integrated into agency operations at all levels, and harmonized with the approaches of other mature regulatory agencies. Examples of such approaches might include the qualification of a particular biomarker, the acceptance of novel clinical trial design methodologies, incorporation of electronic health record technologies, alignment and rationalization of regulatory pathways for the approval of drugs/biologics and companion diagnostics, or adoption of novel methods in predictive toxicology.

Among the Chief Innovation Officer's duties should be the systematic analysis of the recommendations of all internal and external entities involved in advancing regulatory science, such as the FDA Science and Innovation Strategic Advisory Council, the FDA Science Board, the National Center for Toxicology Research, the FDA/NIH Joint Leadership Council, the Reagan-Udall Foundation, and key public-private partnerships such as the academic Centers of Excellence in Regulatory Science, the Biomarkers Consortium, the Patient Reported Outcomes Consortium (PROC), and the Predictive Safety Testing Consortium (PSTC).²⁵ Analyses should be published for public comment for at least 30 days.

²⁵ FDA, Existing Public Private Partnerships, *available at* <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/PublicPrivatePartnershipProgram/ucm166082.htm>.

Further, the Chief Innovation Officer’s responsibilities should include the development of implementation plans for pilot programs to incorporate recommendations from governmental, public/private organizations and academic regulatory science initiatives into agency regulatory decision making. Implementation plans should be published for public comment for at least 60 days prior to initiation of any pilot program.

Most importantly, the Chief Innovation Officer should have the authority, with input from Center representatives, to establish and oversee the implementation of pilot programs within the Centers, and ensure participation by cross-disciplinary pilot teams.

At least every two years, the Chief Innovation Officer should submit a report to Congress every two years detailing FDA’s progress with respect to the integration of new scientific and regulatory approaches into agency operations, and explaining why any recommended approaches were not implemented.

ENHANCE FDA’S ACCESS TO EXTERNAL SCIENTIFIC AND MEDICAL EXPERTISE

Executive Summary

The Federal Food, Drug, and Cosmetic Act (FFDCA) establishes the Food and Drug Administration (FDA) as the preeminent agency charged with evaluating cutting edge science as it is applied to the prevention, diagnosis, and treatment of human disease. FDA has also been perceived by many as the global standard bearer for regulatory review of drug and biologic applications. However, scientific and medical knowledge, techniques, and technology are advancing at a more rapid pace today than at any other time, and FDA’s capacity to access information about these advances has not kept pace. It is essential that FDA’s access to scientific and medical advice be enhanced by improving the operations of FDA Advisory Committees, establishing Chief Medical Policy Officers in the immediate offices of the Center Directors and providing FDA staff with additional avenues for accessing external scientific and medical expertise.

Background

Improving the Operations of FDA Advisory Committees. FDA regularly looks to outside experts to provide the Agency with independent opinions and recommendations on a variety of complex medical and scientific issues, typically through the use of Advisory Committees. Federal Advisory Committees were initially established under the Federal Advisory Committee Act (FACA), which defines an advisory committee, in the broadest sense, as any committee, board, commission, or similar group of independent experts established or used by one or more federal agencies to obtain advice or recommendations.²⁶

The FFDCA requires FDA to establish panels of independent experts (*i.e.*, Advisory Committees) for “the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug” or

²⁶ 5 U.S.C. App. 2, § 3(2)(C).

biologic.²⁷ Currently, there are approximately 20 standing Drug Advisory Committees. The activities of FDA Advisory Committees are subject to detailed requirements and procedures, set forth in 21 C.F.R. Part 14. As an example, any meeting of an FDA Advisory Committee must be announced in the *Federal Register* at least 15 days in advance of the meeting, except in very limited circumstances when authorized by the Commissioner of Food and Drugs.²⁸

In recent times, FDA has found it more difficult to populate Advisory Committees with qualified members. This is in part due to the establishment of new conflict of interest requirements under the Food and Drug Administration Amendments Act of 2007 (Title VII), and FDA's interpretation of that statute. Over time (FY2008-FY2012) the new requirements progressively limit FDA's ability to grant waivers permitting individuals with essential expertise, but who also have a conflict of interest, to participate with respect to a particular matter before the committee. The waiver caps apply even though the type, nature, and magnitude of the individual's financial interests must be disclosed on FDA's website.

FDA Advisory Committees have historically used the most knowledgeable and highly qualified individuals to obtain the best available information. This authority is critical for reviews of the cutting-edge science and next generation innovation that is the bailiwick of biotechnology companies. In many cases, only a handful of qualified experts may exist to provide the agency with appropriate review of complex and technical issues surrounding new products. For example, for certain rare diseases areas or product categories, the universe of highly knowledgeable and qualified individuals may be quite small. In some circumstances, virtually the only experts in an area are individuals who are involved as advisors or participants in the research and development leading to the innovation being reviewed by FDA.

