

Final Report of the Committee to Review Proposals to the 2008 Biomedical Research and Commercialization Program of the State of Ohio

Committee to Review Proposals to the Ohio Third Frontier BRCP Program

Board on Life Sciences
Division on Earth and Life Studies

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June 16, 2008

Lt. Gov. Lee Fisher
Chair, Third Frontier Commission
Ohio Department of Development
77 S. High Street
Columbus, OH 43215-6130

Dear Lt. Gov. Fisher:

This letter details the work of and transmits the final report of the Committee to Review Proposals to the 2008 Biomedical Research and Commercialization Program of the State of Ohio. This activity was supported by a contract of the Ohio Department of Development (ODOD) with the National Academy of Sciences and was performed under the auspices of the National Research Council's Board on Life Sciences.

The goal of the Biomedical Research and Commercialization Program (BRCP) is to provide funds to help Ohio universities, research institutions, medical centers, and private companies work together to commercialize technology-based products and improve the health of Ohioans. The Request for Proposals (RFP) listed a number of criteria against which applications were to be measured, including:

- Building on Third Frontier Program (TFP) Investments
- Consistency with Roadmaps for Success
- Consistency with State and Regional Priorities
- Degree of Customer Readiness
- Degree of Sustainable Competitive Advantage (Fly Wheels)
- Demonstrated Leadership Assets
- Identified Stage of Market Development
- Impact on Ohio
- Importance to Key Existing and Emerging Ohio Industry Drivers
- Involvement of Anchor Companies
- Involvement of Statewide Research Capacity
- Level of Scientific Merit
- Past Performance (if applicable)
- Potential for Leverage
- Potential for Products
- Size of Opportunity

At the request of the state of Ohio, the National Research Council convened a committee of experts to consider the applications submitted in response to the state's RFP. The committee of 20 was chaired by Alastair Wood, a member of the Institute of Medicine, Managing Director of Symphony Capital LLC and Professor of Medicine and Pharmacology at Weill Cornell Medical College in New York. Committee

members were chosen not only for their expertise in the subject areas represented in the 31 applications but also for their experience in commercializing research. Half of the committee members hold patents, 5 have founded or co-founded companies, 2 are employed in venture capital, 3 are or have been CEOs of medical device companies and 4 are or have been directors at major pharmaceutical companies. Of the committee members who are academic scientists, most have chaired departments, managed large interdisciplinary centers or served as deans. Many of the committee members have extensive experience in regulatory issues. The committee included 5 women and 5 members of underrepresented minorities. Biographies of the committee members can be found in Appendix C.

The process used by the committee to review the proposals was as follows: each proposal was read by a primary and secondary reviewer. Reviewers evaluated each proposal using a score sheet that included each requirement in the RFP (Appendix B). At its first meeting, in Washington, D.C. on April 23-24, committee members were asked to summarize their reviews of the proposals for which they were responsible. Proposals which were deemed uncompetitive by both the primary and secondary reviewers were not discussed further (unless another committee member requested a full discussion), but the two reviewers were asked to provide feedback in the form of a short review for each of these proposals. The remaining proposals were discussed at length. Stephen Berger, who served as a volunteer consultant to the committee, provided the committee with information on the performance of the various applicants on previous TFP funded projects. The committee reached a consensus that 9 of the proposals should be further evaluated through an interview with their project leaders. A set of questions was developed for each of these applicants to address in meetings that were held in Columbus, Ohio on May 15.

On May 15, 10 members of the committee met in Columbus with groups representing the 9 proposals for follow-up interviews. Two additional committee members participated in some of the interviews by conference call. Each group was given 30 minutes to address the committee's questions, followed by 15 minutes of questions from the committee. On May 16, the committee met to finalize its recommendations.

The committee concluded that six proposals substantially complied with the criteria set forth in the RFP. In the case of two of the proposals, the committee found that parts of the proposals were consistent with the RFP, while others were not. The detailed reviews of these proposals explain which projects the committee found most consistent with the RFP and the committee recommends that the state of Ohio consider working with the applicants to revise their requests to focus on the projects that are most likely to meet program goals. In one case, the committee was enthusiastic about the proposed project, but found a critical need for immediate business expertise and recommends that the state of Ohio consider requiring the recruitment of an experienced business collaborator as a condition of funding. In rank order, the proposals that the committee recommends the state consider funding are:

08-031 Rapid rehabilitation for amputee soldiers

The goal of this proposal is to develop a more functional prosthetic limb for transfemoral amputees. The team includes bioengineers, clinical experts and an industrial partner with production, marketing and distribution experience, as well as a strong commitment to the state of Ohio. The design concept is innovative, interesting, and reasonably likely to be successful. The potential market size of amputee users is

large. The business plan rests on the existing business establishment at Ohio Willow Wood to manufacture, market, and distribute the product. The potential for job creation in the state of Ohio as a result of this product's development may be modest, but the value of the product, both to amputee soldiers and other patients, lends this proposal a value beyond its immediate economic impact.

08-061 Treatment of acute and chronic wounds with tissue engineering strategies

The Clinical Tissue Engineering Center (CTEC) was initially funded by the TFP in 2004 with a plan to act as the hub of a network to bring scientists, tissue engineers, clinicians and private companies together to advance basic research findings to clinical practice. The Center has successfully established itself as a provider of resources to help establish collaborations and facilitate commercialization. The aim of this proposal is to extend CTEC's network and programs beyond musculoskeletal applications into the areas of wound healing, treatment of burns and scars and repair of peripheral nerves. The overall level of scientific merit is high and the integration of the projects is well laid out. The commercial potential of the proposed projects is high and will be supported by the relationships the PI and the project team have detailed in the proposal. The leadership and the management of this project are outstanding. The structure, collaborative relationships and mechanisms put into place for this and the group's previous proposal could be used as a model for successful encouragement of translational research and commercialization.

08-055 Therapeutic DNA Nanoparticles and Molecular Imaging

This consortium is comprised of individuals from Case Western Reserve University, University Hospitals of Cleveland, Copernicus Therapeutics, Polgenix and a new company, Akrotome Imaging. The application includes three complementary activities. The first aim is to develop novel therapeutic nanoparticles to treat cystic fibrosis and retinitis pigmentosa. The preliminary data are excellent, and the scientific rationale is quite strong. The proposal reflects a realistic understanding of the time needed for and complexity of the experiments proposed. The second aim is to develop a two-photon ophthalmoscope that can be used to image retinal cells in vivo. This has a great deal of potential, as it will allow in vivo monitoring of both retinal health and of response to drug treatments (thus complementing Aim 1). The final aim is to develop contrast agents to detect clean margins in breast lumpectomy tissue. The preliminary data are very compelling, and the potential marketability of this approach for detecting cancer cells in tissue while surgery is still underway is large. The studies described in this proposal have a very strong potential for successful completion and commercialization.

08-049 Breath Analysis: Targeted Sensor Development and Commercialization for Health Care Diagnostics

This proposal aims to develop a nitric oxide (NO) sensor that will enable asthma patients to monitor their asthma at home. The scientific merit of this proposal is acceptable, although there will be a number of challenges to overcome. The very great need for such a device heightened the committee's enthusiasm. The commercial potential of this device is very high. The ability to measure inflammation via NO with a handheld device at home – one that can replace the peak flow meter – would be an important step in asthma treatment. However, the committee is concerned that the

team lacks the business expertise to carry this device through the complex process of commercialization. The potential impact on Ohio for additional revenues and jobs, and the impact on the comfort and health of millions of people around the world are both significant if this project is successful. Therefore, the committee recommends that Ohio consider working with the team to ensure that adequate business management is incorporated into the project.

08-058 Neuroregenerative Therapies

The project seeks to develop small molecules that can enhance repair of the brain in multiple sclerosis (MS). The goal is not only to delay progression of disability but to reverse it. This is a highly innovative proposal, with two major commercial strategies. The first is to develop MS drug discovery screen assays and offer them as a commercial service. This goal looks achievable as the screens are already being used successfully for research purposes. Consolidating the tests in one place and optimizing them for high-throughput and commercialization should generate several jobs. The second goal is drug discovery by running commercially available compound libraries through those screens, generating leads, and chemically modifying those leads to obtain drug candidates. The drug discovery efforts are desirable, and if successful, would fill a critically important unmet medical and market need. However, this part of the proposal is still very premature. The committee would have preferred to see more detailed information on the already identified compounds and greater evidence of successful implementation of medicinal chemistry. The committee recommends that if the state of Ohio decides to fund this proposal, the applicants should be asked to provide a new budget and business plan for establishing the screening business and that the remainder of the proposal be re-submitted in the future when the drug discovery efforts are more advanced and therefore more consistent with the goals and timelines expected under the BRCP.

08-047 Platform for Antiviral Resistance Testing and Vaccine Development

In this proposal, Diagnostic Hybrids, Inc. proposes to collaborate with researchers at Case Western Reserve University (CWRU) to further develop a yeast-based cloning system for viral diagnostics/treatment monitoring and to market these assays to hospitals, clinicians and pharmaceutical companies. The scientific merit of this application is high. While there are many tests for identification of HIV and HCV infection, there are few platforms that can readily identify or track the origin of drug resistance. The HIV application holds significant and immediate value as a genotyping tool for viral identification. There is real near-term need for a fast, inexpensive platform for HIV genotyping, particularly in monitoring for and determining the origins of drug resistance. This would be of tremendous value to doctors and patients, who would benefit from a more rational drug therapy for the “when to switch” cocktail strategy. The committee had some skepticism about the commercial potential of two of the three programs in the Diagnostic Hybrids consortium proposal. Specifically, the programs for HCV and influenza vaccines are likely to require nearly a decade of research and development rather than the 2-3 year timeline proposed and therefore, the committee does not believe that these programs meet BRCP criteria. The committee recommends that the state consider working with the applicant to revise the proposal to pursue only the HIV application.

The remaining 25 proposals each contained significant deficiencies in meeting the requirements of the RFP. In general, these deficiencies fell into three categories. First, in many cases, the committee found that the projects were not sufficiently advanced to have a realistic expectation of reaching commercialization within a reasonable time frame. In several other cases, the committee had doubts whether a significant market would exist for the proposed product or service even if the project were successful. Finally, in many cases, the special difficulties that attend bringing a novel drug, diagnostic tool, device, or treatment approach to market were seriously underestimated by the applicants. The triple challenges of demonstrating efficacy, safety and cost-effective production are more difficult, time-consuming and expensive to achieve than many of the applicants acknowledged or planned for. The proposals that garnered the most enthusiasm combined innovative ideas with solid intellectual property positions, an important unmet need with room in the market for new approaches, and a clear-eyed view of the path to commercialization. At the same time, the committee did not choose only “safe bets.” It is not unlikely that even with BRCP funding, some of these projects may fail and this is consistent with the goal of the BRCP to provide support for promising ideas before the stage when private capital is willing to invest. Conversely, certain of the projects that were not selected may succeed with future funding should the applicants refine their respective projects’ focus and direction. The committee tried to identify those projects where the high risk of supporting early stage commercialization and development is justified by the magnitude of the potential payoff.

The committee wishes to thank the state of Ohio for the opportunity to review these proposals and to provide its recommendations as to which of the proposals best met the requirements set forth in the RFP. As in years past, many of the committee members were vocal in their enthusiasm for Ohio’s commitment to the Third Frontier Program and honored to be a part of helping the state determine how best to invest this important resource.

Sincerely,

Alastair Wood
Chairman

cc: Warren Muir
Frances Sharples

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APPENDIX A

Individual Summary Evaluations

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Proposal 08-001
Nanomedicines for Cancer and Leukemia
The Ohio State University Research Foundation

Proposal Summary:

This proposal is to commercialize a nanoparticle formulation consisting of lipids, polymers and nucleic acids (siRNA or ODNs) for treatment of cancer, specifically leukemia. A novel microfluidic synthesis process that can be scaled up for use in this project has been developed to generate the nanoparticles. The project leverages existing infrastructure and prior TFP funding and includes multiple Ohio academic entities and companies.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,799,764	\$4,899,925
Capital Funds	\$200,000	\$100,000
Subtotal	\$4,999,764	\$4,999,925
TOTAL	\$9,999,689	

Detailed Review:

- **Level of Scientific Merit**

The scientific merit of this proposal was judged to be high. Although the LPD (lipopolyplexes) and similar nanocomplexes have been around for many years, their commercialization is relatively recent. The use of microfluidic technology was deemed to be novel and could provide new IP protection for the commercialization process. It was not clear how long the IP protection of the LPD particle would last. This group is not the first to invent pegylated nanospheres. Even after meeting with the team, the committee still questioned whether the group would be able to protect its IP in such a competitive field. The proposal adequately describes pre-clinical models and the particle synthesis process but particle composition and rationale needed further explanation, which was provided at the follow-up interview in Columbus.

- **Commercial Potential**

Although proof of concept has been nicely demonstrated, the panel had less enthusiasm about the commercialization plan and hence the overall potential. It is widely accepted that an efficient siRNA delivery formulation would be welcomed by the industry, but the specific business plan of this project was deemed inadequate. Do they plan to partner with larger siRNA companies, especially since many of the large companies are partnering with and/or acquiring companies like theirs? How will that affect the business plan? Moreover, there was no license agreement in place with Lomus; a written agreement would have increased the committee's confidence. A clear process of commercialization with attention to competition, entry barriers and funding leverage was not provided. This is a highly evolving and competitive market and hence it is critical to start with an excellent plan for commercial success.

- **Leadership and Management Quality**

The assembled team is impressive and includes significant academic and industry participation. Unfortunately this did not translate into a convincing business and commercialization plan. The infrastructure is already established and well funded and the researchers have made significant progress with prior TFP funding. More attention to the specifics and details of commercialization would have greatly enhanced the proposal. During the follow-up interview, the PI expressed his intention to take a leave of absence to serve as the president and CEO; identification of a full-time CEO is important, but an experienced business leader would have increased confidence in the project's prospects for success.

- **Impact on Ohio**

If successful, such an endeavor would be beneficial to Ohio, provided the IP stays within the state. Concerns were raised that there might be a significant chance of acquisition by large, out-of-state, pharmaceutical and siRNA companies. Nevertheless, the overall impact on Ohio and its economy was deemed likely to be positive. The proposal is consistent with the TFP objectives and the state's priority areas and has leveraged existing commercial entities in the state of Ohio significantly.

- **Budget and Cost Share**

The panel was somewhat concerned about the budget and cost sharing. Much of the cost sharing provided is "in kind" and details of the cash cost share are not adequately described. The values provided in the cost sharing letters and the budget form seemed different, especially for OSU.

Review Summary:

Overall the panel was enthusiastic about the science and the technology, although a more convincing argument of the competitive advantage is necessary. The panel was less enthusiastic about the business and commercialization aspect of the proposal. The management team should have leadership experience in industry. Overall, the panel felt that this project is not quite at the stage of successful translation and commercialization.

Proposal 08-007
Commercial Development and Commercialization of Pegylated Albumin
ADS Biotechnology

Proposal Summary:

The goal of this proposal is to commercialize a blood volume replacement product for use in critical and emergent clinical scenarios. The proposal aims to develop a modified form of human serum albumin for the treatment of capillary leak. TFP funding will be used for product commercialization efforts over the next three years, including the development of GMP (Good Manufacturing Practices) commercial manufacturing processes, toxicological testing and Phase I human clinical trials. TFP funding will also support ADS Biotech’s collaborative relationship with the University of Toledo and allow it to pursue possible alliances with other Ohio based institutions.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$2,376,000	\$3,062,174
Capital Funds	0	0
Subtotal	\$2,376,000	\$3,062,174
TOTAL	\$5,438,174	

Detailed Review:

- **Level of Scientific Merit**

Availability of a blood volume replacement in addition to existing saline and albumin products would be revolutionary. A new therapy to address the problem of leaky capillaries after systemic inflammation, infection, sepsis, burn, or major blood loss would be a major breakthrough. Also, massive diffuse injuries, such as blast or trauma, can also cause leaking capillaries. If this can be addressed many lives will be saved and complication rates will decrease. Thus, the panel was enthusiastic about the basic idea.

This team proposes to use a pegylated human albumin to slow or stop hypotension brought about by septic shock and capillary leakage. The addition of PEG to albumin will increase the size of the albumin and the application presents information that appears to show that the larger PEG-albumin stays in the capillaries, slowing the loss of blood. Although Pegylated Albumin (PEG) has been shown to be safe in humans, there are many questions still unanswered for this type of work. The quality of the work described appears to be very high. However, there are many additional questions might have been addressed, including: whether a “PEG alone control” has been performed; whether the material causes an immune reaction if used more than once; whether PO₂ was measured to ensure that the blood will maintain O₂ carrying capacity; and whether the material occludes blood vessels causing small ischemic events. The committee would like to have known what happens to the PEG in this type of animal model. Also, no histology is presented to show tissue viability after treatment. Finally, extending the application of the product to cover treatment of blast injuries would require a great deal more justification, given the many unknowns in that application.

- **Commercial Potential**

If they are successful in developing this technology there will be a large commercial impact. However, the timeframe for commercialization is unrealistic. The accomplishment of phase II and III trials in this time frame is very optimistic.

- **Leadership and Management Quality**

Though the leadership is very experienced in science they need additional depth in business, as reflected in the unrealistic development schedule.

- **Impact on Ohio**

This could have an impact on Ohio. However, the panel had concerns that, in the long term, manufacturing in Ohio may be problematic because the source of the primary materials, blood albumin, would dictate that production be close to a major source of blood.

- **Budget and Cost Share**

Though well thought out, there are major areas that need to be addressed. In typical licensing agreements there is a “substantial use of resource” test for future IP. It appears that use of the equipment in the University of Toledo will be compensated for but this may bring the IP ownership into question. Also, the IP budget, given the type of product, is very light. One would expect it to be closer to \$500K for the three years. This would take into account future filings and any additional challenges that might come into play.

Review Summary:

The committee had a number of concerns about the underlying science as well as the likelihood that production would eventually take place in Ohio. The substantial cash contribution offered by the company is notable and the committee expects that with further development, this application may well be more consistent with the goals of the BRCP program in future rounds.

Proposal 08-011
BRCP Center for Personalized and Genomic Medicine
Children’s Hospital Medical Center

Proposal Summary:

This proposal aims to establish a Center for Personalized and Genomic Medicine (CPGM) to generate and commercialize intellectual property that will advance the ability to individualize the prevention and treatment of disease. Central to the CPGM value proposition is the Computational Medicine Center (CMC) which is a previous Third Frontier Investment to the Cincinnati Children’s Hospital and the University of Cincinnati. The goal of the CPMG is to work with commercial partners to develop intellectual property created by researchers into personalized medicine products. In this application, six cross-disciplinary teams and projects are proposed: 1) to develop and implement a clinically motivated decision support system for pediatric epilepsy and depression; 2) to develop a novel generalized method for natural language processing called Neurocognitive Natural Language Processing (nNLP – patent pending) that can be applied to multiple biomedical domains; 3) to exploit a new broad-genome approach to dramatically improve the diagnosis and treatment of congenital sensorineural hearing loss (SNHL); 4) to validate a clinical test for distinguishing reflux esophagitis and eosinophilic esophagitis based on genomic analysis of esophageal tissue obtained during routine endoscopy; 5) to develop a novel, personalized therapy for ischemia reperfusion injury -induced acute renal failure; and 6) to develop a new approach for molecular analysis of two of the most frequently mutated pathways in human cancer: the p53 and Akt pathways.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$5,000,000	\$3,940,000
Capital Funds	\$0	\$1,110,000
Subtotal	\$5,000,000	\$5,050,000
TOTAL	\$10,050,000	

Detailed Review:

- **Level of Scientific Merit**

The scientific merit of this proposal was judged to be fairly high. However, the committee did not see a defensible thematic rationale linking the proposed scientific programs. Specifically and as stated above, the central value proposition seemed to be the strength of the CMC and the fact that it leveraged a past Third Frontier project grant. That being said, only 2 of the 6 proposed work plans/technical approaches seemed directly related to the CMC; the proposal for Neuropsychiatric Pharmacogenetics (1) and the proposal for Natural Language Processing (2).

- **Commercial Potential**

In general, the CPGM pipeline and portfolio approach was viewed as a positive with the potential to mitigate both scientific as well as investment/funding risk. However, the committee was not convinced that the projects selected demonstrated sufficient commercial potential. As just one example, the Kohl proposal for Renal Failure (5) is directed to the use of a polypeptide analogue of C5aR which acts as a C5a receptor antagonist, but such antagonists have yet to demonstrate human clinical utility. While such CPGM compounds may indeed demonstrate clinical utility with future funding, other C5a receptor antagonists have failed in prior human clinical studies (Neurogen) and a clear differentiation should be established by CPGM as to the rationale for moving

forward a single antagonist for human studies without back-up candidates with demonstrated pre-clinical evidence. While it was beyond the scope of the committee's review to analyze the relevance of the patent literature on any of the CPGM projects, a cursory literature review of the Kohl proposal revealed the presence of certain patent references related to polypeptide analogues of human C5a which are C5a receptor antagonists (for example, US Patent Number 5,807,824) which indicates that commercial freedom-to-operate should be clearly evaluated prior to funding.

- **Leadership and Management Quality**

The committee felt that the team and institution were well-qualified in the areas proposed. Primarily, the committee was unconvinced that the CPGM had established the necessary portfolio structure for success and felt that the CPGM had failed to adequately address the commercial relevance of each of the proposed projects.

- **Impact on Ohio**

The committee felt that the CPGM had the potential for a positive impact on Ohio, but such impact would be strongest where CPGM projects had a direct linkage to previous Third Frontier Investments and the CMC. Consistent with other sections of this review, the committee felt that the CPGM failed to demonstrate a compelling linkage of the entire CPGM portfolio to the CMC.

- **Budget and Cost Share**

The budget and cost share seemed reasonable, especially the commitment of Cincinnati Children's \$3,680,000 in matching funds over a three year period and the commitment of other institutions and organizations to provide both direct and in-kind contributions to the cost sharing.

Review Summary:

Overall, the committee viewed the CPMG proposal favorably as a potential extension of the success of the CMC. However, the committee was not convinced that the proposed pipeline of projects demonstrated a cohesive programmatic theme and furthermore, that the proposal failed to clearly demonstrate a compelling linkage to the CMC core resource. Therefore, the committee did not feel this proposal was consistent with BRCP goals in its current form.

Proposal 08-012
Brain Injury Diagnostics through Engineering Research & Development
University of Cincinnati

Proposal Summary:

The objective of this proposal, a collaboration between researchers at the University of Cincinnati and Xanthostat Diagnostics, Inc. (Cincinnati, OH), is to develop, building on earlier work, a spectroscopic device for detecting hemoglobin (oxy-, deoxy- and met-), bilirubin, and blood cells in cerebrospinal fluid. The device would be used in intensive care units to determine whether or not a patient has intracranial bleeding. The ultimate goal is to sell a product that can be used at the patient’s bedside, either for immediate evaluation of emergency-room lumbar puncture samples, or as a continuous monitor on cranial shunts in neurological ICUs.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,361,527	\$3,289,772
Capital Funds	\$102,000	\$180,000
Subtotal	\$3,463,527	\$3,469,772
TOTAL	\$6,933,299	

Detailed Review:

- **Level of Scientific Merit**

The proposal has a number of strengths; a reagent-free, online approach to looking for blood components in CSF is a good idea and preliminary research shows correlation between bilirubin and intracranial bleeding (subarachnoid hemorrhage or TBI-derived). The medical team is experienced and works in an excellent medical environment with good patient availability. However, even a library of 30,000 spectra may not be able to overcome the fact that it is hard to get quantitative data from overlapping, broad, spectra. Furthermore, the scattering method for blood cell determination is very sketchily described and it is not clear that blood cells are the only objects found in pathological CSF. Not enough information was given to convince the committee that the spectral library can give truly quantitative data.

- **Commercial Potential**

The team seems to have a good grasp of the neurology marketplace, but the market penetration estimate (75% in a few years) seems unrealistic and 5000 units also seems overly optimistic. Nevertheless, the product potential is moderate – this technology could be useful, and point-of-care monitoring is increasingly more important. The team has a good understanding of the needs of the medical professionals who would be using these units.

The relationship with Xanthostat, Inc. and early product development efforts make the commercialization path believable. However, the competitive position is relatively weak, since the proposal does not offer a unique intellectual property position. Other spectral processing algorithms may be as effective as the “minimum distance” approach and offer

serious competition. A discussion of IP management, which might have addressed this question, was not included.

- **Leadership and Management Quality**

There is some discussion of management structure in the proposal but it showed no evidence of the “Level A,B,C Metrics” prominently called for in the RFP. It seems likely that Xanthostat will support this project with additional funding, but the amount of follow-on funding available is unclear.

- **Impact on Ohio**

The job projections appear appropriate for the size of the grant request, and the collaborator, Xanthostat, is an Ohio company. The proposal leverages University of Cincinnati faculty and other UC resources. All of these aspects would have a positive impact on the state of Ohio.

- **Budget and Cost Share**

The budget is realistic and cost share support is good.

Review Summary:

Overall, the committee found the idea and the partnership attractive. However, concern about whether the group’s approach would prove successful and its intellectual property position, as well as a certain skepticism about the market projections reduced the committee’s enthusiasm for the proposal. More convincing preliminary data and more realistic marketing analyses would greatly strengthen this proposal.

Proposal 08-015
Comprehensive Eye Disease Initiative
Cole Eye Institute, Cleveland Clinic

Proposal Summary:

This is a complex proposal, with a large number of modules and submodules, focusing on ophthalmologic devices, diagnostics and pharmacological products. The group lists 5 separate modules for product or service development and commercialization. *AngioQuest* will focus on anti-angiogenesis compounds. In *OptoQuest* they propose the development of two ophthalmic devices, a corneal elastography device and a femtosecond laser for use in tractional vitreoretinal surgery. A third module is the *Clinical Research and Testing Site (CRTS)*, a center offering fee-for-service research and development assistance for ophthalmologic products and devices. Included also is a submodule for developing mouse models of ophthalmic diseases. Fourth is *Retinopathy of Prematurity (ROP) Therapeutics* which will focus on commercialization of small molecule candidate drugs for the treatment of ROP. Fifth, *Complement Diagnostics and Therapeutics* comprises 1) development of a diagnostic for the early detection of age-related macular degeneration (AMD), and 2) development of a non-viral AMD gene therapy.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,828,476	\$7,548,327
Capital Funds	0	0
Subtotal	\$4,828,476	\$7,548,327
TOTAL	\$12,376,803	

Detailed Review:

- **Level of Scientific Merit**

Module 1: The goal of this component is based on the work of Dr. Anand-Apte demonstrating inhibition of angiogenesis with TIMP3. The outline of studies proposed is reasonable, doable, and within the expertise of the module director. The approach is interesting, and there is sufficient evidence to suggest it is well worth investigation for potential therapeutic use in conditions characterized by abnormal vessel growth, including wet AMD, diabetic retinopathy and ROP.

Module 2: The goal of this component is to develop a non-invasive clinical technology for mapping corneal elastic properties to visualize corneal abnormalities that would aid in surgical decisions and outcomes. A good deal of background science to support this device development is provided. The second part of this module is less compelling. There is little evidence that this laser will be able to be focused adequately to treat tractional vitreoretinopathies without injury to the retina. Since the femtosecond laser is currently being used to disrupt corneal tissue, it needs to be demonstrated that it could be used without injury to the retina. Cadaver eyes or animal studies are needed to demonstrate efficacy and safety.

Module 3: The main part of this module, to set up a testing lab, is a sound idea. The group proposes to set up a laboratory that will provide preclinical validation of investigational drugs on a fee-for-service basis. Dr. Singh is well suited to lead the

development of this facility. They also propose to use this site for the development of additional models of ophthalmic diseases. While this sounds good, it is in fact extremely hard to develop good disease models and this goal is not particularly realistic. The committee was unenthusiastic about the proposed licensing of a mouse model where manipulations result in an inflammatory disease that causes in retinal degeneration; the potential of this model is overstated in the proposal and a great deal of additional work would be needed before one could be assured that the retinal injury in this mouse resembles that the disease process that is AMD. That being said, the investigational drug and device testing portion of this module could provide a needed resource to the ophthalmic community, and this is quite an exciting aspect of the proposal.

Module 4: This focuses on identification of small molecular drugs that could lead to coordinated angiogenesis. However, the investigators have no track record in this area. The other rather serious concern is that systemic treatment with drugs that induce blood vessel development could cause angiogenesis where it would have a negative effect, particularly worrisome for its proposed use in infants. Preliminary data from the group in this area is needed.

Module 5: This module has two components. The first is to use complement C3 binding to regulatory factor H as the basis for developing a diagnostic blood test for AMD. The scientific rationale for this is extremely unclear. The second component of this module incorporates very innovative technology from a new company, Copernicus Therapeutics. The preliminary data looks strong, and the application of this technology to AMD therapy is novel. The ability to get DNA into a cell without viral vectors is critically important for the potential treatment of many, many diseases. This has become an even more attractive approach with the recent demonstration that viral vectors result in antibody formation in the host. This is one of the more exciting studies in the application, and it has a very strong chance of commercialization.

- **Commercial potential**

The proposal includes a diverse portfolio of products, some of which have greater commercial potential than others. Focusing on a narrower portfolio including only the projects with the greatest commercialization potential would strengthen this proposal.

- **Leadership and Management Quality**

The group includes prominent ophthalmic researchers and a strong administrative team.

- **Impact on Ohio**

Again, given the diverse portfolio, and the uneven nature of the various components, it is difficult to assess the eventual impact of Ohio. It could conceivably be high if some of the projects reached successful commercialization.

- **Budget and Cost Share**

The committee raised no concerns in these areas.

Review Summary:

Prominent clinical and basic scientists, with long track records of innovative research and productivity, have put together a well-written proposal with a great deal of detail on the commercialization processes to be put in place for a number of devices, diagnostics and pharmaceutical drugs in an attempt to treat a wide array of ophthalmic diseases. Overall, the application is quite interesting, but uneven. Within this group of proposed commercialization initiatives, some have excellent potential both to further our understanding of the disease in question as well as the potential to develop new therapeutic strategies, with a clear basis in excellent science, and will be managed scientifically by experts in the field of ophthalmology. Two modules, however, are particularly weak, with little evidence that they would be successful. They lack a strong grounding in scientific proof, and while conceptually interesting, are really not much more than ideas at present. The proposal suffers from being overambitious and uneven in the potential of the proposed products relative to the scientific basis on which they rest.

Proposal 08-016
NOvel THERapeutic ApplicatiONs For Stromal Cell DerIved
Factor-1 (SDF-1) to TReat Organ DySfuncTion (OHIO FIRST)
AcelleRX Therapeutics, Inc.

Proposal Summary:

This application presents a proposal by AcelleRX Therapeutics, a venture-backed Cleveland-based biotechnology company to lead a collaboration between Ohio-based biotechnology companies (Copernicus, Ricerca), academic centers (Cleveland Clinic, Case Western Reserve University, University of Cincinnati, University of Toledo) and Ohio Centers of Excellence (Center for Stem Cell & Regenerative Medicine, Global Cardiovascular Innovation Center), to develop and commercialize therapeutic applications for stromal cell derived factor-1 (SDF-1). The initiative calls for AcelleRX and Copernicus to co-develop multiple SDF-1 products for treatment of stroke, wound healing and urinary incontinence, delivered through Copernicus’ proprietary DNA nanoparticle (DNAN) delivery system with pre-clinical and clinical development support coming from all collaborators.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,685,176	\$4,724,963
Capital Funds	0	0
Subtotal	\$4,685,176	\$4,724,963
TOTAL	\$9,410,138	

Detailed Review:

- **Level of Scientific Merit**

Stem cell therapies have generated significant excitement for improving repair after myocardial infarction, stroke, and degenerative disease. However, stem cells are challenging to deliver and we do not know yet the exact roles of the cells in repair, how long they remain at the site and even how they get to the site – either mobilizing host cells to the site or honing injected cells. SDF has been found to be involved in the migration of stem cells. Delivery, therefore, of this factor may be useful for helping to attract host stem cells to a site of injury (avoiding the need for cell therapy) or may help in the retention, survival, or activity of exogenously delivered cells. Therefore, the development of SDF-based therapies is a promising idea.

The scientific merit of this proposal was judged to be moderate and varied by sub-project. The preliminary evidence of the utility of SDF-1 in repairing ischemic injury is promising and likewise the evidence of utility of the DNAN as a means to deliver gene to tissue. In wound healing, lack of preliminary evidence of efficacy of applied SDF in animal models, and lack of clarity on why gene therapy vs. protein therapy would be useful in this indication dampened enthusiasm. This part of the project is more “research” than a timely entry into commercialization. A similar argument applies to the urinary incontinence area. The small molecule discovery project has insufficient detail to be adequately reviewed.

- **Commercial Potential**

The commercial potential of these projects was deemed modest, especially in the area of stroke, where it was felt that stereotactical application of the product was impractical and potentially harmful in a stroke patient. The wound and urinary indications have greater promise, but additional research and proof of concept are required, which probably puts commercialization beyond the horizon of the BRCP. The small molecule sub-project could have good promise, but 3 years was seen as insufficient to proceed from screening to having a candidate clear all pre-clinical work.

There was also some concern about the nanoparticle technology. Although an efficient DNA delivery formulation would be welcomed and valued by the industry, the specific business plan related to the proposed DNA delivery is inadequate. As presented, there is insufficiently detailed information about the technology and its potential for future scale-up. What kind of quantities could be manufactured and at what cost-of-goods? A satisfactory answer to this question is essential for a successful product. More information about the properties of the nanoparticles would be useful in understanding their commercial potential

- **Leadership and Management Quality**

The panel felt that the team assembled is impressive and includes significant academic and industry participation. The infrastructure is well established and the coordination established between the companies and universities is excellent.

- **Impact on Ohio**

If successful, such an endeavor would be beneficial to Ohio. Many of the companies are well-established.

- **Budget and Cost Share**

The panel did not have any issues with the budget or cost share.

Review Summary:

Overall the panel felt that the likelihood of generating commercial value with the aggregate of sub-projects was low, but was enthusiastic about project leadership and the potential of the technology. Several of the sub-projects are not yet at a stage to be consistent with the goals of the BRCP. A more persuasive argument of the potential advantages over competing delivery modalities and a discussion of freedom-to-operate in this space would have been helpful.

Proposal 08-019
Bioartificial Pancreas with Novel Immunoisulatory Polymer Membranes
The University of Akron

Proposal Summary:

This proposal is to commercialize a device that can serve as an implantable, artificial pancreas. The device consists of an immuno-isolating polymer membrane, a supporting nanomaterial structure, a scaffold and pancreatic islet cells. The collaboration is between various Ohio Universities and a few existing and proposed start-up entities. The target market at the beginning would be diabetic pets eventually leading to human applications.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,400,000	\$4,850,265
Capital Funds	\$600,000	\$150,000
Subtotal	\$5,000,000	\$5,000,265
TOTAL	\$10,000,265	

Detailed Review:

- **Level of Scientific Merit**

The ability to treat diabetes using implantable pancreas-like devices is a critical need in healthcare and in that regard the application addresses a critical problem. The team assembled is highly qualified and possesses the necessary scientific expertise. The ideas presented were well thought through and somewhat innovative. However, the panel felt that adequate proof of concept for the device has not yet been provided and it remains much too early in its stage of development to warrant commercialization and capital investment. More data needs to be generated and provided regarding the efficacy and safety of this device in small animal models (e.g. diabetic rats). There is discussion of the biocompatibility of the membrane, however no data are shown, especially those related to implant-associated inflammation and foreign body response that could lead to fibrous encapsulation, a problem that has long plagued such implants. The idea of creating a bio-artificial pancreas using encapsulated islet cells is decades old. Although the researchers provide some new and innovative approaches, adequate data to support the superiority of their device is missing.