These individuals, who may have financial interest and thus a potential conflict, can be essential to a meaningful discussion of the issues surrounding review of a new product. Disqualifying them, or limiting their ability to meaningfully participate, could adversely impact the ability of an advisory committee to comprehensively evaluate a particular issue. Allowing such individuals to participate in an FDA advisory committee is vitally important because making decisions based on the best and most relevant science depends on the Agency's ability to seek and use the advice of these experts. Flexibility in the issuance of waivers is crucial to achieving this goal.

As with efforts to reduce private financing of research, policies that prohibit participation on advisory committees or impose other rigid standards contain a flawed, underlying assumption – that certain experts are necessarily biased simply because they work with industry. Basing national policy on that assumption undervalues the expertise and professional integrity of many of the scientists and researchers who participate in FDA deliberations.

The best way to achieve the twin goals of maintaining research integrity while promoting innovation is to enact policies that ensure maximum disclosure of possible conflicts as well as

²⁷ 21 U.S.C. § 355(n)(1).

²⁸ *Id.* § 14.20(a).

provide regulators or other oversight bodies the discretion to make case-by-case decisions. This has been the federal regulatory framework that has led to the discovery and development of hundreds of biotechnology products over the years.

In addition, patient groups and patient research foundations, are in a strong position to characterize benefit. They tend to have a broad understanding of the state of the patient population, and include individuals able to understand intimately the clinical benefits and risks of an approval. Such individuals should have a stronger role in Advisory Committee deliberations.

Providing FDA staff with additional avenues for accessing scientific and medical expertise.

FDA also has the ability to utilize an external expert (a “consultant”) or a group of external experts outside of the Advisory Committee process, including providing advice to FDA on particular drug applications. The following groups are *not* considered an Advisory Committee: (1) a “group of persons convened on an ad hoc basis to discuss a matter of current interest to FDA, but which has no continuing function or organization and does not involve substantial preparation;” and (2) a “group of two or more FDA consultants meeting with the agency on an ad hoc basis.”²⁹ An internal CDER policy addressing clinical review procedures explains that FDA reviewers sometimes use information not contained in an application, including from “consultations with others outside the review team, such as internal or external consultants.”³⁰ For example, the Agency will, at the request of a sponsor, engage in a “special protocol assessment” in order to assess whether a particular protocol is adequate to meet scientific and regulatory requirements.³¹ In assessing a protocol under these procedures, FDA “can seek Advisory Committee review of a clinical protocol or can obtain advisory review from selected advisory committee members, special government employees, or other consultants.”³²

However, no adequate mechanism exists to ensure that FDA makes best and well-coordinated use of its ability to seek advice from external experts outside the Advisory Committee process. Such external experts could be invaluable in providing the agency with advice on broad (not product-specific) emerging medical and scientific issues, for example acceptance of surrogate endpoints in oncology, clinical trial design and post-market monitoring methods for medicines that may have rare but several adverse events, and appropriate benefit-risk balance for medicines to treat serious and life-threatening diseases.

Proposals

Fix FDA Advisory Committee policies to improve committee operations:

- Repeal financial conflict of interest waiver caps (while retaining appropriate disclosure requirements) to ensure that FDA has, and uses, significant discretion to grant financial

²⁹ *Id.* § 14.1(a)(5)(i), (ii).

³⁰ CDER Manual of Policies and Procedures (MAPP) 6010.3, Att. A, at 12-13 (effective Dec. 10, 2010).

³¹ FDA, Guidance for Industry: Special Protocol Assessment, at 1-2 (May 2002).

³² *Id.* at 8.

conflicts of interest waivers on a case-by-case basis for potential advisory committee members whose expertise is essential.

- Amend Section 505 of the FDCA to include language requiring that committees considering the safety or effectiveness of drugs or biologics include at least one medical or scientific expert chosen by a patient group or research foundation whose interests are in the specific disease or diseases proposed to be treated by the drug or biologic under consideration. Such representatives would be in addition to any consumer representative already present on a given committee, and should be full voting members of that committee.

Create Chief Medical Policy Officers with responsibility for identifying and addressing broad medical and scientific policy disputes, and ensuring that FDA staff have access to the external expertise necessary to resolve those disputes: Create Chief Medical Policy Officers (CMPOs) within the immediate Offices of the Directors for the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). CMPOs would:

- work with review divisions to develop proactive and consistent strategies for the Centers to address emerging medical and scientific policy issues, including new peer learning and peer review mechanisms.
- be empowered to coordinate and improve reviewer access to external advice via advisory committees, working with the Office of Special Medical Programs³³ which currently has oversight of FDA Advisory Committees. For example, CMPOs could work to determine whether FDA is making the best and most efficient use of its Drug Advisory Committees. Among other things, a CMPO could examine whether the right type and number of issues are being referred to Advisory Committees, whether Advisory Committees have the necessary expertise to advise on the matters referred to them, and whether new Advisory Committees should be established at the FDA or Center level. In this connection, note that the FDA Science Board has recommended the establishment of Scientific Advisory Boards for each Center.
- be empowered to coordinate and improve reviewer access to external experts outside the advisory committee process. Such external experts would be Special Government Employees, and thus subject to conflict of interest and confidentiality requirements, and their findings would be made public. As appropriate, the CMPO and Review Divisions could hold public forums with presentations by industry, academia and patient organizations on key emerging scientific and medical issues.
- be charged to work closely with any new Chief Innovation Officer in the implementation of regulatory science pilot programs that impact on policy development.