- **Commercial Potential**

The commercial potential of such a device would be significant since the market for diabetes therapy is huge. However, it is critical to understand that the whole diabetes market would not be immediately suitable for such a device, especially the sectors of young children and elderly patients. Since it is so early in development, not enough animal data has been generated to assess commercial potential and a thorough comparison of its efficacy with existing technology has not been made. Although addressing the veterinary market first is a good idea, it is critical to provide adequate analysis of competing technology and show direct performance and cost comparison to assess commercial potential both in the near term and in the longer term.

- **Leadership and Management Quality**

The PI and the collaborators are well established in the field and suitable to carry out the research aspect of the project. The business, IP and regulatory development leadership would benefit from addition of appropriate business leadership. Although the end goal is identified, the proposal fails to realize that it is too early and more feasibility and cost analysis is necessary for commercializing such an endeavor.

- **Impact on Ohio**

If successful such an entity could have significant impact on Ohio creating new technology companies and jobs. The proposal did not leverage any established companies on the technology or business development. Start-ups have been proposed but adequate and detailed business plans for such endeavors are not provided. More existing industry involvement and a better business plan would aid the proposal significantly.

- **Budget and Cost Share**

The budget and cost share sections are strengths of the proposal. Good supporting letters describing the cost share plan have been provided.

Review Summary:

Overall the panel felt that although the area of research and the approach are significant and worth pursuing, the project is too early in its stage of development and adequate proof of concept has not yet been demonstrated. In-vivo efficacy in small (diabetic) animals and comparison with existing technologies are necessary. Addressing the major problem in the field, device encapsulation and subsequent reduction in blood sugar control, must be addressed. In addition, more industry leverage and a better management plan/team would greatly enhance the proposal.

Proposal 08-023
MRI Guidance of Radiotherapy, a New Ohio Development and Commercialization
AllTech Medical Systems America

Proposal Summary:

This application from a consortium of Ohio-based companies aims to develop MRI guidance of cobalt radiotherapy technologies to provide continuous imaging during the delivery of radiation to tumors. The goal is to use real-time MRI (with no radiation) to ensure that radiation is delivered only when the tumor is being targeted, reducing side effects and increasing radiation dose to the tumor.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,006,000	\$4,347,700
Capital Funds	\$994,000	\$3,743,700
Subtotal	\$5,000,000	\$8,143,700
TOTAL	\$13,143,700	

Detailed Review:

- **Level of Scientific Merit**

Today the main shortcoming of radiation therapy is that it is difficult to determine the dose actually being delivered. Body motion causes the tumor to move during therapy delivery, unnecessarily exposing healthy tissue to radiation. With the proposed technology, radiation delivery would be targeted to the area of interest and shut off in a fraction of a second when the tumor has moved off target to spare healthy tissue and allow an accurate treatment. When the tumor is on target the real time imaging will capture the real dose received by the patient, reducing side effects and providing accurate and precise delivery. The team assembled is excellent and very experienced in this field. The ideas and implementation plan are very well thought through and solid. However, the committee was not convinced that there have been enough preliminary studies to demonstrate proof of principle. The use of 0.35T and some of the gradient specifications and performance are not well demonstrated and justified. The committee was not convinced that the proposed dynamic imaging can be performed. Also, no plan to evaluate the therapy in patients is presented.

- **Commercial Potential**

Sales over \$250M are projected within the first five years of the program. The applicant estimates that capturing approximately a 0.8% market share (6 systems installed) in two years post-funding would generate \$16.8 million in gross revenues in late 2009. Additional revenue will be generated from the sale of service maintenance contracts at the industry standard rate of approximately \$150,000 per year per system. Some of these projections seem overly optimistic. Another concern is failure to address considerable competition in this market.

- **Leadership and Management Quality**

The consortium includes three medical device companies, each of which has an

established internal reporting structure and operates under a quality system consistent with the requirements of the Medical Device Directive as well as other relevant regulations. The PI and the collaborators are well established in the field and suitable to carry out the research aspect of the project. There is outstanding business, IP and regulatory development leadership.

- **Impact on Ohio**

AllTech and ViewRay are providing funds from non-Ohio-based VC's. Funding of this program will result in more non-Ohio VC funds making investments in Ohio for two reasons. The funding of this proposal will facilitate the relocation of ViewRay to Ohio and with it a major expansion of imaging cluster development past diagnosis and into radiation therapy.

- **Budget and Cost Share**

The budget and cost share sections are strengths of the proposal. Good supporting letters describing the cost share plan has been provided.

Review Summary:

Overall the panel felt that although the area of research and the approach are significant and worth pursuing, the project is still too early in its stage of development and adequate proof of concept has not yet been demonstrated.

Proposal 08-024
Commercialization of a Non-Invasive Ocular Glucose Measurement Device for
Persons with Diabetes
Freedom Meditech

Proposal Summary:

This application, from Freedom Meditech, Inc. proposes to develop and commercialize a non-invasive device to measure glucose levels in the eye as a substitute for blood tests currently used by diabetic patients. Requested funds would be used to reduce the size of the current system, work toward obtaining an Investigational Device Exemption from the FDA and prepare for pilot studies in humans. The applicants have assembled a team that includes researchers at the University of Toledo and Case Western Reserve University and several private sector partners to shepherd the technology from its current stage through the commercialization process. In the long term, the team hopes to develop their optical technology for other applications.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$2,585,000	\$2,520,000
Capital Funds	115,000	\$180,000
Subtotal	\$2,700,000	\$2,700,000
TOTAL	\$5,400,000	

Detailed Review:

- **Level of Scientific Merit**

The application was judged to have scientific strengths and weaknesses. The approach taken by the applicants is to shine polarized light in a linear path across the space between the cornea and the lens. The optical activity of the glucose in the aqueous humor rotates the plane of polarization; polarization is resolved after the light passes through the eye and is then used to calculate the concentration of glucose.

The strengths of this approach are that it provides reagent-free measurement without having to use a finger stick to obtain blood, and, purportedly, will not require contact with the eye. New data on this aspect of the eye will be scientifically useful and the block-diagram of optical design shows a system designed to counteract birefringence in cornea (previously a confounding factor). Aqueous humor glucose equilibrates with blood glucose in 5 minutes, so it is probably a better medium than vitreous humor for glucometry.

On the other hand, the application provides no detail on device design, except for a vague statement that the device might look like a pair of binoculars. Among key factors that appear to be overlooked are: light delivery/collection; packaging of optical components; and signal acquisition and processing (for example, will it use modulated/CW light? A PMT/p-i-n photodetector? Optical referencing?) In particular, there is no information on how the device would be miniaturized. The applicants provide no in vivo proof of principle that the instrumentation can work in a living animal without anesthesia, and no prototype of the device. The committee was skeptical that this measurement could be done properly without contacting the eye, since motion artifact alone would cause severe

problems. How path length will be measured is not obvious; this is a key weakness as its absence will make the device impossible to calibrate. Also, no evidence is provided that glucose is the only optically active substance in the vitreous humor; many other molecules (e.g., most proteins) are optically active. It is unclear that the timeline for development of this complex instrumentation is realistic, as they have been working on this for 14 years. And finally, the authors may be overstating the pin-prick as “great bodily pain”, and underestimating the reluctance of most people to do things that involve their eyes.

- **Commercial Potential**

The commercial plan also had strengths and weaknesses. The market for noninvasive glucometers could indeed be enormous (literally billions of dollars), and there are currently no acceptable products. The proposers are to be commended for creating a detailed, measurable (“Level A,B,C”), stage/gate commercialization process and their plan is realistic. The group truly is requesting seed money. However, early, and repeated, attempts to develop similar products have failed, creating a large barrier of skepticism in the business community. Also, there is intense competition from public and private groups, large and small, around the world, to develop such products. The marketing plan is not well developed; unspecified “vendors” would initially target clinicians as customers

- **Leadership and Management Quality**

While the connection with Ohio business/technical resources is reasonable (Battelle and Case Western Reserve both being highly regarded and Ohio-centered), the proposed business effort does not appear to have gained significant concrete support from **industrial** partners.

- **Impact on Ohio**

Development of a noninvasive glucometry product would have a huge positive impact on the health of people in Ohio, and the rest of the world. On the other hand, if successful, the proposed business would almost inevitably be acquired by a large medical equipment firm – making the projected impact of this product on Ohio uncertain.

- **Budget and Cost Share**

The proposed budget is reasonable and the cost share is well supported.

Review Summary:

The goal of glucometry without a blood sample has been pursued by many groups for several years, with limited success. The proposed approach uses no reagents, but this could lead to potential problems with specificity (since other optically active substances may be in the aqueous humor). The committee was not convinced that the proposed measurement could be done reliably without contacting, or even immobilizing, the eye, which would undermine the benefit of “no finger stick.” There was also concern that individual eye shape variation could easily confound the measurement. Nevertheless, the

market for noninvasive glucometers is enormous (literally billions of dollars), and no acceptable products currently exist. The team paid very close attention to creating a measurable stage/gate commercialization process and their plan is realistic for the amount of funding requested. However, the degree of skepticism in the business community and the intense competition for this market require that scientific strengths of any entrant to this market be exceptional.

Proposal 08-028
Novel Therapeutics for Neuro Rehabilitation
CSF Therapeutics, Inc.

Proposal Summary:

This proposal, submitted by CSF Therapeutics, Inc., aims to develop and commercialize a system to increase cerebral blood flow (CBF). The proposed approach, called Cadence, utilizes the dynamic effect of cranial fluid spaces on cerebral blood vessels. Use of Cadence for traumatic injury is the near-term commercialization goal but the applicants anticipate that the technique could be extended to various acute and chronic low flow neurological diseases. Current funding would be used to support pre-clinical studies, clinical trials, technology and team development, and fundraising.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,577,346	\$4,623,948
Capital Funds	\$335,835	\$350,000
Subtotal	\$4,913,181	\$4,973,948
TOTAL	\$9,887,129	

Detailed Review:

- **Level of Scientific Merit**

While there was general agreement that the applicants had demonstrated that the Cadence system had the ability to affect CBF, there was considerable skepticism amongst the reviewers about the potential for changes in CBF to affect such neurodegenerative diseases as stroke or Alzheimer’s disease. Previous clinical studies using pharmaceutical agents such as vasodilators have been uniformly unsuccessful, creating doubt that an increase in CBF would necessarily have a beneficial effect. The design of the proposed pre-clinical animal studies would not necessarily address these questions since almost all of the study endpoints are focused on CBF rather than other derivative clinical factors. The level of concerns about safety raised during committee discussions also suggests that the approval process for such a device would be lengthy and difficult.

- **Commercial Potential**

The market potential for a successful device treating different forms of neurodegenerative diseases is extremely large and currently unmet.

- **Leadership and Management Quality**

The development team assembled to conduct the research is extremely strong with areas of weakness (such as GLP animal studies) being sub-contracted to professional organizations.

- **Impact on Ohio**

Presuming a successful outcome for the project, the potential for CSF Therapeutics to provide a positive impact on Ohio through the creation of high-paying jobs is high.

- **Budget and Cost Share**

The budget and cost sharing is fair and reasonable

Review Summary:

Overall the reviewers were excited about the potential for a successful device but extremely concerned that the link between increasing CBF and achieving beneficial **clinical** effects is unproven. Strengthening this link, either directly or indirectly, would significantly enhance enthusiasm for this proposal.

Proposal 08-031
Rapid Rehabilitation and Return to Function for Amputee Soldiers
Lerner Research Institute, Cleveland Clinic

Proposal Summary:

This goal of this proposal is to develop a more functional prosthetic limb for transfemoral amputees. The proposed prosthetic would use electrorheological fluids (ER – fluids whose viscosity changes with electrical charge), combined with an internal spring, sensors and control systems to allow the prosthetic to capture and return energy allowing a more normal gait. The aim of the research effort is to develop an above-knee (AK) prosthesis that will enable rapid rehabilitation and a sustained ambulatory lifestyle. The team includes faculty at Cleveland State University (who will focus on the ER fluid aspects), engineers at Ohio Willow Wood (experienced in prosthetic limb technology) and investigators at the Cleveland Clinic (who provide expertise on the human gait). The necessary patents have been provided by Lubrizol Corporation to researchers in Cleveland, on the understanding that these patents would be used to develop spin-off products and jobs in Ohio.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$2,104,502	\$2,132,426
Capital Funds	\$0	\$0
Subtotal	\$2,104,502	\$2,132,426
TOTAL	\$4,236,928	

Detailed Review:

- **Level of Scientific Merit**

The scientific basis for the proposed prosthetic device is sound. The innovative part of this proposal is the engineering design of the prosthetic knee joint damper which combines the ER fluid and an imbedded spring, the development of control algorithm and the electric circuitry to implement the algorithm. The innovative design concept has been made available through a patent donation from Lubrizol Corporation. The selection of electric circuitry is adequate given the low-power requirement for the device. The control design is also achievable using available technology. The testing of the prototype is realistic.

- **Commercial Potential**

The population of amputees around the world is increasing, and stands to reach around 3.5 million. The estimated market size is 15,000 new users per year for each of US and EU regions alone. There is also an additional potential market of replacements which was not included in the market estimates. The proposed prosthetic device is more expensive (\$2,000 to \$3,000 each) than the current low end of the market, which may limit its potential market to those who can afford a higher cost, but the projected price is considerably lower than currently available electronically enhanced prosthetics. The company already has an established distribution channel in the US and a growing one outside of the US. The company is also beginning to tap the market in India.

- **Leadership and Management Quality**

The leadership of the team is strong and experienced. The proposed activities primarily focus on the research and design phase of the prosthetic device, where the scientific and technological leadership is adequate.

- **Impact on Ohio**

The potential impact to the state of Ohio is high. Ohio Willow Wood was founded and based in Ohio and will remain in Ohio to provide jobs and their associated economic impact. New job creation will occur in and benefit Ohio. Interactions between the company and Ohio university graduate programs will also impact positively on Ohio.

- **Budget and Cost Share**

The budget and cost share is reasonable. The company would benefit by exploring funding opportunities with SBIR/STTR grants and also partnering with the DOD on a commercial basis.

Review Summary:

This proposal relies on innovative engineering design and aims to lead to the manufacturing of a testable prototype. The IP and future investment of venture capital will be contingent upon successful testing of the prototype. The design concept is interesting and is reasonably likely to be successful. The potential market size of amputee users is large. The business plan rests on the existing business establishment at Ohio Willow Wood to manufacture, market and distribute the product. The potential job creation for the state of Ohio as a result of this product's development may be modest, but the value of the product, both to amputee soldiers and other patients, lends this proposal a value beyond its immediate economic impact.

Proposal 08-034
Cardiovascular BioEngineering and Therapeutics (CBET)
Ohio State University Research Foundation

Proposal Summary:

The proposed project, Cardiovascular BioEngineering and Therapeutics (CBET), builds on the Cardiovascular Bioengineering Enterprise (CBE) funded by the State of Ohio's Third Frontier Program (TFP) in 2002. CBET will be focused on the intersection between advanced diagnostic imaging and therapeutics development, specifically the early detection, prevention, and treatment of atherosclerosis. The applicants state that the market for improved cardiovascular diagnostic and therapeutic technologies is expected to continue to grow exponentially in the next 20 years as the baby boomer generation ages. Specific products proposed include 32-channel coils for cardiovascular MRI at multiple field strengths, an MRI-compatible treadmill system, wireless 12-lead MRI-compatible electrocardiography technology, rapid pulse sequences for cardiac and vascular imaging, multimodality cardiovascular image analysis software and workstations, and reverse cholesterol transport and high-density lipoprotein therapeutics for clinical trials.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,903,000	\$3,711,078
Capital Funds	97,000	\$1,472,500
Subtotal	\$5,000,000	\$5,183,578
TOTAL	\$10,183,578	

Detailed Review:

- **Level of Scientific Merit**

The committee was impressed by the scientific reputation and past accomplishments of the collaborating groups. They have extensive expertise in the field of medical imaging and have productively utilized previous funding from the state of Ohio. The proposed imaging technologies are realistic, if not innovative, and the committee was convinced that these groups could successfully develop working versions of the technologies that they propose. The committee also noted that the applicants have access to large numbers of patients, which is an additional strength of the proposal.

The committee was concerned primarily with the commercialization potential of the proposed products (see below) and with the scientific justifications for pursuing some of the products. Of greatest concern was the plan for small molecule therapeutics, since there is no evidence that improved imaging resolution will improve the success of cardiovascular drug development. It was also unclear why the proposed image analysis software would first be tested using SPECT-CT rather than MRI. The committee commended the applicants' technical approach to improve rapid imaging, but noted that their product would suffer from the same signal-to-noise ratio problems as other types of rapid imaging.

- **Commercial Potential**

Some of the proposed products are relatively low-risk, low-return and could be successful on the market. These include the image analysis software, which would be useful to the imaging community, and the MRI-compatible treadmill system, which could benefit research institutions. However, the committee questioned the commercial potential of most of the proposed products. There is already significant competition in coil development, so the proposed 32-channel coils for MRI will probably have limited market penetration. Another serious problem is that the rapid imaging technologies will compete on the market with cardiac CT, which already gives rapid images (40-50ms) that most physicians consider sufficient. In fact, some physicians question whether the information obtained from fast CT scans is really useful for their clinical decision-making. Given that the market may not be particularly eager for new rapid imaging technologies and that MRI has a long way to go before it will compete with fast CT, the committee felt that this product has very limited commercial potential.

- **Leadership and Management Quality**

The success of team members with previous state funding has apparently been high. The lack of enthusiasm for the commercial prospects of several of the proposed projects in this application suggests, however, that greater leadership from one of the commercial partners might have been helpful.

- **Impact on Ohio**

Again, given that the prospects for commercialization resulting from the projects proposed are deemed to be poor, the likely impact of the current investment would largely be in jobs funded directly by the grant rather than additional jobs leveraged by the state's investment.

- **Budget and Cost Share**

No concerns were raised about the budget and cost share, but again, the level of investment requested is high for projects with limited commercial potential.

Review Summary:

The primary strength of this proposal is the expertise of the imaging teams and the inclusion of a few low-risk, low-return technology products. The imaging technologies proposed are realistic and are likely to succeed in development. However, the committee felt that most of the proposed products do not have significant commercial potential. In particular, the proposal for small molecule therapeutics was unconvincing. Given the scientific and technical quality of the applicants, the committee felt that other products could have been suggested, such as a simpler interface for MRI, which would be significantly more marketable.

Proposal 08-035
Functionalized Nanoparticle-Mediated Delivery of Therapeutic Agents
Lerner Research Institute, Cleveland Clinic

Proposal Summary:

The goal of the proposed project is to develop commercially viable products based on the patented composition of biodegradable nanoparticles for the delivery of macromolecular and other small molecular weight therapeutics to treat cancers and other age-related disorders. Proof of principle and efficacy have been demonstrated in pre-clinical animal models of breast and prostate cancers. The proposal group includes the Taussig Cancer Center, the Department of Biomedical Engineering at Lerner Research Institute and Telomolecular Corporation. Telomolecular Corporation, headquartered in Rancho Cordova, California, is committed to establishing a Cleveland, Ohio based subsidiary under this project.

	State Funds	Cost Share
Operating Funds	\$3,997,423	\$4,584,773
Capital Funds	44,700	\$530,000
Subtotal	\$4,842,123	\$5,114,773
TOTAL	\$9,956,896	

Detailed Review:

- **Level of Scientific Merit**

The scientific merit of this proposal was judged to be moderate. The modified nanoparticles have been around for many years and their commercialization is challenging. As presented, there is inadequate detail about several aspects of the technology, including detailed information about the method of fabrication, efficiency of encapsulation, toxicity and the potential for future scale-up. Such information is essential for evaluating whether the product could be successful. So little detail is provided that it is hard even to understand what the nanoparticles are, what they are made of, how difficult is their modification and whether the modification will be done after or before encapsulation. The committee found that it was unable to judge the scientific merit of the proposal with so little information.

- **Commercial Potential**

Proof of concept needs further validation, and the prospects for regulatory approval and adoption of the new products are not clear. Most of the sunscreens on the market today are nanoparticulate in nature, however, delivery of proteins transdermally and their long term stability was not laid out, nor was a market analysis provided to justify the optimistic adoption rates. Another issue not addressed was the use of antioxidants on skin and the possible tumorigenesis that could result from the use of topically applied antioxidants. Penetration depth needs to be understood before such a product could be used on humans and this was not clear in the data presented. Finally the IP position and the future allocation of IP were briefly mentioned but the work plan did not clarify who has IP ownership. The commercial prospects of the initial product require greater

justification, and the regulatory and clinical challenges facing the cancer treatment applications have not been sufficiently addressed. In general, the timelines appear unrealistic.

- **Leadership and Management Quality**

The assembled team is impressive and includes significant academic and industry participation. The infrastructure is well established and the coordination established between the companies and universities is excellent.

- **Impact on Ohio**

If successful, such an endeavor would be beneficial to Ohio.

- **Budget and Cost Share**

It appears that the proposers are slightly naive in thinking that they can complete phase I and II trials in this round of funding. Greater justification for the very aggressive budgets would have been helpful.

Review Summary:

Overall the committee was enthusiastic about the business partnership and leadership. The committee was less enthusiastic about the scientific quality of the proposal. Future applications would be strengthened by greater clarity in the technical descriptions and more rigorous commercial models. Although the use of nanoparticles for delivery of therapeutics looks very promising, the technical ability to deliver on that promise is not adequately demonstrated by the applicants, and there are many potential competitors in this endeavor. Ability to ramp up production and to demonstrate the safety of the resultant complex are major challenges that the current application does not adequately address.

Proposal 08-038
Early Lung Cancer Detection Alliance (ELCDA): Integrated Breath Analysis and Imaging Techniques for Early Lung Cancer Detection
Cleveland Clinic Foundation

Proposal Summary:

In this proposal, the Cleveland Clinic, Riverain Medical, BreathSensing Inc., the Ohio Tobacco Treatment Clinics and SRI International, are requesting funds to develop early-stage lung cancer diagnostics. Two companies (ChemSensing and BreathSensing) have committed to moving to Ohio if the proposal is funded. The applicants aim to leverage prior Third Frontier investment in x-ray based lung cancer detection to develop breath-sensing approaches to this diagnostic area.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,149,438	\$5,283,636
Capital Funds	\$850,000	\$0
Subtotal	\$4,999,438	\$5,283,636
TOTAL	\$10,283,074	

Detailed Review:

- **Level of Scientific Merit**

The state of Ohio Third Frontier Commission has previously provided funding for an Early Lung Disease Detection Alliance (ELDDA) grant focused on developing, testing, and commercializing Computer Aided Detection (CAD) chest x-ray of lung nodules. The current application proposes working with SRI International, Inc. (SRI) and ChemSensing (CSI) – BreathSensing (BSI) to develop breath analysis technologies for commercial lung cancer detection products. The scientific merit of the proposal was difficult to judge because the proposal’s experimental design was not adequately detailed. The application calls for recruiting subject populations from many different subpopulations in an effort to determine differences between these subpopulations and lung cancer patients. Inadequate information is provided about the recruitment strategy, number of subjects per population, rationale behind the subpopulation designations, and the statistical data analysis models to be used to differentiate the data obtained from these subpopulations and the lung cancer patients. Additionally, there is no discussion of institutional review board (IRB) requirements. Although the applicants state that a combined analysis using both the CAD modality and the breath analysis will be pursued for improved diagnosis of lung cancer, no discussion is given in the proposal as to the advantage of detecting the presence of lung cancer by both methods. No discussion is given of how the two results will be combined to indicate a positive diagnosis. What does it mean if one method indicates the presence of lung cancer and the other one does not? What selection criteria will determine which detection method provides the correct answer? There is no discussion of interfering breath volatile compounds that may originate from sources such as recently ingested foods or drink or other possible exposures. Little information is provided on the analytical statistical plan for advancing the breath analysis system other than improving the collection system. The nature of the chemical indicator for the array “spots” is unclear – what metalloporphyrins will be used?

What other compounds? What is the evidence that these will be adequate to screen for lung cancer? Is a 36-element array large enough to get specificity? In short, a great deal more detail would be needed to judge this proposal's chances of success.

- **Commercial Potential**

The commercial potential of the breath analysis is probably overestimated. Breath analysis is not yet acceptable by clinicians, at least partially because reproducibility among individuals and groups is unproven at this stage. Market readiness is not addressed by the proposers, and a plan to address this challenge is not presented.

- **Leadership and Management Quality**

Dr. Phillips is proposed as the Administrative Principal Investigator and Dr. Mazzone as the Technical Principal Investigator, despite instructions in the RFP that these roles be filled by a single individual. The leadership and management, however, appear to be adequate.

- **Impact on Ohio**

While the RFP emphasizes the importance of linking proposed research to previous Third Frontier Project investments, continuation of funded projects is not allowed. This project claims to build on the currently funded ELCDA project, adding breath analysis as a complementary approach. The committee believed that it would be equally valid to consider this project a continuation of the ELCDA project and therefore, possibly not appropriate for additional investment. Two companies have committed to relocating to Ohio if the project is funded, which will add jobs and revenue to the state. However, given the committee's lack of enthusiasm about the scientific merit and commercial prospects of the proposed products, the commercial impact is likely to be small.

- **Budget and Cost Share**

The budget may be reasonable to achieve the project objectives but this not definite since the magnitude of all of the subpopulations is unclear. Adequate cost share has been committed to the project.

Review Summary:

The scientific merit of this proposal was judged weak because the experimental design was unclear as presented, particularly for the recruitment and selection of the subpopulations for testing and the statistical data analysis for subpopulation discrimination. Reviewers were also unconvinced that the proposed sensor array could actually detect incipient lung cancer. Overall, the commercialization plan, while well written, probably overestimates commercial impact and does not adequately address the potential lack of wide-spread acceptance of breath analysis by the clinical community.

Proposal 08-041
Clinical Development of an Adult Stem Cell Product for Treatment of
Ischemic Stroke
Athersys, Inc.

Proposal Summary:

This proposal from Athersys, Inc., a biotech company that has licensed university technology for multipotent adult progenitor cells (MAPC) derived from adult bone marrow, aims to extend the application of these cells from graft vs. host disease (GVHD) and cardiac applications (for which it previously received similar funding) to

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,637,297	\$3,848,699
Capital Funds	\$466,000	\$283,000
Subtotal	\$4,103,297	\$4,131,699
TOTAL	\$8,234,996	

treatment of stroke using IV administration of cells. There is in vivo efficacy data in a rat model and pre-investigational new drug (IND) discussions with FDA to determine necessary components for IND application. The company has substantial venture funding to execute the initiation of product scale up and stroke clinical development program. The funding request is aimed at determining the scientific mechanism of action and the safety profile of this novel approach to treatment of stroke. The specific project goals for this submission are: 1) Submit, gain approval and successfully execute a Phase I clinical safety study for delivery of MultiStem in stroke; 2) Determine the mechanism(s) of therapeutic benefit the MultiStem cellular product exerts in in vitro ischemic injury experiments; 3) Validate mechanism(s) of benefit using in vivo animal ischemic stroke experiments including generation of novel imaging technologies; 4) perform GLP safety and efficacy experiments using cells and reagents defining a mechanism of therapeutic benefit, sufficient to submit a Phase II Safety Protocol for using MultiStem to treat acute ischemic stroke in humans.

Detailed Review:

- **Level of Scientific Merit**

Athersys, Inc. has developed a method for production of MAPCs that has been approved by the FDA for clinical use. This is critically important for both patient safety and from a commercial use perspective. These cells are notoriously difficult to maintain in vitro, but apparently Athersys has developed stringent conditions that keeps the cells stable which is assessed using a variety of gene and protein expression profiles. The culturing system is important in itself. The main concern with this proposal is not so much with the scientific merit of the proposed cells, but rather with their application in stroke. There have been some reports of tumors in the brain reported in animals treated with these cells so the imaging/tracking studies would need to be taken out longer to validate safety. Studies showing karyotypic stability and lack of tumor development in Nude mouse tumor models support their safety for use in transplantation, and other mice experiments show efficacy of these cells in reducing symptoms in stroke models. However, it would

seem to be more appropriate to go from mouse models to a large mammal, such as the non-human primate or pig, prior to injecting these into human stroke patients. A major concern is that it will be hard to dissect therapeutic effects of MAPC transplantation compared to drugs and treatments given simultaneously to the stroke patients. The vast majority of these cells die after injection into animals. It is critical to follow where these cells end up, in what tissues they reside, what structures they contribute to, and the like. It is also important to determine what trophic factors are being produced that result in therapeutic effectiveness.

- **Commercial Potential**

Athersys has a strong record for getting a challenging cell therapy into a phase I trial for other applications. They are one of the leaders in application of cell therapy to CNS disorders. The functional restorative approach in treatment of sub-acute stroke is different from previously failed cytoprotective approaches, as strong in vivo efficacy has been established in mouse models. Mechanistic studies will provide important insights that will have an impact on both the scientific and commercial communities. The patient population that could benefit from the proposed technology is large and has few options available today. However, it is unclear what the cells are actually doing after transplantation. The committee also feels that a large animal model may be imperative prior to human patient trials.

- **Leadership and Management Quality**

Leadership to date has successfully driven and executed business plans as demonstrated by the clear pathway to the clinic that has been delineated and combined with mechanistic studies. The management and leadership team are very strong, and they have recruited a number of staff and secured substantial funding for the company. The combination of strong business experience with scientific expertise is excellent.

- **Impact on Ohio**

The group's cell therapy efforts are in part a result of prior BRCP stem cell funding, which has been leveraged to translate similar cell therapy to GVHD and cardiac clinical applications, creating a history of success with this funding mechanism. Because of the potentially high impact and large stroke market, there is potential for spinning out the technology just for stroke, which would create a new entity. The imaging work is based in Ohio and would help build that small company since the technology will be useful for other companies engaged in cell therapy.

- **Budget and Cost Share**

BioInvision will contribute about a million dollars (via an STTR grant). There are significant costs such as a confocal for 300K in the first year. However, overall the budget is reasonable.

Review Summary:

This is a well written proposal from a company that has demonstrated that it has developed a stringent cell production method to reproducibly generate large numbers of MAPCs which appear to be stable based on genetic and proteomic analyses. FDA approval of these cells for a human clinical trial will help in moving this towards a clinical trial. The combination of management and scientific work proposed will work in a complementary fashion to move the cell therapy to stroke applications. However, serious scientific concerns remain about mode of action, efficacy in a large-animal stroke model, and the long term safety of MAPCs within the brain. Furthermore, it is anticipated that demonstrating efficacy in humans will be exceptionally difficult, making the path to commercialization lengthy. Overall, the committee agreed that the number of hurdles facing this particular application make it inconsistent with the timelines expected in the BRC program.

Proposal 08-043
Development and Commercialization of Antibody Based Products
The Research Institute at Nationwide Children’s Hospital

Proposal Summary:

This proposal seeks to establish collaboration between Ohio-based private industry, academic institutions, and research institutions to discover, develop and commercialize antibody-based products. Monoclonal antibodies are currently marketed as diagnostic and therapeutic agents and comprise a significant portion of the large-molecule market. The requisite technology is well established in this area and the vision of this proposal is to become a leader in recognizing new biomedical applications of monoclonal antibodies and rapidly discovering and developing new antibody therapeutics. Competitive advantage is seen to be derived from combining a robust screening, lead, and candidate development process pipeline with a business development arm.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,885,409	\$4,631,760
Capital Funds	101,870	356,000
Subtotal	\$4,987,280	\$4,987,760
TOTAL	\$9,975,040	

Detailed Review:

- **Level of Scientific Merit**

The merit of this proposal is derived not so much from innovative science (the respective technologies are established and practiced at many institutions), but the sequential organization of the core facilities within the NuImmune pipeline.

- **Commercial Potential**

The committee had little enthusiasm for the commercial potential of the proposed enterprise. The main revenue generator is the diagnosis and therapy of Norovirus. The main commercial application proposed is as a prophylactic for travelers and tourists. Norovirus is seen as a self-limiting disease, so a key question is how much travelers would be willing to pay for the product, and whether cost-of-goods would support a reasonable cost/treatment (\$150). Other MAb therapies are priced on the order of thousands of dollars/dose. In addition, supporting data for the market of existing prophylactic agents in the travel industry were not provided, nor was a detailed examination of NuImmune's freedom to operate with respect to intellectual property. A commercial assessment of the markets for non-typeable haemophilus influenzae (NTHI) and anthrax (aside from a potential DoD grant) was not provided. The proposed business in antibody libraries and screening is small and has the prospect of little growth given existing competitive services and platforms.

- **Leadership and Management Quality**

The lead applicant is well established in virology and has led a small group of researchers in his laboratories. The level of difficulty in leading, managing, and coordinating the organization in this proposal is an order of magnitude higher than that of leading a small research group. Sub-division of the effort into discreet projects with associated leaders along with leaders of the pipeline core activities is sound.

- **Impact on Ohio**

The impact on Ohio could be substantial if a new significant diagnostic or therapy would emerge from this program. The impact of the library and screen business would be small.

- **Budget and Cost Share**

Both are reasonable for this plan.

Review Summary:

There is a lack of enthusiasm for the commercial promise and market potential of the antibody-based products developed in the three projects described in this application. In addition, lack of differentiation of the services to be provided by NuImmune and the modest growth potential of these services represent significant challenges to achieving a sustainable business.

Proposal 08-044
Bridging the Valley of Death: Enabling Commercialization of New Therapeutics
PrimeDP, LLC

Proposal Summary:

The goal of this proposal is to support the creation of a management company that will facilitate the translation of low-value, early-stage compounds into high value Phase II clinical trial stage drug candidates for sale or licensing to mid- and large pharmaceutical companies. By arranging for discount services from contract research organizations (CROs) in exchange for equity, the company aims to bring

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,988,003	\$4,988,003
Capital Funds	12,000	23,000
Subtotal	\$5,000,003	\$5,000,003
TOTAL	\$10,000,006	

compounds from discovery to Phase I clinical trials at a cost of \$2 to \$5 million per compound, which can then be sold for \$10 to \$100 million. Because the CROs are Ohio companies, the proposal would have a beneficial impact on Ohio even if the products are licensed out of state. The investigators believe that the proposed activities will help to overcome the discrepancy of 18% of NIH funding but only 4.3% in venture capital funds going to the Midwest, as success in bridging “the valley of death” would attract further interest from venture capital firms. PrimeDP has developed a portfolio of 4 entities, ranging from minimal risk (a reformulation) to a cancer therapeutic that is at an early stage of development, with three of the four being for topical administration and therefore facing a lower FDA hurdle.

Detailed Review:

- **Level of Scientific Merit**

The lead applicant is a management company as opposed to a scientific company. Alliances have been arranged with four scientific companies. The companies have licensed IP from different sources including Abbott Labs, Procter and Gamble, and Cincinnati Children’s Hospital Medical Center. The various companies and products are:

Akebia Therapeutics: Cincinnati, OH: The IP was licensed from Procter and Gamble. While the lead compound has been shown to stimulate PGK and VEGF expression in cells, the concentrations required for activity are high (uM range). In addition, the absence of proof-of-concept in an animal model for wound healing, and the relatively modest plan to prepare and test an additional 30 analogs, make the probability of having a Phase I asset in the third year low. The structure of the compound is not included in the proposal, making it difficult for the committee to assess the synthetic challenges and understand the SAR strategy.

Bexion Pharmaceuticals, Cincinnati, OH: The IP was licensed from Cincinnati Children’s Hospital Medical Center. Bexion currently has an NIH SBIR/STTR

grant. A key question here is whether there are data to support the reproducible preparation and scale-up of the nanovesicles.