³³ FDA Staff Manual Guides (SMG 1140.1), Office of Special Medical Programs (effective Aug. 7, 2009).

ENABLING MODERNIZED PATIENT-CENTRIC CLINICAL DEVELOPMENT

INCREASE ACCESS TO INNOVATIVE TREATMENTS AND THERAPIES THROUGH PROGRESSIVE APPROVAL

Executive Summary

Patients, industry, Congress, and others are eager to find ways to deliver safe and effective new drugs and biologics to patients. Patients, particularly those with illnesses for which no adequate therapy exists, want access to promising new therapies earlier in the drug development process. Smaller biopharmaceutical companies that develop those therapies are sometimes unable to maintain operations through extensive phase III testing without revenue from marketing of products. Expanding and improving the accelerated approval pathway into a progressive approval mechanism would provide patients timely access to needed therapies. This pathway would be limited to innovative products for unmet medical needs, significant advances to standard of care, targeted therapies, those that have been approved by the EU and other mature regulatory agencies. Additionally, this pathway would ensure risk-benefit analysis that incorporates the safety and needs of patients in the real world.

Background

The current new drug development and approval process is uncertain, lengthy, and expensive. It can take 10 to 15 years for a molecule in the earliest stages of development to be translated into a finished and approved drug product available for use by patients. The cost of developing an approved drug has been estimated between \$800 million and \$1 billion.

The current drug approval process and standards at the Food and Drug Administration (FDA) date to the early 1960s. Following preclinical work that provides an adequate assurance of safety for human testing, a drug's sponsor will typically conduct several phases of clinical trials that begin with small safety studies and conclude with large-scale controlled trials for clinical effectiveness. FDA regulations describe three phases of testing, but federal law does not require three phases. In fact some drugs have been approved on the basis of testing that combined two phases (Phase I/II or Phase II/III), and some have been approved on the basis of Phase II studies.

FDA then reviews each new drug application for proof of safety and effectiveness. The Federal Food, Drug, and Cosmetic Act (FFDCA) requires "substantial evidence" of the drug's effectiveness for its intended use, which is defined by statute to mean that "adequate and well-controlled investigations" demonstrate the drug will have the intended effect. When FDA finds a new drug safe and effective, it is essentially concluding that the drug's benefits outweigh its risks when the drug is used as described in the proposed labeling. This is in essence an exercise in risk/benefit balancing. A similar standard applies to biological drugs, which are the subject of a different type of application.

Federal law generally prohibits the distribution and marketing of new drugs prior to FDA approval. Patients, particularly those suffering from life-threatening or serious medical

conditions, have long sought access to drugs earlier in the drug development and approval process. Advocacy by HIV/AIDS patients in the 1980s led to the accelerated approval scheme, and advocacy by terminally ill patients in the 1990s led to improvements in compassionate use programs while drugs remain investigational.

First, FDA may grant accelerated approval to new drugs for serious or life-threatening diseases that represent a meaningful therapeutic benefit over existing treatment. The agency may approve such a drug on the basis of a surrogate endpoint “reasonably likely” to predict clinical benefit or another clinical endpoint other than survival or irreversible morbidity. Surrogate endpoints are markers, such as tumor shrinkage or CD4 cell counts, used in clinical trials as an indirect measurement of a clinical outcome, such as patient survival. The use of surrogate endpoints permits approval earlier than the use of clinical endpoints. The sponsor of a drug approved under the accelerated approval pathway must perform adequate and well-controlled clinical trials after approval, to verify the anticipated clinical benefit of the therapy.

Second, under its expanded access regulations, FDA permits the use of an investigational drug for treatment of patients with “immediately life-threatening” or “serious” medical conditions when there is no comparable or satisfactory alternative treatment as well as during an emergency. FDA grants expanded access for patient groups of varying sizes, depending on the state of the evidence on safety and effectiveness.

Accelerated approval and expanded access, while helpful, are narrow in their scope. In fact, most patients do not benefit from them. These pathways do not provide subpopulations of patients access to promising therapies that may help them. For example, cancer patients identified using a biomarker, for which targeted drug therapy has been shown effective, would not receive early access to the therapy under any existing program. Terminally ill patients do not receive early access to promising therapies, despite the fact that the risks they face from the disease may far outweigh risks they face from taking the drug. Accelerated approval only applies to a subset of drugs that have the potential to treat serious diseases; thus, fewer drugs are made available via that pathway. Last, no existing program provides a method for companies to fund continued research of a promising drug. As a result, promising drugs may never be made available to patients because companies do not have the resources to continue developing the drug.