Pep Therapeutics: The IP was licensed from Abbott Laboratories. The physical location of this company is not clear though it was stated that they may establish operations in Cincinnati or Columbus. Given the number of products on the market to prevent/treat sunburn, the commercial assessment should include proposed points of differentiation which will make this product the preferred product. In addition the cost-of-goods for ADPR will be substantially higher for ingredients in existing products. The business case would have been strengthened by the inclusion of estimates of market penetration and expected profit margins.

RxDino, LLC: The project seeks to reformulate current OTC products for use in dermatitis, specifically (hydrocortisone-dihydroepiandrosterone, HCT-DHEA). The physical location of this company is not clear although it was stated that they may establish a physical laboratory in Cincinnati. Given that this product is a combination of two existing marketed products, it is unlikely that any sort of marketing exclusivity could be obtained and hence profitability would be linked to a compelling (and expensive) marketing strategy. Such a plan is absent from the proposal.

There is minimal innovation involved in the proposed projects. The level of scientific merit of the proposal was deemed moderate. It is not clear how funding this proposal will lead to increased scientific innovation; the proposal's aim is to build an organizational structure to facilitate commercialization in general.

- **Commercial Potential**

Prime DP lists eight commercial challenges that it expects to meet. Only the first three of these challenges: marketing novel therapeutics to established pharmaceutical companies; enabling commercialization of therapeutic products based on intellectual property generated in Ohio; and providing an experienced management team to handle drug development projects, have significant value. The rationale for the other five challenges is weak. The commercial plan appears to be to use the funds from the BRCP to advance the current portfolio of candidates in the expectation that at least one will be successful, thus funding the development of further candidates. The proposal emphasizes that its innovative equity arrangements with the CROs are a key strength of the plan, but these arrangements are not described and the letters of commitment from the companies contain no details of the special relationship they are committing to.

The commercialization plans for the individual projects appear reasonable.

- **Leadership and Management Quality**

PrimeDP has excellent leadership (including the Advisory Board) and a sound management plan. They have experience in drug development and therefore know the challenges ahead and ways to overcome them. Even so, the business model is

inadequately described to be able to evaluate this team's ability to succeed in this particular venture.

- **Impact on Ohio**

The CROs already exist in Ohio. PrimeDP will serve as middle-man between the identified discovery entities and the CROs. A major unresolved issue is the possibility of the discovery company having alliances with CROs outside of Ohio. How will PrimeDP handle such situations? There is no focus on any disease and therefore no development of a center of excellence in any disease area. Once the NCE has been sold or licensed out, the discovery company might actually fold up or be dismantled by the acquiring company. Nothing appears to be in place to prevent such an outcome. PrimeDP has negotiated "in house" prices with Ohio's CROs. Does this mean guaranteed lowest prices as compared to anywhere within the US? How do these compare with academic prices, for example? Without greater detail on the nature of the arrangements between PrimeDP and these CRO's, the impact on Ohio is difficult to assess.

- **Budget and Cost Share**

The funds requested are for hiring PrimeDP personnel and payment of services to help move the projects forward. It is not clear how many personnel will be hired by each of the collaborating four companies as a result of funding the proposal.

Review Summary:

The lack of coherence and focus of the "product" portfolio is troubling. The SapC-lipid nanovesicle looks to be the most promising and certainly addresses an unmet medical need. The challenge associated with bringing the wound treatment to the investigational new drug (IND) stage given the current state of development has been addressed above. The two topicals leave many questions unanswered from a business perspective. It is true that many NCEs are not able to cross "the valley of death" to realize their full potentials. So, there is a need for the gap that PrimeDP is trying to fill. Also, the idea of bringing Ohio's CROs together and negotiating in a coordinated way on behalf of the client companies to get a better deal is an interesting one, and the CROs may have incentive to provide a discount in exchange for a stake in the products' success. The project, however, is basically to set up a management company and overall, the level of scientific innovation is low. Since the goal is to move the products to certain level and then sell them to mid- to big-pharma, the number of scientific and manufacturing jobs that would be created in Ohio is unclear.

Proposal 08-047
Platform for Antiviral Resistance Testing and Vaccine Development
Diagnostic Hybrids Inc.

Proposal Summary:

Diagnostic Hybrids, Inc. (DH) is a private, Athens, Ohio-based company focused on delivering diagnostics tools to clinical virology laboratories, providing reagents for known cultivable viruses such as herpes, respiratory viruses and enteroviruses. Diagnostic Hybrids proposes to work with researchers at Case Western Reserve University (CWRU) to further develop a yeast-based cloning system for viral diagnostics/treatment monitoring and to market these assays to hospitals, clinicians and pharmaceutical companies.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,474,500	\$6,248,649
Capital Funds	\$525,500	\$787,500
Subtotal	\$5,000,000	\$7,036,149
TOTAL	\$12,036,149	

Detailed Review:

- **Level of Scientific Merit**

The scientific merit of this application is high. While there are many tests for identification of HIV and HCV infection, there are few platforms that can readily identify or track the origin of drug resistance. The yeast-based cloning system offers significant promise as a model for assay and diagnosis of genetic variation of disease. The identified areas of application of HIV, HCV and influenza (in that order of priority) are significant and appropriate targets for this technology.

One concern about the underlying science is whether the yeast expression system presents an accurate model for each disease. The proposal however, does identify a variety of methods for validation, using historical clinical data and comparison to competitive products.

- **Commercial Potential**

The committee had some skepticism about the commercial potential of two of the three programs in the Diagnostic Hybrids consortium proposal. Specifically, the programs for HCV and influenza vaccines are likely to require nearly a decade of R&D rather than the 2-3 year timeline proposed. While there may be some value in an influenza research platform, there is very low probability of commercial success with a vaccine in the medium term – and the applicants did not address the fact that there are many well-established competitors in vaccine manufacturing and significant barriers to entry in that market. The proposal’s explanation of the value of an influenza library in speeding the delivery of influenza vaccines in the event of a pandemic was unconvincing.

However, the HIV application does hold significant and immediate value as a genotyping tool for viral identification. There is real near-term need for a fast, inexpensive platform for HIV genotyping, particularly in monitoring for and determining the origins of drug resistance. This would be of tremendous value to doctors and patients, who would benefit from a more rational drug therapy for the “when to switch” cocktail strategy. To their credit, the DH consortium lists the HIV program as its primary focus, with rational (albeit highly ambitious) plans for revenue generation and job creation in the service business model. DH has already demonstrated a strong commercial interest, along with good prospective partners already in the service and customer sectors.

DH may be able to claim significant market share of what is currently a limited and expensive process. The application indicates that the DH diagnostic would cost 25% of the individual assays offered by current competitors, and would replace three separate assays with one for further cost savings.

The yeast-based expression system appears to hold significant promise as a screening and diagnostics platform for infectious disease. DH is a well-established and profitable enterprise, and seems well-positioned to exploit the clinical diagnostics business model. The clinical service business leverages existing expertise within the company and provides a fast (demonstrated) source of revenue. CLIA certification will be required and is outlined in this proposal.

By identifying the molecular origin of drug resistance, there also is benefit for clinical drug development, ably demonstrated by the \$300+K revenue for their early pharma partnerships. There was some concern whether DH intended to pursue drug development itself – for the scope of this application; the reviewers felt strongly that it was not appropriate for DH to anticipate an internal drug development strategy.

A final concern is the IP surrounding the hepatitis C application. While IP has been developed for the yeast-based assays, the underlying Chiron/Novartis position needs to be clarified to determine whether they maintain a blocking position. A better IP assessment for the HCV application would have strengthened this part of the proposal.

- **Leadership and Management Quality**

This application’s leadership has demonstrated proven expertise in both research and business sectors.

- **Impact on Ohio**

The development of a clinical service center could generate significant business for the state of Ohio.

- **Budget and Cost Share**

Budgets and cost share is reasonably split between the academic and business partnership.

Review Summary:

For the impact of the HIV genotyping platform alone, the committee believes that this proposal is consistent with the goals of the BRCP RFP. However, given that near-term commercialization, not merely platform development and interim revenue generation, are the stated goals of the program, the committee does not believe that the HCV or influenza platforms meet the program's criteria. The committee recommends that the state consider working with the applicant to revise the proposal to pursue only the HIV application.

Proposal 08-048
Ohio Consortium for Metabonomics
Frantz BioMarkers, LLC

Proposal Summary:

This proposal seeks funding to establish the Ohio Consortium for Metabonomics using instrumentation (namely NMR spectroscopy, mass spectrometry and MALDI-TOF) to detect small, rare biologic molecules in order to diagnose and track diseases. In the first phase, funds would support the launch of a diagnostic test for ovarian cancer discovered by Frantz

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,514,819	\$9,140,639
Capital Funds	380,000	0
Subtotal	\$4,894,819	\$9,140,639
TOTAL	\$14,035,458	

BioMarkers and the building out of a reference laboratory. The second phase is focused on discovering, validating and commercializing additional biomarkers from a supply of patient biological samples provided by clinical partners.

Detailed Review:

- **Level of Scientific Merit**

The scientific objectives of the proposal are not entirely original and innovative—the use of instrumentation to detect rare biologic molecules is not novel. The project, however, is scientifically and technologically feasible and the proposal lays out its design and framework adequately.

- **Commercial Potential**

The first planned product for ovarian cancer could be promising having shown some initial proof of principle in patient plasma samples. A more detailed commercialization plan, however, would be helpful to assess, for example, whether a charge of \$125 per sample is reasonable or viable. It was also difficult to assess whether the ovarian cancer product would have a sustainable competitive advantage versus other technologies and diagnostics that are currently in development. The committee was less convinced of the merit of the follow-on potential products identified by Frantz BioMarkers with their clinical partners. Biomarker targets for cardiovascular disease and Crohn’s disease are broad and will likely have little impact on changing medical standards of care either medically or surgically; biomarker targets for necrotizing enterocolitis and Kawasaki disease may not be very useful without the availability of proven disease modifying therapeutics. A stand-alone esoteric metabonomic-based reference laboratory may be feasible, but a more detailed proposal of this would be needed for the committee to evaluate its merit.

- **Leadership and Management Quality**

The lead applicant, Frantz BioMarkers, led by its founder Mark Frantz, has had good experience executing scientific and business ventures. However, the level of difficulty in commercializing a new diagnostic service and transitioning the company to a CLIA-certified laboratory is much higher.

- **Impact on Ohio**

The impact on Ohio in terms of job creation and new sales could be large if a new diagnostic service is adopted as standard of care and a large reference laboratory is successfully established. However, the committee deems the likelihood of this as low.

- **Budget and Cost Share**

Both are reasonable for this plan.

Review Summary:

While the scientific objectives of the plan are not entirely original, the initial plan to commercialize a product for ovarian cancer could be promising. The follow-on products appear less exciting in terms of commercial potential. A more robust commercialization plan would be helpful and a proposal detailing progress on the ovarian cancer product or proposing a stand-alone metabonomic based reference laboratory might garner more enthusiasm.

Proposal 08-049
Breath Analysis: Targeted Sensor Development and Commercialization for Health
Care Diagnostics
The Cleveland Clinic Foundation

Proposal Summary:

The project described in this application is to develop an NO sensor that will enable asthma patients to monitor their asthma at home. The team includes Cleveland Clinic, NASA, Case Western Reserve University, and Ohio State University and strong industry and commercialization collaborators. BRCP funds will be used to support the development and commercialization of existing sensors. The project’s emphasis will be on testing and commercializing sensors already produced in Ohio.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,634,038	\$4,927,964
Capital Funds	149,100	0
Subtotal	\$3,783,138	\$4,927,964
TOTAL	\$8,711,102	

Detailed Review:

- **Level of Scientific Merit**

The proposers plan to use the funds from this effort to re-develop a sensor used in the aerospace industry so that it can be used as a breath chemistry detection device. Overall, the scientific merit of this proposal is acceptable. Furthermore, the very great need for such a device heightened the committee’s enthusiasm for this proposal. The applicants aim to develop a finished device that uses an array of multiple sensors based on “orthogonal” (different) technologies to cancel out confounding, interfering compounds—a major challenge due to the large number of compounds commonly encountered in breath and in the ambient air being inhaled by the asthmatics. Without prejudicing the committee’s overall judgment that this proposal is highly consistent with the goals of the BRCP RFP, there are several “pitfalls” that need to be considered seriously in the development of the technology for efficacious “in-home” use.

- Although the applicants state that the device will measure NO in breath, in reality it will detect NO_x. The presumption is that since NO and not NO₂ is expired by humans, the measurement of NO_x is acceptable. While this may be true in many ambient environments where levels of ambient NO_x are low, measuring minute differences in NO_x in breath against a high background may not be possible. The applicants have considered some solutions to this problem but more thought should be given to this potential pitfall.
- The potential poisoning of the catalyst from other volatile breath components needs to be considered more carefully. For this device to meet the proposed purpose, it must be useable by the asthmatic whenever necessary without preparation to eliminate confounding compounds in their breath from eating, drinking, teeth brushing, etc. Sulfur-containing compounds could be present in the breath and the inflammatory response during asthma attacks releases lipid peroxidation-derived compounds, both of which could poison the catalyst.

- Maintaining calibration of the system in the home settings needs to be seriously considered.
- The safety of the heated sensors needs to be considered carefully.
- A more detailed plan for the home testing (and clinical testing) phase of development is needed; there is no discussion about the number of subjects, the ages or demographics, or other points needed to assess the adequacy of this testing. As evidence of durability, the proposers point to a space-qualified sensor they have developed for the NASA; this may be germane, but details of in-home testing seem sparse.
- The discussion of the difficulties in obtaining approval for clinical testing and FDA approval of the device also would benefit from greater detail. The applicants may be underestimating the length of time that this process will take and its importance.

None of these challenges appear to be technically insurmountable given the skills of the proposing team. The committee felt that the level of technical risk for the project is acceptable, and that this project is consistent with BRCP goals if the proposers maintain tight focus on solving the practical problems of bringing an NO sensor into the commercial/residential world.

- **Commercial Potential**

The commercial potential of this device is very high. The ability to measure inflammation via NO with a handheld device at home – one that can replace the peak flow meter – is considered to be an important step in asthma treatment. However, the committee is concerned that the team lacks the business expertise to carry this device through the complex process of commercialization. The committee recommends that, should the state decide to fund this project, the group be required to recruit a business manager to guide the team in the realization of product development and commercialization.

- **Leadership and Management Quality**

One of the strongest attributes of this proposal is the enthusiasm and apparent commitment of the applicants. The Leadership and Management Plans for the scientific portions appear to be adequate for the successful completion of this project. However, as discussed above, the business plan as presented is weak. The project would benefit by including an experienced business manager.

- **Impact on Ohio**

The potential impact on Ohio for additional revenues and jobs will be quite significant if this project is successful.

- **Budget and Cost Share**

The budget and cost share are adequate for the proposed effort. A large portion of the cost share is “in cash”, which is preferable based on the RFP.

Review Summary:

The project described in this proposal is to turn a nitric oxide sensor developed for the aerospace industry into one that will enable asthma patients to monitor exhaled NO at home. The market for such a device could be substantial and there are currently no competing products. The committee noted several technical challenges that will need to be addressed, and would have preferred to see a more detailed plan for how the device will be tested in homes and clinically, and for achieving regulatory approval. Most importantly, the committee believes that the success of this promising proposal depends on the inclusion of an experienced business leader.

However, the potential impact on Ohio in terms of additional revenues and jobs, and on the comfort and health of millions of people around the world are so significant if this project is successful that the committee concluded that this project substantially meets the goals of the BRC program.

Proposal 08-051
Novel Detection and Treatment for Cancer Using Specific Targets and Labels
Enlyton, Ltd.

Proposal Summary:

This application, submitted by Enlyton, Ltd., a new company founded by faculty members from the Ohio State University's Schools of Medicine, Engineering and Pharmacy, aims to develop commercial applications of a monoclonal antibody, ATA-1, which Enlyton licensed from the Public Health Service. ATA-1 is proposed as a marker for colorectal and other adenocarcinoma cancers. The three proposed applications are: development of a cancer-specific imaging agent for use with positron emission tomography (PET) to improve cancer detection; development of fluorescent and other non-radioisotope ATA-1 markers for use in determining tumor margins and detecting small tumors; and assessing other members of the ATA-1 family of monoclonal antibodies for cancer imaging and detection applications.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$2,154,997	\$2,154,997
Capital Funds	\$0	\$0
Subtotal	\$2,154,997	\$2,154,997
TOTAL	\$4,309,994	

Detailed review:

- **Level of Scientific Merit**

The project is innovative, in that it would enable both late and early stage tumor detection, including real-time detection during surgery. The group plans to take several approaches—from radiolabeled iodine to organic dyes (fluorescent molecular targets) to gold nanoparticles being conjugated to ATA-1 to development of a hand-held fluorescent probe—and this increases the possibility that something positive will emerge from the work. However, it also means that the project lacks focus. The evidence that the conjugates will target TAG-72 (tumor-associated-glycoprotein 72) in vivo is weak. In general, while the science is promising, it is still at a stage requiring additional research and development before commercialization – an observation shared even by the applicants.

- **Commercial Potential**

There is no prototype for the hand held probe or margin analyzer. Even the 124-I conjugated to ATA-1 that is proposed as an immediate commercialization prospect is no where near such a point, as in vivo parameters (pharmacokinetic, immunogenic, stability and toxicity profiles) are yet to be determined and adverse results on any of these could derail the project. Furthermore, it is possible that labeled antibody could be considered as a new chemical entity and therefore could require further testing even if ATA-1 itself has already undergone all the tests.

Finally, the work is almost entirely ATA-1 dependent. Without success with that molecule, no near-term commercialization prospects remain. There is a great deal promise in this project, and it is possible that it will be appropriate for the BRCP funding mechanisms when the technologies being pursued have reached a considerably more advanced stage.

- **Leadership and Management Quality**

Investigators are highly qualified and have access to excellent facilities.

- **Impact on Ohio**

A successful execution of the project could have a significant impact on cancer treatment and could result in substantial financial return, if not a large number of jobs..

- **Budget and Cost Share**

No concerns were raised about the budget and cost share.

Review Summary:

The application presents interesting and promising science, with the prospects for commercialization being considerably longer than a timeframe consistent with BRCP goals. The project's major reliance on a single molecule increases the risk that any of the early steps in the process of demonstrating safety and efficacy could put the entire project at risk.

Proposal 08-053
Unique Program to Repurpose Drugs for Therapeutics Areas Linked to
Ion Channels
ChanTest Corporation

Proposal Summary:

This proposal seeks funding to establish a pharmaceutical company to develop drugs for the treatment of ion channel-linked diseases utilizing ChanTest’s high-throughput screening ion channel assays through the spin out company CT Pharm. The strategy is to lower drug development risk through repurposing drugs already known to be safe. CT-1 and CT-2 are the lead drug programs; 2-3 additional new drugs are anticipated to be added annually to the pipeline. CT Pharm will partner with ChanTest, ANALIZA and CD3 for drug development.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,799,656	\$2,872,076
Capital Funds	115,000	\$1,175,000
Subtotal	\$3,914,656	\$4,047,076
TOTAL	\$7,961,732	

Detailed Review:

- **Level of Scientific Merit**

The scientific objectives of the proposal are not entirely original and innovative—the targeting of ion based channel drugs is not novel. The project, however, is scientifically and technologically feasible and the proposal lays out its design and framework adequately.

- **Commercial Potential**

While the markets for CT-1 and CT-2 for atrial fibrillation/atrial flutter are potentially large and described adequately in the proposal, it is very difficult to assess the true commercial potential and viability of CT-1 and CT-2 without having more information about these particular compounds. A more detailed commercialization plan for the two products detailing the specific clinical and regulatory pathways, the detailed intellectual property strategy (since composition of matter patents are not likely to be in effect), the specific clinical selling proposition, the reimbursement strategy, and the competitive landscape for similar therapeutics both in medical and surgical development would have been very helpful. There is potential value in future pipeline drugs, but the near term commercialization value appears largely to reside with CT-1 and CT-2 and cannot be properly assessed with the level of detail provided in the application.

- **Leadership and Management Quality**

The lead applicant, CT Pharm/ChanTest, has had good experience executing scientific and business ventures; it is a profitable business with revenues exceeding \$10 million. However, more detail would be helpful regarding the applicant’s ability to run clinical

drug development and the management/ structure of the spin-out to assure that CT Pharm is not just expanding research activities with ChanTest.

- **Impact on Ohio**

The impact on Ohio in terms of job creation and new sales could be large if CT-1 or CT-2 gets approved and the company runs its own sales and marketing efforts. However, it is probably more likely that, if successful, CT Pharm would partner with or be acquired by a larger corporation, which could decrease the direct ROI for the state of Ohio.

- **Budget and Cost Share**

Both are reasonable for this plan.

Review Summary:

While the scientific objectives of the plan are not entirely original, the initial plan to develop CT-1 and CT-2 could be promising. The follow-on platform appears less exciting in terms of near term commercial potential. A more robust commercialization plan providing greater detail on CT-1 and CT-2 would be helpful, a future application detailing advances in the two drugs' clinical development could be more enthusiastically received.

Proposal 08-054
Commercialization of Cartilage Regenerative Technology
Ohio State University College of Veterinary Medicine

Proposal Summary:

The goal of this proposal is to commercialize a novel regenerative cartilage cell therapy (Chondron™) to restore injured cartilage as a treatment for joint disease. The patient’s own cells are harvested, expanded in culture, combined with a biodegradable matrix and re-injected into the affected joint. The proposal team includes SewonCellontech Co. (Seoul, Korea) and the Ohio State University and plans establish a new company in the state of Ohio with production and distribution rights first for the companion animal market and eventually the human market.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$2,399,067	\$1,501,446
Capital Funds	\$100,000	\$1,000,000
Subtotal	\$2,499,067	\$2,501,446
TOTAL	\$5,000,513	

Detailed Review:

- **Level of Scientific Merit**

The proposal provides inadequate justification for the scientific superiority of the proposed technique. There is significant controversy about the efficacy of cell therapies compared to standard surgical therapies such as microfracture that show equivalent results with a much cheaper repair method, even after 5 years. The crux of the authors’ argument in favor of their approach is that there are problems associated with the periosteal flap used in current cell therapies. There are indeed problems with the periosteal flap and that is why Genzyme purchased Verigen in Europe, where a collagen membrane is used instead of the periosteal flap.

Although the therapy is described as injectable, it is unclear how injection will be carried out – for example, the problem of gravity must be overcome when injecting liquid into a liquid environment. Will this require a dry arthroscopy and how will this technique fit into current clinical practice? No evidence is presented that the fibrin matrix is adequate to hold the cells in place for repair in the joint environment. This is particularly a challenge in the horse model where the joint must almost immediately bear weight.

The clinical efficacy data (and even the data from the preclinical dog study), are not interpretable as the control data are not included. Particularly in the horse study, it is not clear how the cells will be tracked or how they will be held in place in a mechanically-challenging environment.

Finally, in the horse study, the control used is an untreated defect. Clinically, however, the procedure likely will be evaluated against a microfracture control and this should therefore be included in the horse study. Also, the fibrin adhesive alone may have some

biological activity (particularly if there is any subchondral stimulation); it is important to establish which element is responsible for the tissue repair.

A minor point, but one that may be a source of confusion is the name of the product, Chondron. In the literature, a chondron is a chondrocyte (or small cluster) with their cell associated matrix, not an isolated or expanded chondrocyte cell population.

- **Commercial Potential**

There are a number of missing elements in the analysis of the market. For example, the next company that is poised to translate cartilage cell therapies in the US, Tigenix, is not discussed. Tigenix has a strong position in Europe and now has a manufacturing facility in the US. There are other competitors introducing non-cell-based, injectable therapies, including Biosyntec. The competitive marketplace therefore has not been thoroughly evaluated. The other aspects of commercialization, cell expansion for example, are well established and therefore low risk commercialization prospects. The competitive landscape of Europe has helped to keep prices lower for the autologous cell therapies so there is significant need in the US for a lower-priced product.

- **Leadership and Management Quality**

The group has strong experience in the vet community but there is a lack in commercialization, product development, and business experience.

- **Impact on Ohio**

The proposed new company and technology, if successfully translated to practice, would benefit Ohio and bring new jobs and technologies to the state.

- **Budget and Cost Share**

The budget includes cost sharing provided by the Korean counterpart that will provide the cell expansion technology capabilities. The revenue estimates appear ambitious and may be unrealistic.

Review Summary:

This proposal addresses a clinically significant target, cartilage repair, which has a potentially large market. The proposal background is poorly written and the sole justification of the product resting on overcoming problems with the periosteal flap is not adequate. The cell expansion technology is low risk since it is being licensed from a Korean company. The committee was not provided adequate information to be convinced of the ability of the fibrin adhesive to hold cells in place, particularly in the large animal studies, and particularly when implanted in a wet environment which can cause further challenges. This potential lack in efficacy in keeping the cells in place at the defect would seriously diminish the product's success in the projected the initial market for horses.

Proposal 08-055
Therapeutic DNA Nanoparticles and Molecular Imaging (TDNMI)
Case Western Reserve University

Proposal Summary:

This consortium is comprised of individuals from Case Western Reserve University, University Hospitals of Cleveland, Copernicus Therapeutics, Polgenix and a new company, Akrotome Imaging. The application includes three complementary activities: development of nanoparticles for treatment of cystic fibrosis and retinitis pigmentosa; commercialization of a two-photon ophthalmoscope for early detection of retinal disease; and development of contrast agents for the detection of clean margins during breast cancer surgery.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,791,270	\$3,966,689
Capital Funds	\$185,419	\$10,000
Subtotal	\$3,976,689	\$3,976,689
TOTAL	\$7,953,378	

Detailed Review:

- **Level of Scientific Merit**

The first aim is to develop novel therapeutic nanoparticles to treat cystic fibrosis and retinitis pigmentosa. The preliminary data is convincing, showing 95% efficiency in getting DNA into retinal cells and 30-50% efficiency in lung cells. In the first human trials, the treatment was well tolerated and corrected the chloride channel defect in 8 out of 12 subjects. The use of non-viral vectors with such high efficiency is exciting. The nanoparticles are very small, from 8-25nm, and either use lineage specific promoters or nucleolin to target them to the nucleus. Due to the small size and effective and rapid nuclear transfer, initial studies suggest the nanoparticles are non-immunogenic. A system for larger-scale production has been developed that can generate 1 gram of the DNA formulation in an afternoon, and the particles are very stable in solution. The preliminary data are excellent, and the scientific rationale is quite strong. Preliminary data is provided for each of the major commercialization goals. The technical approach is carefully broken down into reasonable objectives, and these would appear to be obtainable in the time frame proposed. The proposal reflects a realistic understanding of the time needed for and complexity of the experiments proposed.

The second aim is to develop a two-photon ophthalmoscope that can be used to image retinal cells in vivo. The goal is to detect and analyze cells that are apoptosing (committing cell suicide), an early sign of retinal disease. The scope is based on the scanning laser ophthalmoscopes, and preliminary data is provided showing real-time visualization of retinosomes within an intact animal eye. The preliminary data again look very promising, and the approach, the equipment, and the goals are very clearly and realistically defined. The second part of this aim proposes to assess two-photon microscopy for its ability to visualize retinoid cycle changes in normal and knock-out mice. Again the preliminary data is good, and the descriptions of the scientific basis clear. This has a great deal of potential, as it will allow in vivo monitoring of both retinal health and of response to drug treatments (thus complementing Aim 1).

The final aim is to develop contrast agents to detect clean margins in breast lumpectomy tissue. Clean margins reduce tumor recurrence rate and being able to determine margins in real-time can allow surgeons to remove as little breast tissue as possible. Improved speed of pathologic examination is very important, as it means the patients are still in the operating room when the biopsy material is analyzed. Infrared detection will enable quick analysis without dimming the room lights, and the entire examination should take no more than 15 minutes. The preliminary data are very compelling, and the potential marketability of this clear and fast approach for detecting cancer cells in tissue immediately ex vivo is large.

- **Commercial Potential**

The use of non-viral vectors to bring genetic material to specified cells within tissues with such high efficiency has a great deal of clinical and commercial potential. It appears that the group's patents on the nanoparticles extend to the year 2028, which should protect their intellectual property. The two-photon ophthalmoscope is being developed by Polgenix, who is working with several instrument manufacturers. They have a prototype and are working towards commercialization in 2010. While each scope will be expensive, it has a good deal of potential as a diagnostic tool but even more importantly as a means for analyzing efficacy of drugs in altering retinal health. The ability to assess tumor margins for breast cancer patients is hugely important, as it will allow the surgeons to immediately assess successful removal of the breast cancer. As two of the three aims are instrumentation and not treatments, these ventures should be commercializable relatively quickly. The proposed aims, if achieved, have the potential to impact the quality of health care and change the practice of medicine.

- **Leadership and Management Quality**

The leadership team includes members with very strong science and medicine backgrounds and a good track record of successful completion of research in all the areas included in the proposal: imaging, nanoparticle preparation and gene therapy. The scientists appear to be well supported by a commercialization partnership committee that will help with commercialization strategy, IP management, strategic planning and so forth. The scientific advisory board will help with review and evaluation of the research projects. An executive committee will monitor progress on all aims, and includes two individuals who are not directly involved in any of the research.

- **Impact on Ohio**

The potential impact on Ohio for additional revenues and jobs is significant.

- **Budget and Cost Share**

These seem to be reasonable.

Review Summary:

This is an extremely well-prepared application and builds on the strength of earlier funding from the state. The strengths of this application are the team of prominent research scientists performing and monitoring these studies and the very clear description of the scientific bases for all their commercialization products. The science is well performed, and both the drawbacks and the positives are clearly enumerated. The studies described in this proposal have a very strong potential for successful completion and commercialization.

Proposal 08-056
Ohio Restoration Innovation Advancement Network
Case Western Reserve University

Proposal Summary:

The goal of the Ohio Restoration Innovation Advancement Network (ORIAN) is to accelerate and expand the commercialization of neurostimulation devices. These technologies have been developed through the Cleveland FES Center, Case Western Reserve University, MetroHealth Medical Center, The Louis Stokes Cleveland VAMC and the Ohio Neurostimulation and Neuromodulation Partnership (ONNP). The proposal incorporates a broad collaboration of researchers and aims to develop stimulation devices to treat several neuromuscular related disorders. The devices would stimulate target muscles with bipolar electrodes driven by a small battery-operated unit buried within skin ‘sacks’ such as the upper torso for the scapula control system. The basic premise is to electrically stimulate denervated muscles to increase their bulk and strength. The group plans to develop, obtain FDA approval, and market devices for four medical indications via a partnership with marketing and manufacturing companies that are based in Ohio. Requested funds would be used to support approximately one-third of the overall estimated required costs for personnel, R&D, unit development, and initial marketing, with about two-thirds of the funding coming from other sources.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,889,212	\$5,077,382
Capital Funds	\$110,788	0
Subtotal	\$5,000,000	\$5,077,382
TOTAL	\$10,077,382	

Detailed Review:

- **Level of Scientific Merit**

The principal investigator on this proposal is a leading neurostimulation researcher at Case Western University. The committee does not question the scientific basis of the group’s proposed aims. The scapula/shoulder control system appears to be the program with the best chance of technical success and greatest commercial yield potential. However, questions were raised about the choice of muscles for stimulation. The gluteal stimulation program for bedsores and the other programs such as the hand/wrist control system for quadriplegics are technically less sound and there is a substantially weaker business case for these.

- **Commercial Potential**

A core unit is likely to be used for all indications if approved. The commercial potential is judged to be low overall due to very small markets. Each approved indication if obtained would contribute only a small return individually. The IP protection for this particular unit is unclear and it seems that large competitors could likely follow or enter prior to this group and substantially influence the marketplace.

Two of the proposed products are targeted for HDE (Humanitarian Device Exemption) which implies a patient population of fewer than 4,000 in the US. According to FDA regulations, profit is not allowed for a HDE but a manufacturer may recover costs of R&D, manufacturing and handling. The projected selling prices and expected unit sale numbers of these 2 products do not appear to be consistent with the HDE rules.

The manufacturing and, especially, the marketing plans were also insufficiently robust to rationalize the estimates on the business returns.

- **Leadership and Management Quality**

The principal investigator is highly qualified but the capabilities of the manufacturing and commercial partners are less clear.

- **Impact on Ohio**

This proposal builds upon an earlier BRCP investment in the device arena. The partner, MPM Solutions, is projected to grow to over 50 employees in Ohio about 5 years after completion of the work in the proposal if all products are developed.

- **Budget and Cost Share**

Funds would be used principally for R&D expenses and personnel; the overall estimates appear appropriate.

Review Summary:

In summary, the level of scientific merit is reasonable and builds on accepted knowledge that electrical stimulation can activate muscles. Although collaborators for the manufacturing and commercialization of products have been identified, the business plan is weak and data are not presented that would convince the committee that there is significant market potential.

Proposal 08-058
Neuroregenerative Therapies
The Cleveland Clinic Foundation

Proposal Summary:

The project seeks to develop small molecules that can enhance repair of the brain in multiple sclerosis (MS) with the goal not only of delaying progression of disability but reversing it. The proposed mechanism is myelin repair through generation of new oligodendrocytes which make myelin. Demyelination occurs in several central nervous system (CNS) diseases like MS. The group proposes to screen small molecule libraries to identify compounds that increase oligodendrocyte number and/or differentiation. Positive compounds identified will be put through graduated biological assays, beginning in zebrafish, then proceeding to tissue slice and in vivo mouse models. The lead compounds will be chemically optimized to obtain compounds suitable for licensing by major pharmaceutical companies as drug candidates.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,399,999	\$5,906,933
Capital Funds	\$600,000	\$0
Subtotal	\$4,999,999	\$5,906,933
TOTAL	\$10,906,932	

In the meantime, the group aims to commercialize the various assays that they have developed, offering this service to provide a revenue stream. They have five unique assays: a small molecule screen for oligodendrocyte differentiation; a small molecule screen for Stem/Progenitor cell division; conservation of target in Zebrafish; proof of principle in brain tissue slices; and proof of principle in animal models of human disease

Detailed Review

- **Level of Scientific Merit**

This is a highly innovative proposal. The investigators are at the forefront of research in MS. Collaboration among Drs. Trapp, Miller, Macklin and Ehrhardt could have a major impact on drug discovery for MS. The credibility of the screens is further enhanced by the science and the scientists behind them. Success of proposed goals could also have a significant impact on other CNS diseases as several are thought to be mediated by demyelination.

- **Commercial Potential**

There are two major commercial strategies. The first is to develop MS drug discovery screen assays and offer them as a commercial service. This goal looks achievable as the screens are already being used successfully for research purposes. Consolidating the tests in one place and optimizing them for high-throughput and commercialization should generate several jobs. The second goal is drug discovery by running commercially available compound libraries through those screens, generating leads, and chemically modifying those leads to obtain drug candidates. While the drug discovery efforts are

desirable, this part of the proposal is still very premature. No patent has been filed on any of the already identified compounds and no chemical modification has been conducted. The chemistry information is very scanty with no information as to synthetic schemes or possible challenges at either the laboratory or scale-up levels. No data are provided to suggest that the current lead compound will be bioavailable in the brain if taken orally (which is a key goal of the project) and no toxicity data are provided. The committee concluded that it cannot properly evaluate the scientific merit of this candidate, but it is certainly not ready for commercialization.

- **Leadership and Management Quality**

Renovo was founded by CCF investigators with IP from CCF. This is an excellent example of company spun-off by a non-profit, as CCF has done successfully many times. The scientific leadership of the company is excellent. The business leadership and management component will follow the CCF model which has been used successfully in several commercialization efforts.