Stakeholders and thought leaders have repeatedly suggested that FDA implement, or Congress enact, some sort of “progressive approval” mechanism for promising new therapies to provide earlier access to patients that need them. Progressive approval is not a novel idea. Congress created a progressive approval pathway for some animal drugs in 2004, and the European Commission (EC) also progressively approves some human drugs.

The EC will progressively approve a drug that (1) targets a seriously debilitating or life-threatening disease, (2) can be used in emergency situations, in response to public health threats, or (3) is a designated orphan drug. The drug is approved before all of the relevant safety and effectiveness data are available, subject to the condition that the sponsor meet “specific obligations.” These include conducting confirmatory clinical trials within an agreed upon timeframe. The progressive marketing authorizations are valid for one year, on a renewable

basis. The European Medicines Agency (EMA) assesses each renewal application to determine whether the company will be able to confirm the positive risk/benefit profile of the drug. The EMA considers whether the “specific obligations” associated with the progressive marketing authorization must be modified or whether they have been completed. Once the specific obligations are fulfilled, the EC may fully authorize the drug at any time.

Proposal

Eligibility. Progressive approval should be available for a new drug intended to provide a meaningful advancement in the treatment of serious or life-threatening disease, which offers the promise of one or more of the following:

- first approved therapy for a condition or targeted subpopulation with the condition
- ability to treat patients unresponsive to, or intolerant of, existing approved therapies
- ability to treat rare diseases or disease subpopulations based on biomarkers or genetics (*e.g.*, personalized medicine)
- ability to offer a significant improvement in outcomes for patients compared to existing approved therapies, either alone or in combination with existing approved therapies. Improvement in outcomes may reflect improved efficacy, improved safety, or an enhanced balance of efficacy and safety, compared to existing approved therapies and products that have been approved by the EU and other mature regulatory agencies

The relative risk/benefit profile of these drugs is different from other drugs, which justifies their earlier availability to patients (subject to appropriate controls and additional data gathering). For purposes of determining whether a new drug offers the promise of meaningful advance over existing approved therapies, only therapies with full FDA approval should be considered as existing approved therapies (*e.g.*, drugs available under the Progressive Approval or Accelerated Approval pathways should not be considered as existing approved therapies).

Process for Eligibility and Designation Decisions. The sponsor could apply at, or any time after, a pre-IND meeting. Whether a drug should be considered for, or the subject of, progressive approval can be recommended by FDA, but should be the option of the sponsor. FDA should issue, upon request within 60 calendar days, a written determination explaining whether a drug and a proposed indication is, or is not, eligible for progressive approval. FDA’s written determination should include an explanation of the rationale for FDA’s decision. FDA’s determination should be publicly available at the time the decision is made, but the sponsor can request that the final decision not be disclosed (prior to approval of the product) due to concerns regarding disclosure of proprietary information about product development plans. A decision that the product is not eligible for progressive approval should not preclude a subsequent decision (based on new information) that the product is eligible for progressive approval. There should be no requirement to seek, or obtain, an eligibility determination prior to applying for progressive approval. Products that are under IND at the time of the introduction of this progressive approval pathway, shall maintain the option, at the election of the sponsor, of pursuing approval through the existing accelerated approval pathway or through the progressive approval pathway.

Appeal Rights (Adverse Designation Decisions). In the event of an adverse decision on the progressive approval application, an applicant can invoke a statutory administrative appeal process that includes (at the applicant’s option) stakeholder (public) and expert input. The FDA should provide a response to an appeal within 60 calendar days. If FDA issues an adverse appeal decision, the agency should explain what would be needed to satisfy the standard.

Standard for Progressive Approval. Progressive approval should be granted:

- In general, at the earliest possible time when the available evidence suggests that the drug is more likely than not to provide a favorable benefit-risk tradeoff to its intended patient population
 - For example, progressive approval may typically be granted following completion of one Phase II trial, provided that the available evidence suggests a favorable benefit-risk tradeoff
 - May also be granted earlier, at the Commissioner’s discretion, if the Commissioner concludes that the benefits of immediate availability of the drug outweigh its risks for the intended population
- If necessary to create the conditions whereby the drug is more likely than not to provide a favorable benefit-risk balance, FDA should use all available tools, including REMS, post-market surveillance, controlled distribution, physician training and registries, etc.

Approval should be conditioned on written agreement between FDA and the sponsor regarding further development plans designed to lead to the submission of a supplement for full approval under section 505 of the FDCA, or 351 of the PHS Act, within a period of time to be negotiated on a case-by-case basis. FDA should also have the authority to waive the requirement to obtain full approval, if it finds that the data necessary to satisfy the standard in question cannot be collected, for example due to ethical concerns or scientific limitations (referred to as “exceptional approval”).