- **Impact on Ohio**

The proposed project has the possibility of major impact on Ohio. First, Cleveland Clinic is a center of excellence in the treatment of MS. Achieving proposed goals will enable Cleveland Clinic and associated institutions to become more known as a center of excellence for drug discovery and development in the area of MS. This can lead to several jobs being created and improvement of health for Ohioans and the world.

- **Budget and Cost Share**

The group has been very successful in securing funding from NIH and the MS Society to support its scientific efforts. The budget requested for starting the screening business looks adequate and is consistent with commercialization efforts. The drug discovery efforts are still premature and research grants are a more appropriate source of funds at this stage.

Review Summary:

This is an excellent application with an important goal of moving innovation in MS science to commercialization level. It could have a major impact on Ohio both in terms of job creation and in the reputation of the state as a center of excellence in the treatment, drug discovery and development efforts of MS. The model of starting a screening business followed by drug discovery looks reasonable and is consistent with the criteria of the BRCP. The screening business is ready for commercialization. The drug discovery effort, however, appears to be premature. The committee would have preferred to see more detailed information on the already identified compounds and greater evidence of successful implementation of medicinal chemistry. The committee recommends that if the state of Ohio decides to fund this proposal, the applicants should be asked to provide a new budget and business plan for establishing the screening business and that the remainder of the proposal be re-submitted in the future when the drug discovery efforts

are more advanced and therefore more consistent with the timelines expected under the BRCP RFP.

Proposal 08-059
Commercialization of MicroRNA Assays and Biosignatures
for Biomedical Applications
The Ohio State University Research Foundation

Proposal Summary:

This application proposes to establish The Ohio MicroRNA Commercialization Consortium (OMIRCO) to rapidly expand commercialization efforts and services in the area of microRNA biomarker technologies. The proposal teams Phylogeny Inc. (Columbus OH), an existing Ohio bio-service company that offers customized gene-based diagnostics and molecular evaluations of tissues including gene probe design, tissue procurement and gene expression studies with an research and administrative operations partner, the Ohio State University, and a number of commercialization collaborators.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,923,500	\$4,048,615
Capital Funds	\$76,500	0
Subtotal	\$5,000,000	\$4,048,615
TOTAL	\$9,048,615	

Detailed Review:

- **Level of Scientific Merit**

Biomarkers present a compelling challenge for any screening or diagnostic application. While data appear to link specific mRNA sequences with a particular cellular state, other groups have demonstrated that a single sequence or biomarker is generally insufficient to accurately identify cellular differentiation and/or pathology; rather a panel of tens or hundreds of biomarkers is necessary for unambiguous identification. Thus while the approach proposed is credible, the scientific challenge faced by the group is high.

- **Commercial Potential**

This program appears to be primarily focused on development of a comprehensive microRNA biomarker program for a variety of cell states and disease conditions. The product development plan was well described, but the commercialization plan was fairly superficial and lacked a well-defined market assessment and competitive analysis.

- **Leadership and Management Quality**

The leadership in the research programs is well described and appears to be highly qualified; however no leadership was identified for the commercialization efforts.

- **Impact on Ohio**

It would appear that funding would primarily support programs within existing organizations of the OMIRCO consortium, and thus may not have a significant additional impact.

- **Budget and Cost Share**

The bulk of the requested funds are earmarked for the research program at Ohio State University, the primary member of the OMIRCO consortium, with appropriate detail for disbursement of the requested funds. Funds that are requested for the identified commercialization partner, Phylogeny Inc., are vague and lack appropriate detail, i.e. the bulk of Phylogeny's request is for specified but unidentified positions for a senior scientist, study manager and lab technician. Furthermore, it would appear that the cost share identified does not match the amount of funding requested from the state.

Review Summary:

This application presents a comprehensive research plan, rather than a development program with a high probability of commercialization. While the research programs are well described, this application presents only rudimentary details of a practical commercialization plan. While key elements of intellectual property are described (relevant patents and an intent to license), no clear plan for technology transfer or implementation is presented. The review panel would have expected to see preliminary licensing arrangements between the academic centers and the commercialization partner(s). Similarly, very little detail was presented for marketing and operations of the downstream product development.

While the scientific merit of this program may have long-term potential, this application lacks a clear path to commercialization within a reasonable time frame.

Proposal 08-061
Treatment of Acute and Chronic Wounds with Tissue Engineering Strategies
Clinical Tissue Engineering Center

Proposal Summary:

The goal of this proposal is to expand the activities of the Clinical Tissue Engineering Center (CTEC) in the areas of burn care, wound healing and nerve repair through partnership with collaborators at the Cleveland Clinic, Case Western Reserve University, University Hospitals of Cleveland, Cincinnati Shriners' Hospital, Akron General Medical Center, University of Akron, Northeastern Ohio Universities Colleges of Medicine and Pharmacy and industrial partners. CTEC was initially funded by the Third Frontier Program in 2004 with a plan to act as the hub of a network to bring scientists, tissue engineers, clinicians and private companies together to advance basic research findings to clinical practice. The Center has successfully established itself to provide resources to help establish collaborations and facilitate commercialization. The aim of this proposal is to extend CTEC's network and programs beyond musculoskeletal applications into the areas of wound healing, treatment of burns and scars and the repair of peripheral nerves.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,977,748	\$5,001,219
Capital Funds	\$0	\$15,000
Subtotal	\$4,977,748	\$5,016,219
TOTAL	\$9,993,967	

Detailed Review:

- **Level of Scientific Merit**

The overall level of scientific merit is high and the integration of the projects is well laid out. Each of the projects builds on what has happened in the past, but these projects strike out in new directions to meet unmet needs in the general area of wound care. The increase in the speed of cell sorting will be a great advance in the operating room if this project can be realized and, given the players, there is every reason to expect success. Also, the several levels employed to approach the cell sorting problem, though not unique, may change how harvesting cells for transplantation in this type of setting will evolve. Several of the new projects will bring new materials to the handling of large wound beds and the issue of wound bed structure and revascularization, although this area is not without competition. Work to extend the existing technology in alginates should also result in extended IP.

- **Commercial Potential**

The commercial potential of the proposed projects is high and will be supported by the relationships the PI and the project team have detailed in the proposal. Though some of the IP is already licensed, new IP will result from the work and the collaborations formed during this project. The licensing of work is presented well and the existing and future contracts appear to be well handled. The private sector partners appear to have excellent working relationships with the PIs.

With a group like this and the expertise of the Center's leadership, Ohio will draw students and companies to utilize this resource, so the long term outlook is very favorable.

- **Leadership and Management Quality**

The leadership and the management of this project are outstanding. The structure, collaborative relationships and mechanisms put into place for this and the group's previous proposal could be used as a model for the state. It is also clear that they are in the process of slowly gathering collaborators across the state as they gather additional resources. The management and the succession plans are actively planned for as they grow their group of collaborators.

- **Impact on Ohio**

This could have a large impact on Ohio in the following ways: First, having a world class group performing this type of research will draw students and companies from all over the world. Second, since several premier medical institutions are in Ohio, a unique cluster is starting to form there that will bring patients and unique medical challenges that few are able to deal with anywhere else in the world. Finally, with these institutions working in concert, training will be available for the future workforce that will be required to sustain this type of industry in the local Ohio area.

- **Budget and Cost Share**

The budget is generally reasonable.

Review Summary:

This is an exceptionally well-written proposal. The review of accomplishments based on the previous grant is outstanding and shows the strong attention to detail present in the leadership of this group which is critical to the successful execution of its plans. The application is fully responsive to the RFP. The group will benefit from the award and will be able to put the state's investment to work in a way that will derive the maximum return to Ohio.

Proposal 08-066
Intradiscal Pressure Sensor for Back Pain Assessment and Treatment
OrthoMEMS LLC

Proposal Summary:

This proposal requests funds for the development of the OrthoChip, a miniature, wireless sensor designed to be implanted in the intradiscal space to continually assess pressure. The applicants assert that such measurements will allow improved diagnosis of the source of lower back pain, and guide patients and surgeons to the most appropriate treatment, thus improving treatment outcomes.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$3,999,408	4,228,229
Capital Funds	\$0	\$105,000
Subtotal	\$3,999,408	\$4,333,229
TOTAL	\$8,332,637	

Detailed Review:

- **Level of Scientific Merit**

The proposal involves some very interesting and exciting technology by a group with the necessary experience to further its development according to the plan. If successful, the device would enable for the first time a determination of the way(s) in which the Panjabi model for the neutral zone is clinically applicable for patients exhibiting low back pain.

- **Commercial Potential**

There were several major concerns about the commercial potential of the OrthoMems device. First, there is concern about proposing the use of an invasive device (albeit one that can be introduced through a reasonably small trocar) to provide a diagnostic test. A second concern is that the insertion of the device in a patient subsequently found unsuitable for surgery as a result of the test could have an adverse effect on that patient's long term clinical results. Also, a very large database of clinical data will be required before any significant commercial adoption of the system could be expected. This database would need to involve the obvious variables of patient age and disc condition but would undoubtedly also need to include such additional variables as device placement and multi-level discogenic pain. On the other hand, a MEMS device like this may have other potential commercial uses and the team is encouraged to explore other applications in veterinary and human medicine, and the development of research tools.

- **Leadership and Management Quality**

The team assembled for this proposal is first rate and fully able to complete the proposed development objectives. The team combines the necessary expertise in electronics, business, biomechanics, manufacturing and regulatory affairs.

- **Impact on Ohio**

Presuming a successful outcome for the project, the potential for OrthoMems to provide a positive impact on Ohio through the creation of high paying jobs is reasonable.

- **Budget and Cost Share**

The budget and cost sharing is fair and reasonable

Review Summary:

As indicated above, the committee was intrigued and excited by the technology but concerned about the significant issues associated with the use of this device for the proposed indication. There was considerable fear that clinical testing, regulatory approval and eventual acceptance in the market would prove much more difficult than the team has estimated. There was, however, a great deal of interest in the OrthoMems device as a research tool or for other applications and the committee would encourage the team to consider alternate applications.

Proposal 080-070
The Ohio Cancer Consortium
The Ohio State University

Proposal Summary:

This proposal aims to establish a consortium of cancer research centers from seven Ohio institutions in order to provide value-added clinical trials to the biotechnology and pharmaceuticals industry by providing access to a greater number of patients and reducing the time and cost of the cancer drug development process. The value proposition of the Ohio Cancer Consortium is the proposed integration of currently disparate clinical research process and regulatory functions at individual institutions into a coordinated process to be managed by a central business entity.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,916,254	\$5,858,684
Capital Funds	\$83,748	\$580,000
Subtotal	\$5,000,002	\$6,438,684
TOTAL	\$11,438,686	

The proposal has three major goals: (1) to establish a single business entity to organize and coordinate state-wide clinical studies, (2) to recruit pharmaceutical and biotechnology companies to conduct clinical studies of innovative cancer treatments, and (3) to generate and retain intellectual property by conducting proprietary drug discovery leading to venture creation.

Detailed Review:

- **Level of Scientific Merit**

The scientific merit of this proposal was judged to be low. Not being predicated on innovative scientific breakthroughs per se, the proposal’s value proposition is to establish an innovative process of conducting value-added clinical trial services. The proposed bioinformatics grid infrastructure was viewed favorably from an informatics perspective.

- **Commercial Potential**

The commercial market for providing clinical trial service is well established, but without clear differentiation, clinical sites are often selected based on cost and time efficiencies. The panel did not feel that the Ohio Cancer Consortium demonstrated significant differentiation as compared to the clinical trial activities that are currently being conducted at the consortium institutions. For example, a clear differentiation would be the implementation of a single regulatory review process that would be mandated to be used by all participating consortium institutions. The same IRB process (Western IRB) is currently being used at each institution, therefore IRB approval at one institution should be acceptable at another with only minimal administrative review, but the panel felt that there is a fundamental distinction between a single regulatory process that would be integrated and mandated across the consortium members versus the current regulatory process that is simply shared by – but not mandated for – all consortium members.

Without a commitment to a single mandated IRB process, one consortium member is free to decide during the funding period to switch their IRB process, and if this occurs, the consortium's commercial value proposition is significantly diminished.

The panel was also concerned about potential competition between the consortium and the consortium's member institutions. Specifically, the value of the consortium would be enhanced if consortium member institutions extended the equivalent of a "first right-of-refusal" to conduct all proposed clinical trials to the consortium. This would ensure that the consortium management company has the authority to effectively market the consortium to industry without competition from its own members.

The panel was less optimistic, at least without further information, about the consortium's potential to assist in the development of innovative therapies in a way that would lead to the retention of proprietary intellectual property.

- **Leadership and Management Quality**

The panel felt that the leadership team and consortium institutions are impressive and well-qualified in the area of cancer treatment and clinical trials. The critical feature of the proposal is how well the team and institutions can work together in a coordinated fashion to integrate these currently disparate functions and processes. The panel was unconvinced that the consortium has established the necessary management structure for success. Namely, and as addressed further below, there was no indication given to the panel that dedicated personnel to manage the entity was in the initial budget allocation and the panel felt such an allocation would be critical for success.

- **Impact on Ohio**

If successful, such an endeavor would be beneficial to Ohio, regardless of the retention of the IP from proprietary drug development. The proposal leverages well-established Ohio "assets" – comprehensive cancer centers, University entities, and the necessary expertise that is resident within the state of Ohio currently – and could result in a profitable entity, although its nature would be that of a management company, not the kind of advanced technology company the BRCP generally seems designed to encourage.

- **Budget and Cost Share**

While much of the cost sharing seems to be provided through in-kind contributions and personnel time, the letters of commitment and some cash contributions from the comprehensive cancer centers were viewed favorably. Additionally, cost sharing through the contribution of Oncore software, equipment, and maintenance was viewed favorably as this system seems to be a key component of the infrastructure and value proposition. The panel did not feel that the budget allocations were in alignment with the initial objective of the proposal which is to establish a single entity to coordinate the activities of the member organizations in the consortium. Specifically, the proposal calls for a "dedicated Executive Director" (p. 22) yet there was no indication given that such a Director was even contemplated in the initial budget allocations. To the contrary, the initial budget allocations would go to existing personnel within the member institutions.

This was seen as a key risk factor by the panel in that the lack of dedicated personnel will significantly hinder the establishment of the management company which, as proposed by the Applicant, is viewed as a key rate limiting step to success in executing the “single-point-of-service” model.

Review Summary:

The idea of leveraging existing cancer centers of excellence is promising and there is a critical need to enable more innovative and efficient clinical trials. This proposal relies on the promise that a single managing entity can implement the proposed “single-point-of-service” for conducting clinical trials in a time and cost efficient manner within the cancer institutions. However, the success of the proposal is dependent on developing an organizational structure that guarantees incentives such that the member institutions prefer to work through the consortium rather than independently. The committee was not convinced that the member organizations have agreed on this critical organizational structure; such an agreement is critical for the committee to feel that the consortium is consistent with the demands of the BRCP RFP.

In summary, the panel did not feel that this proposal was likely to be successful in its current form, in part due to the lack of a mandated, integrated regulatory processes and the lack of immediacy in the hiring of dedicated full time employees, especially an Executive Director. Both deficiencies were viewed as necessary for the consortium to be successful in delivering the proposal’s central value proposition; integration and coordination of the member institution clinical trial activities that would yield a time and cost commercial advantage to industry.

Proposal 08-073
Development and Clinical Assessment of New Applications
for Deep Brain Stimulation
Intellect Medical Inc.

Proposal Summary:

This proposal, from Intellect Medical, a Cleveland, OH based implantable medical device company, requests support to develop a Deep Brain Stimulation (DBS) System for the treatment of Traumatic Brain Injury (TBI) and Post-Stroke Hemiparesis. Intellect was formed as the commercialization venture for the Cleveland Clinic-based Brain Neuromodulation Center (BNMC), which was previously funded through the Ohio Third Frontier BRTT program.

Proposed Budget		
	State Funds	Cost Share
Operating Funds	\$4,996,687	\$12,513,750
Capital Funds	\$0	\$0
Subtotal	\$4,996,687	\$12,513,750
TOTAL	\$17,510,437	

Neurostimulation is among the most rapidly developing areas in neuroscience, growing approximately 30% annually with many emerging applications. Currently, neurostimulation therapies and devices are available for Deep Brain Stimulation (DBS) for movement disorders, Spinal Cord Stimulation (SCS) for extremity pain, and Peripheral Nerve Stimulation (PNS) for pain and urinary incontinence. This proposal aims to extend DBS as a treatment for patients with post-TBI cognitive disability and patients with Post-Stroke Hemiparesis. Current funding would be used to complete necessary feasibility trials and initiate large scale, multi-center pivotal studies to prove safety and effectiveness.

Detailed Review:

- **Level of Scientific Merit**

This proposal is from a company looking to develop and sell deep brain stimulators for cognition improvement in 1) traumatic brain injury and 2) post-stroke/TBI hemiparesis. The premise for the first application is that electrodes placed in regions of the thalamus can activate forebrain projection and thereby increase alertness and cognition in certain forms of TBI. The science is supported by a reasonable set of data supporting activation of forebrain with electrical stimulation of thalamic regions but rather limited animal model data for functional improvements. The investigators repeatedly cite a proof of concept for the procedure and device in a Nature article describing the observations in a single patient with a rather severe TBI-caused vegetative state. The committee is unconvinced that this description of a single patient is adequate to demonstrate proof of concept.

The stroke/TBI hemiparesis stimulation portion of the proposal involves placing electrodes in the cerebellar dentate. Animal data for this is very limited and this proposal aims to prove the hypothesis and then to develop and market a stimulator to treat patients.

The proposal incorporates collaborations broadly across a number of university based laboratories. Intellect is a very small, nearly virtual, company that has an engineering development agreement with Greatbatch DES, a company in Cleveland.