Expiration and Renewal. Progressive Approval should remain in effect unless and until FDA determines that the conditions for Progressive Approval (*i.e.*, that the available evidence suggests that the drug is more likely than not to provide a favorable benefit-risk balance) no longer apply, as described below under “Withdrawal of Approval”). The holders of NDAs and BLAs approved via progressive approval should submit supplements to convert their products to full approval when they have gathered the data needed for that approval.

Postmarket Restrictions. Same post-marketing reporting requirements as drugs approved under the traditional approval process (*i.e.*, recordkeeping and safety reporting). FDA may use all available tools, including REMS, post-market surveillance, controlled distribution, physician training and registries, etc. to ensure a favorable benefit-risk balance in the post-market.

Withdrawal of Approval.

- Withdrawal of approval (with an opportunity for a post-withdrawal hearing) should be available in the event the Commissioner concludes that it is no longer more likely than not that the benefits of the product outweigh its risks.
- Sponsor will be required to submit a report to the FDA once every two years, until full approval is obtained or progressive approval is revoked. This report will provide

an update on the progress of the agreed development program toward full approval; and will update all available evidence regarding the efficacy and safety of the drug in the approved indication and population; and will provide an updated assessment of the benefit-risk balance based on all available evidence at that time

- Following submission of each such report, FDA will conduct a review of the product's Progressive Approval status. The FDA may convene an Advisory Committee in conjunction with such review. If the Commissioner concludes that it is no longer more likely than not that the benefits of the product outweigh its risks in the intended population, then the FDA may initiate withdrawal procedures.
- FDA should utilize all available tools in order to maintain a favorable benefit-risk balance, including labeling changes, REMS, etc., prior to withdrawing Progressive Approval
- If FDA determines to withdraw Progressive Approval status, the sponsor should be notified of the FDA's assessment, in writing. FDA's written assessment of the benefit-risk balance should be made publicly available.
- The sponsor should be entitled to appeal the FDA's decision to withdraw Progressive Approval status.
- Prior to ruling on an appeal, the FDA should convene an Advisory Committee, if it has not already done so in conjunction with its original withdrawal assessment.
- The appeal process should be completed within [180 days]
- The product should retain its Progressive Approval status and remain commercially available until final resolution of the appeal process.

Labeling and Promotion. The package insert of a progressively approved (or exceptionally approved) drug should disclose its status. Marketing and promotional claims should be permitted, in accordance with the product label, in the same manner as with drugs granted full approval.

Charging and Reimbursement. Drugs approved under this pathway are not considered investigational drugs, thus, are subject to the same coverage and reimbursement policies applicable to drugs approved under the traditional process.

Generics and Biosimilars. Once full / traditional approval has been obtained, the drug may be a reference product for purposes of generic or biosimilar drug approval. A regular period of data exclusivity will apply at that point (and protect the data just submitted for the full approval).

EMPOWER FDA TO UTILIZE A WEIGHT-OF-EVIDENCE APPROACH

Executive Summary

The Federal Food, Drug, and Cosmetic Act (FFDCA) requires that the Food and Drug Administration (FDA) approve applications for new drugs when they have been demonstrated to be safe and effective under the intended conditions of use. Under Section 505(d), effectiveness is established when FDA is satisfied that there is "substantial evidence" that the new drug has the intended effect that it is purported to have. FDA typically requires two "adequate and well controlled" studies under this standard. A weight of evidence approach to data analysis,

however, allows the decision-maker to look at all data and information, whatever its value, and give each appropriate consideration.

Background

FFDCA grants FDA significant latitude in defining the contours of the studies establishing “substantial evidence”. Statistical significance is generally demonstrated by meeting the standard of $p < 0.05$ with respect to pre-determined endpoints.³⁴ This means that there is a less than one in twenty chance that the observed difference between test articles (*e.g.*, an investigational drug and placebo) is “just” a product of random variability within a data set. Said differently, if there truly was no difference and the same experiments were conducted twenty times, we would expect to falsely “find” a difference just once.

Ultimately, however, the $p < 0.05$ standard for statistical significance is an arbitrary one. Observations that clearly have practical meaning may fall short of statistical significance due to the statistical power of a given study. For example, if one drug in a given class demonstrates effectiveness with a p value of 0.04 after a very large clinical trial, and a second drug within the same class – and as to which all scientific principles suggest would act similarly – demonstrates effectiveness with a p value of 0.06 after a smaller study, it would not make good sense to say that the first is effective whereas the second is not. It would also be an inefficient use of resources (and potentially unethical) to force the sponsor of the second drug to recruit additional subjects when the result of doing so, lowering the p value to reach 0.05, is more or less a foregone conclusion.

Data analysis may also show that a statistical significance exists when such significance has no meaning in practice. For example, a clinical study for a topical antibiotic ointment may show that individuals given the treatment, as opposed to placebo, had a small, but statistically significant increase in the development of gastric ulcers. Given that there is no reason to expect that local, topical application of an antibiotic would have any causal relationship to ulcers, it should be unnecessary to conduct a full follow-up study to demonstrate the lack of such a relationship, particularly when other similar medications are already known not to have such an effect. In each of these cases, the statistical analysis fails in that it becomes divorced from basic first principles of science.

A weight of evidence approach to data analysis, on the other hand, would allow a reviewer to consider a study whose data demonstrate a statistical p value that, while not technically meeting a standard definition of “significance”, nonetheless provides evidence of safety or effectiveness. When reviewing an individual set of data and the question of causation, the reviewer would look

³⁴ The measure of statistical significance being at the 5% level is more or less an artifact of historical chance, when full statistical tables were difficult to manually produce. As a result, Ronald A. Fisher’s seminal 1925 text on the subject, although providing tables with multiple levels of significance for other values, only provided the 5% level for one particular table. This value subsequently became the standard of significance for the biological and medical sciences. See Stephen Stigler, Fisher and the 5% Level, 21 CHANCE 12 (2008).

at the strength of the association (the statistical analysis) in the context of the data's internal consistency as well as its coherence with first principles of science.³⁵

Such an approach to data analysis is not new to FDA or to other governmental agencies. The Environmental Protection Agency regularly utilizes a weight of evidence approach to determining acceptable levels of various substances in drinking water and the atmosphere. FDA also regularly invokes the weight of evidence concept when communicating issues of causation; for example, when considering the toxicity of a regulated product or a qualified health claim for a food. In a 2009 briefing on the status of FDA regulatory science, the agency stated that regulatory and public health decisions promulgated by the FDA are based upon the weight of scientific evidence. Nonetheless, FDA rarely articulates what it means when it says "weight of evidence." Conducting a weight of evidence evaluation requires scientific expertise and judgment, but it enables regulatory decision makers to consider and give weight to a broader range of data, including information that might otherwise fail the traditional, yet somewhat arbitrary, definitions of statistical significance.

Proposal

The last sentence of FFDCA Section 505(d) should be amended to state that if the Secretary determines either, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation), or that the overall weight of the evidence (including all relevant scientific data and information not otherwise prohibited from reliance or reference by the agency) is sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence.

LEVERAGE ELECTRONIC HEALTH RECORDS TO FACILITATE CLINICAL RESEARCH

Executive Summary

Every new drug's sponsor spends years designing and conducting clinical trials to show the drug is safe and effective. Using health information technology (IT) such as electronic health records (EHRs) in clinical research will improve and speed up the drug development process, and decrease costs. However there are significant barriers preventing wide-spread use of health IT in clinical research, including slow adoption by providers, and lack of standards development. FDA can help remove those barriers. Congress should create a Clinical Informatics Coordinator in the Office of the Commissioner of Food and Drugs charged with developing processes to validate and encourage the use of health IT in clinical research, and establishing pilot projects to use health IT in clinical research.

Background

³⁵ It is important to note that such an approach does not abandon statistical analysis, but rather borrows from the Bradford Hill criteria for causation when considering the question of whether the data are indicative of real differences.

Health IT can improve the quality, and efficiency, of the health care system. Congress has passed legislation promoting the use of health IT by encouraging the adoption of electronic health records to reduce medical errors, reduce health care costs, and improve health care quality. The widespread adoption of interoperable EHRs can facilitate the secure exchange of electronic health information, which can be used to speed the drug development process by improving the efficiency of clinical research.

To develop a new therapy for use by patients, companies spend the majority of the drug development phase conducting clinical trials to demonstrate that the drug is safe and effective. The clinical trials generally proceed in three phases, beginning with smaller studies to gather preliminary safety information about the drug, followed by larger studies to gather information about safety and effectiveness. This process can take six to seven years. EHRs can be used to improve how clinical research is conducted.

Specifically, EHRs can help companies more effectively identify, recruit, and enroll patients for clinical trials. Companies often face challenges recruiting subjects to participate in clinical trials studying drugs for a rare disease or for trials that require a large number of patients. Difficulty recruiting eligible subjects increases the time (and cost) to develop a drug. But electronic health records can be used to notify a physician if a patient is eligible for a clinical trial. This functionality will allow clinical trial investigators to more efficiently identify potential study participants eligible to participate in a trial.

Sponsors can also use health IT to better inform clinical study design. Data from EHRs can allow companies to simulate different clinical research models to determine the most efficient study design to assess the safety and effectiveness of a drug. Using health IT, sponsors can better understand the physiology of the target disease, the pharmacology of the drug compound to be tested, and the statistical methods that will be used to analyze the clinical trial results. This information can be used in designing the trial, which may improve the chance of clinical trial success.

Further, health IT can be used to more efficiently collect study data. Sponsors can eliminate redundant and time-consuming manual data entry by using EHRs to automatically populate case report forms.

Health IT can also allow investigators to protect subjects enrolled in a clinical trial by more effectively monitoring for adverse events. Sponsors can enroll patients in an electronic registry that allows the sponsor to track the patient's experience with the drug in real-time, relying on information contained in the patient's EHR. As a result, safety signals may be detected and addressed more rapidly, helping to ensure patient safety.

Despite the vast potential for improving clinical research through the use of health IT, significant barriers remain. Although Congress has provided funding to encourage the adoption of EHRs, the use of EHRs in clinical practice remains relatively low at this time. Work must be done to ensure interoperable standards and the secure exchange of data. In addition, validation methods for clinical research health IT tools are needed. But most importantly, FDA must issue standards governing activity in this area. Companies are less likely to use different approaches to clinical

trial research, even if those methods lead to more efficiency and better protections for clinical subjects, if FDA is unwilling, or unprepared, to apply data generated in clinical research using health IT in drug approval decisions.

Proposal

The Federal Food, Drug, and Cosmetic Act (FFDCA) should be amended to provide that the Commissioner of Food and Drugs appoint, within the Office of the Commissioner, a Clinical Informatics Coordinator. The Clinical Informatics Coordinator should develop a process to validate the use of health IT in clinical research and encourage the use of new health information technologies in clinical research protocols. FFDCA should also require that the Clinical Informatics Coordinator establish pilot projects to explore and evaluate the methods of incorporating emerging health IT to make the clinical research process more efficient. Not later than one year after the conclusion of the pilot programs, FDA should issue guidance for the conduct of clinical trials incorporating health information technology. The guidance should explain how FDA will evaluate such information when reviewing medical product applications.

REQUIRE FDA TO DISCLOSE TO THE SPONSOR REASONS FOR NON-APPROVAL

Executive Summary

The Federal Food, Drug, and Cosmetic Act (FFDCA) implies that licensing or approval applications are a binary question – approve or deny – due to phased, investigational review of applications; however, there is in practice a third response. In this case, the Food and Drug Administration (FDA) neither approves nor officially denies the application (which would require FDA to give the sponsor specific procedural rights such as a hearing), rather it finds the application to be incomplete in some way that makes the application ineligible for approval. When FDA makes such a finding, it should communicate to sponsors in clear terms why risk was determined to outweigh benefits and why authorities such as Risk Mitigation and Evaluation Strategies (REMS) – which are designed to mitigate risk – are insufficient (in addition to indicating what must be done to address any deficiencies). Such an approach would help create a consistent and transparent evaluation of risk-benefit, and provide the sponsor with better information on what, if any, additional studies are required to achieve approval.

Background

FDA, like most regulatory agencies, tends to be relatively risk-averse – there is a gravitational pull toward issuing a request for additional data when faced with data that does not clearly and greatly exceed the approval standards for safety and effectiveness. FDA has, however, been given the authority to implement a number of strategies to mitigate potential risks associated with the use of a given product. The first and least restrictive way is to limit the approved conditions of use. Here FDA can effectively exclude certain higher risk use scenarios without being forced to deny an application. Second, FDA can include warnings, and even black box warnings, to expressly contraindicate a treatment under certain high risk uses. Third, under the FDA Amendments Act of 2007, FDA can require the implementation of a REMS to manage a known or potential serious risk associated with a drug or biological product and ensure that the benefits of a drug or biological product outweigh the risks of that product when prescribed. In

each case, these mechanisms can be utilized to manage risk, and thereby alter the benefit-risk analysis.

Proposal

Section 505 of FDCA should be amended to include a requirement that when the Secretary has determined that submitted Phase 3 clinical investigations are inadequate to support approval or the application otherwise results in the Secretary denying approval, sponsors of applications under this section or section 351 of the Public Health Service Act shall be provided with a written explanation as to the reasons for that conclusion. That document should include detailed justifications for why FDA believes that (a) label warnings, (b) a REMS (including each possible REMS element to assure safe use), or (c) post-approval research, are inadequate to ensure that the benefits of an approval outweigh the risks.

ATTACHMENT IV: FOOD & AGRICULTURE PROPOSALS

THE ROAD TO A BRIGHTER FUTURE FOR AGRICULTURAL BIOTECHNOLOGY

For the past two decades, the United States has played a leadership role in agricultural biotechnology innovation, contributing billions of dollars to the U.S. GDP. Unfortunately, the U.S. regulatory system for plant and animal biotechnology, which was designed in the mid-1980s to facilitate product development, is fast becoming an impediment to the development and commercialization of safe, beneficial products. Today, developers of agricultural biotechnology are less certain about the length and scope of federal regulatory approvals and the susceptibility of approvals to legal challenge. Greater certainty is needed to drive scientific innovation and reassure international trading partners, which is essential to U.S. producers of genetically-engineered products.

PROPOSED LEGISLATION

While the underlying statutory authorities and regulatory framework for agricultural biotechnology are sound, to improve the process, Congress can provide direction to the federal agencies responsible for implementing the governing statutes that most directly impact genetically-engineered plants and animals.

SENSE OF CONGRESS:

- A. Congress recognizes the important role that biotechnology innovation has played the past 15 years in:
- * improving the environment by reducing soil erosion, improving soil health, reducing consumption of fuel for farming equipment, allowing for the return of beneficial wildlife around farm fields, and less chemical runoff;
 - * helping U.S. growers' competitiveness in an increasingly competitive global market;
 - * creating jobs and stimulating economic growth; and
 - * maintaining healthy rural economies.
- B. Congress acknowledges that science and the history of safe use have shown biotechnology crops to be safe for human health and the environment. As such, existing and future biotechnology products have the potential to make a significant contribution to the major challenges facing society: feeding, fueling and clothing the world's growing population in a manner that is sustainable.

- C. Congress recognizes the importance of this technology to the national interest, including energy security, trade, competitiveness, food security, environmental protection and sustainability.
- D. Congress directs that USDA and EPA consider the benefits of technological innovation in agriculture in achieving the goal of environmental protection and stewardship in carrying out their statutory authorities and complying with environmental statutes.
- E. Congress affirms that regulatory decisions should be consistent with the World Trade Organization Agreement on the Application of Sanitary and Phytosanitary Measures and that regulatory decisions for agricultural biotechnology products shall be based on science and not socio-economic issues or the so-called “precautionary principle.”
- F. Congress reasserts the fundamental principles that guided the early development of the U.S. regulatory system: a) risk depends on the product and not the process by which it was produced; b) the extent and type of regulatory oversight should be commensurate with the relative safety of the product.
- G. Congress affirms the Coordinated Framework for the Regulation of Biotechnology as the basis for regulation of agriculture biotechnology.
- H. Congress supports regulatory agencies, which oversee biotechnology products, having sufficient resources and funding to perform their review in an effective and efficient manner.
- I. Congress urges the creation of educational initiatives to improve the understanding of students in grades K-12 of basic elements of biotechnology, including agricultural biotechnology, and enhance their ability to pursue higher education and careers in the biological sciences.
- J. Congress supports funding to the National Institute for Food and Agriculture and its programs to conduct further research in biotechnology.

CONGRESS DIRECTS THE SECRETARIES OF AGRICULTURE AND HEALTH AND HUMAN SERVICES, AND THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY:

- A. To recognize the division of authorities as established in the Coordinated Framework and to eliminate and avoid unnecessary duplication of regulation.
- B. To maximize agency resources by increasing the efficiency and effectiveness of the regulatory process, particularly for familiar products; providing greater predictability in data requirements, timeliness and decision making; and improving review and authorization timelines.

- C. To take administrative actions designed to reinforce plant, animal and human safety and sound science as the sole basis for decision making; to endorse a history of safe use as an appropriate basis for regulatory reform; and to emphasize product over process as basis for regulatory jurisdiction and action.
- D. To promptly submit a joint report to Congress on how each agency will accomplish these objectives.

CONGRESS DIRECTS THE SECRETARY OF AGRICULTURE:

- A. To meet timeframes for decisions as reflected in regulations.
- B. To provide support for maintenance of germplasm banks as a biodiversity resource.
- C. To provide financial support for developing and commercializing biotechnology-derived minor use crops and commodity crops with value-added traits to benefit small farmers.

CONGRESS DIRECTS THE SECRETARY OF HEALTH AND HUMAN SERVICES:

- A. To appoint experts in the field of genetically-engineered animals to Veterinary Medical Advisory Committees when genetically engineered animals are being reviewed as a result of a new animal drug application;
- B. To permit interactions between FDA staff and Veterinary Medical Advisory Committee (VMAC) members to: 1) clarify data and questions during meetings of the VMAC when reviewing genetically engineered animals as a new animal drug; and 2) guide VMAC processes to ensure discussions stay on track.
- C. To support small business innovation by continuing small business exemptions under the Animal Drug Use Fees Act.

CONGRESS DIRECTS THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY:

- A. To maintain the Agency's long-standing policy of utilizing FIFRA Section 25(b) to avoid duplication of regulatory requirements for those plants and other macro organisms, seeds, and other plant parts that are already subject to regulation under the Plant Protection Act of 2000 and other statutes administered by the Secretary of Agriculture.
- B. To ensure that the recordkeeping, reporting, data, and other requirements for plant-incorporated protectants and other biological products are based solely on considerations of safety and sound science and that the requirements traditionally required for chemical pesticides are not automatically applied to these biological products.

CONGRESS DIRECTS THE U.S. TRADE REPRESENTATIVE WITH SUPPORT FROM THE SECRETARIES OF AGRICULTURE AND HEALTH AND HUMAN SERVICES AND THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY:

- A. To negotiate trade agreements with key U.S. export markets on: a) adoption of low level presence policies consistent with Codex guidance to advance trade in products authorized in the United States; b) minimizing/eliminating barriers to wood trade related to certification schemes that prohibit wood from genetically engineered trees; c) minimizing/eliminating barriers to cloning and genetically engineered animals and plants.