Some animal based hypotheses for electrode placement but the animal disease model data are rather limited and the single human observation although interesting is not a sound proof of concept. Note for the hemiparesis rehabilitation or functional restoration portion, another company, Northstar, recently stopped development of a cortically placed stimulator for functional motor restoration in stroke patients. It is not clear what advantage, if any, DBS has over the cortical stimulator approach.

- **Commercial Potential**

There is a very large market opportunity for the hemiparesis project but the technical risk is very high. The cognitive TBI device has limited market opportunity.

- **Leadership and Management Quality**

This is a very weak area, as reflected in the lack of details and clearly established business model in the proposal.

- **Impact on Ohio**

This project follows on the state's investment to date in the neurostimulation R&D arena. A small impact is anticipated on job creation in Ohio in the near term.

- **Budget and Cost Share**

There is a very large reliance on cost share from Greatbatch DES. Otherwise, the proposal would use funds to support further DBS research, personnel and a more formal proof of concept for the TBI treatment approach. The clinical costs seem low.

Review Summary:

In summary, the scientific premise for DBS as a treatment for cognitive improvement and restoration of function in hemiparesis is rather weak and further basic research needs to be done. The outcome value proposition and business model for TBI need to be re-evaluated. For stroke, the market opportunity is quite large but more basic research needs to be done to support the rationale for investment in this aim of the proposal.

APPENDIX B

Evaluation Criteria	BRCP 08- Score 0-5*
A. Level of Scientific Merit	
Scientific objectives are original and innovative; novel concepts, approaches or methods are employed	
Project has potential for new discoveries and understanding; advances beyond previous studies can be expected	
Project is scientifically and technologically feasible; conceptual framework, design, methods and analyses are adequately developed	
B. Commercial Potential	
Size of opportunity: <ul style="list-style-type: none"> • Proposal accurately assesses market and has realistic assumption about market share that could be captured • Proposal demonstrates understanding of global marketplace and can compete for international business opportunities 	
Identified stage of market development: Proposal demonstrates understanding of the commercialization process and the resource requirements for commercialization	
Potential for products: <ul style="list-style-type: none"> • Focused commercialization opportunity areas are identified • Project has achieved proof of principle • Technologies and products have a competitive advantage over existing and alternative technologies 	
Degree of customer readiness: <ul style="list-style-type: none"> • Proposal addresses needs of end-users • A collaborator is a potential customer whose input has been built into the proposal 	
Degree of sustainable competitive advantage: Proposal demonstrates that a competitive advantage can be maintained beyond the three-year Project period	
C. Leadership and Management Quality	
Demonstrated leadership assets: <ul style="list-style-type: none"> • Proposal demonstrates commitment of the Lead Applicant and Collaborator(s) • Leadership is demonstrated in all critical phases, including research, IP protection, regulatory compliance, product development, leveraging of funding, and commercialization 	
Vision for Success: Proposal presents a compelling vision of the project's goals, potential achievements and importance to the state of Ohio	
Potential for Leverage: Lead applicant and Collaborators demonstrate potential to leverage additional funds during and beyond requested initial State support	
Past Performance (if applicable): Lead applicant has demonstrated successful performance on prior Third Frontier grants	

* A score of 0 should be used to indicate that the applicant either did not address the requirement or that the applicant completely failed to meet the requirement. A score of 5 should be used to indicate that the applicant meets the requirement exceptionally well.

	BRCP 08-
	Score 0-5*
D. Impact on Ohio	
Proposal demonstrates key impacts including job creation, new sales, companies created or attracted to Ohio, leveraged funding	
Proposal demonstrates industrial support from the State's relevant industry sector	
Proposal demonstrates integration with existing relevant State research capabilities	
Proposal involves and engages relevant anchor companies within the State of Ohio	
Proposal integrates and builds on prior Third Frontier Project investments	
Proposal is consistent with State and Regional Priorities	
E. Budget and cost share	
Budget is justified and adequate to meet the goals of the proposal	
Cost share letters are provided and are sufficiently detailed	

* A score of 0 should be used to indicate that the applicant either did not address the requirement or that the applicant completely failed to meet the requirement. A score of 5 should be used to indicate that the applicant meets the requirement exceptionally well.

APPENDIX C

BIOGRAPHICAL SKETCHES OF COMMITTEE MEMBERS

CHAIR

Alastair J.J. Wood, M.D. (IOM), is currently Managing Director of Symphony Capital LLC and Professor of Medicine and Professor of Pharmacology at Weill Cornell Medical College, New York. In 1978 he joined the Faculty at Vanderbilt University School of Medicine, where he became tenured Professor of both Medicine and Pharmacology and Attending Physician at Vanderbilt Medical School. He was Assistant Vice Chancellor for Clinical Research (1999-2004), and Associate Dean, Vanderbilt Medical School (2004-2006) before being appointed Emeritus Professor of Medicine and Emeritus Professor of Pharmacology in 2006. Dr. Wood was the chairman of the FDA's Nonprescription Drugs Advisory Committee until 2006, and chaired the 2005 FDA Advisory Committee on Cox-2 inhibitors. He previously served as a member of the Cardiovascular and Renal Advisory Committee of the Food and Drug Administration, and the FDA's Nonprescription Drugs Advisory Committee. He has served as a director of pharmaceutical companies including Antigenics (AGEN), Symphony Neurodevelopment, and Symphony Evolution. Dr. Wood is a member of many societies and has received numerous honors, notably election to membership of The National Academy of Sciences' Institute of Medicine, The American Association of Physicians (AAP), The American Society for Clinical Investigation (ASCI), Honorary Fellow, American Gynecological and Obstetrical Society (AGOS). Dr. Wood has served on a number of Editorial Boards. He was a member of The New England Journal of Medicine Editorial Board (2004-2006); he was the Drug Therapy Editor of The New England Journal of Medicine from 1985 to 2004, and is also on the Editorial Board of Clinical Pharmacology and Therapeutics and The Scientist. His research interests have been focused on understanding the mechanisms for interindividual variability in drug response, with a particular focus on the molecular genetics of adrenergic receptors, ethnic differences in drug response, vascular response, and the genetics of drug metabolism. His research has been continuously funded by NIH, and has resulted in over 300 publications.

MEMBERS

Adeboye Adejare, Ph.D., is Professor and Chair of the Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences in Philadelphia. He received his Ph.D. in Medicinal Chemistry from The Ohio State University in 1985 and did postdoctoral studies at the National Institutes of Health for 3 years prior to beginning his career in academia. His research is geared towards discovery of compounds that can be used to probe mechanisms of neurodegeneration as observed in stroke, Alzheimer's disease and related disorders, pharmaceutical profiling, and drug targeting. His research was/is funded by the Commonwealth of Pennsylvania, the National Institutes of Health, the Office of Naval Research, and several pharmaceutical companies. These efforts have resulted in over 30 publications, one issued patent, two patent applications, and over 80 presentations at meetings, including invited presentations at national and international conferences. Dr. Adejare serves on several national panels, including grant review panels for the National Institutes of Health, National Science Foundation, and Alzheimer's Association.

Charlene W. Bayer, Ph.D., is a Group Leader and Principal Research Scientist with the Georgia Tech Research Institute (GTRI) in the Electronic Systems Laboratory (ESL) and is a leading national expert in the field of environmental analysis and design. Dr. Bayer is leading a multi-university research program in the development of breath analysis as a means of disease detection, particularly for breast cancer detection. Another of Dr. Bayer's recent research programs, funded by HUD, successfully resulted in a real-time wearable sensor array system (SAS) to nearly continuously measure airborne exposures of

asthmatic children with periodic pulmonary function measurements designed to investigate the impact of airborne exposures on asthma exacerbations. She is leading the Green Schools Program through the state funded program Environmental Health and Occupational Safety Program at GTRI and she is teaching a graduate level course in the GT School of Architecture on High Performance Schools. For more than 20 years, she has led research programs investigating all aspects of the indoor environment, such as building diagnostics; product emissions; contaminant sources identification and control; air cleaner technology development; strategic ventilation strategies; effects of airborne exposures on asthma and respiratory health; schools indoor air quality; real-time instrumentation development, methods development for airborne species; methodology development for measurement of gas-phase filtration removal efficiency; indoor air quality management plans development; and interfacing indoor air quality and energy efficiency. Her research is conducted for a wide variety of industrial and governmental sponsors, much of this research being multi-university/partner research efforts. Dr. Bayer is the holder of two patents and is the author and presenter of more than 100 technical papers. Prior to joining the Georgia Tech Research Institute, Dr. Bayer was a researcher for the US Geological Survey, running their mass spectrometry laboratory and developing methodology for pollutant analysis in water, sediment, and aquatic life. She also conducted research for the Toxicology Department of Emory University, investigating drug metabolic pathways, and Smith-Kline Corporation in antibiotic structure elucidation and isolation.

Alastair J. Clemow, Ph.D., serves as President and Chief Executive Officer and is a member of the Board of Directors of Nexgen Spine, a leading developer of innovative spinal devices. Dr. Clemow has over 20 years of experience in managing orthopaedic companies, most recently at Gelifex which he founded, secured funding for and ultimately sold to Synthes Spine, one of the three largest spinal companies. From 2000 to 2003, Dr. Clemow provided strategic planning assistance to a wide range of companies, including Abbott Labs, BTG, Synecor, and Johnson & Johnson. Prior to that, Dr. Clemow enjoyed a successful career at Johnson & Johnson where he was a Vice-President of Business Development. In this role, he was responsible for numerous acquisitions, including DePuy and Joint Medical Products. For 5 years before that, he was Director of Research and Development at Johnson & Johnson Orthopaedics with responsibility for the development of the PFC Sigma Total Knee System as well as many other innovative orthopaedics. Dr. Clemow is the inventor of eight patents in the area of arthroscopy and spinal implants as well as the author of over 40 papers, books and presentations. Dr. Clemow is a Past President of the Society for Biomaterials and has served as an Associate Editor of the Journal of Applied Biomaterials as well as a reviewer for the Brown Foundation. Dr. Clemow obtained his B.Sc. and Ph.D. in metallurgy from the University of Surrey in the U.K. and has an MBA in Finance from Columbia University. Dr. Clemow serves on the Boards of BioMedical Enterprises and Hydrocision, Inc.

Jennifer H. Elisseff, Ph.D., is an associate professor of biomedical engineering at Johns Hopkins University with an adjunct appointment in Orthopedic Surgery. Her biomaterials and tissue engineering laboratory at Johns Hopkins focuses on developing new biomaterials and minimally invasive technologies for tissue repair, stem cells, and musculoskeletal tissue engineering. She has collaborations with plastic surgery, orthopedics, ophthalmology and otolaryngology clinical departments. Dr. Elisseff has published over 50 articles and book chapters, has 6 patents issued and pending, and has given over 70 invited national and international lectures. She serves on a number of NIH and foundation review panels, the science advisory board for Bausch and Lomb and Cellular Bioengineering, Inc, and recently cofounded a company that is developing new materials and therapies for cartilage repair. Dr. Elisseff has received awards including the Carnegie Mellon Young Alumni Award, Arthritis Investigator Award from the Arthritis Foundation and was named by Technology Review magazine as a top innovator under 35 in 2002 and top 10 technologies to change the future. In 2005, the Urbanite magazine voted Elisseff one of the up and coming in Baltimore and the Baltimore Business Journal recently named her to Baltimore's 40 under 40.

Rutledge Ellis-Behnke, Ph.D., is an associate professor in the Department of Anatomy at the University of Hong Kong Li Ka Shing Faculty of Medicine and a research scientist in the Brain and Cognitive Sciences Department at Massachusetts Institute of Technology. His primary interest is using

nanobiotechnology to reconnect disconnected parts of the central nervous system (CNS). He received his PhD in neuroscience from MIT, BS from Rutgers University, and graduated from Harvard Business School's International Senior Manager's Program (AMP/ISMP). Prior to returning to school to pursue his PhD, Dr. Ellis-Behnke held various management positions including Senior Vice President of a public company for testing and consulting services and Co-founder/CEO in 1995 of one of the first internet companies to do online commerce in computer memory. Dr. Ellis-Behnke is a Fellow and founding board member of the American Academy of Nanomedicine, Associate Editor of Neurology for the journal Nanomedicine, Scientific Advisory Board member for the Glaucoma Foundation, member of the China Spinal Cord Injury Network, Society for Neuroscience, American Chemical Society, Association for Research in Vision and Ophthalmology, American Society of Neurochemistry and Sigma Xi. Technology Review named his nanotechnology discoveries one of the "Top 10 Emerging Technologies of 2007."

Zahi A. Fayad, Ph.D., FAHA, FACC, serves as Professor of Radiology and Medicine (Cardiology) at the Mount Sinai School of Medicine. He is the Director of the Translational and Molecular Imaging Institute, Director of the Eva and Morris Feld Imaging Science Laboratories and Cardiovascular Imaging Research, Director of the General Clinical Research Center Imaging Core at the Mount Sinai School of Medicine and Mount Sinai Medical Center. Dr. Fayad's current research is in the development and use of multimodality cardiovascular imaging including, Cardiovascular Magnetic Resonance (CMR), computed tomography (CT), and positron emission tomography (PET), and molecular imaging to study cardiovascular disease. His recent focus has been on the noninvasive assessment of atherosclerosis. He holds 7 US and Worldwide patents in the field of imaging. He is currently the principal investigator of two federal grants funded by the National Institutes of Health's National Heart, Lung and Blood Institute totaling over four million dollars. Dr. Fayad has authored more than 200 peer-reviewed publications, 50 book chapters, and over 400 meeting presentations. He is Deputy Editor of Magnetic Resonance in Medicine (MRM), immediate past-president of the Society of Atherosclerosis and Prevention (SAIP), fellow of the American Heart Association (AHA) where he is currently serving on the National Research Committee and on the Council on Cardiovascular Radiology and Intervention (CVRI), fellow of the American College of Cardiology (ACC), where he serves on the Cardiovascular Collaborative Imaging (CCI) Committee. He is a member of the NIH's National Lung, and Blood Institute (NHLBI) Cardiovascular Strategic Planning Working Group on Vascular Disease and Hypertension and a past member of the board of trustees of the Society of Cardiovascular Magnetic Resonance (SCMR). Dr. Fayad is also on the editorial boards of the Arteriosclerosis, Thrombosis and Vascular Biology (ATVB), Journal of Cardiovascular Magnetic Resonance, Nature Clinical Practice Cardiovascular Medicine, Atherosclerosis, and Journal of the American College of Cardiology Imaging (JACC Imaging). He is the recipient of numerous awards and recently was the recipient of the 2006 John Paul II Medal, Krakow, Poland. Dr. Fayad trained at the Johns Hopkins University and at the University of Pennsylvania.

John A. Grosso, Ph.D., is Executive Director of Analytical Research and Development at Bristol-Myers Squibb Co. in New Brunswick, NJ. He is responsible for the leadership of areas which are involved in the development and execution of analytical methods to support API and drug product release, process chemistry, structure elucidation, atomic spectroscopy, powder property characterization, and materials characterization. Prior to joining the analytical division, Dr. Grosso was Director of Process Research and Development at Bristol-Myers Squibb in Lawrenceville, NJ. In that role, he led a department whose mission was identification of practical synthetic routes and refinement of synthetic organic transformations leading to reliable, rugged and safe, plant-worthy chemical processes. He and his group have been involved in the development of chemistry for the preparation of the phosphinic acid-containing ACE inhibitor, fosinopril (Monopril®), the antitumor agent paclitaxel (Taxol®), and a variety of small-molecule drug candidates for the treatment of cancer, inflammation, depression, migraine, hypercholesterolemia, hypertension, fungal infection, and sexual dysfunction. He received his B.A. in Chemistry from New York University and his Ph.D. in Organic/Medicinal Chemistry from Purdue University studying under Prof. David Nichols. He is the author of a number of publications and patents in both analytical chemistry and process chemistry.

Patrick Lee is currently a Regulatory Affairs professional at Micrus Endovascular Corp. in San Jose, CA where he is involved in regulatory activities worldwide. Prior to Micrus, he co-founded and was a director of iMedic Devices, Inc., in Sunnyvale, CA. At iMedic Devices, he was involved in the development of drug-delivery devices. Mr. Lee has over 20 years of experience in the food, medical device, and other hi-tech industries including over 16 years at Fortune 500 companies. He has experience in food, nutrition, and medical products. Mr. Lee received his Chemical Engineering BS from Cornell, MS in engineering from Columbia, and MBA from the Anderson School at UCLA. He is a licensed Professional Engineer in the states of New Jersey and California and holds several patents. Patrick holds the US Regulatory Affairs RAC (US) designation.

Robert A. Lieberman, Ph.D., is President and Chief Technical Officer of Intelligent Optical Systems, Inc. He received a Ph.D. in Physics with an emphasis on solid-state physics and biophysics from the University of Michigan. After working at AT&T Bell Laboratories for 10 years, Dr. Lieberman joined Physical Optics Corporation (POC), where he became Vice President and General Manager of Research and Development. In 1998, the R&D Division of POC spun-off and became Intelligent Optical Systems, Inc. (IOS), where he served as Senior Vice President and CTO. After a year as CTO of OpTech Ventures, LLC, a company founded to commercialize IOS technologies, Dr. Lieberman returned to IOS to serve as President and CTO. Among his accomplishments is the formation of Optical Security Sensing LLC, a company created with the explicit goal of manufacturing and selling chemical sensor systems for security and industrial applications.

Dr. Lieberman has been the Principal Investigator on numerous federally funded projects, holds 29 U.S. patents, and is the author of many scientific articles. He has chaired more than 30 sensor conferences and has presented invited talks around the world on biological and chemical sensors. He is the Chairman of ASTM Subcommittee E13.09 on Fiber Optics in Molecular Spectroscopy, a Fellow of SPIE, and a Senior Member of IEEE, and has served on the editorial boards of Optical Engineering and the Journal of Measurement Science and Technology.

Edith Mathiowitz, Ph.D., is a tenured Professor of Medical Science and Engineering, and the Director of the Artificial Organs, Biomaterials and Cellular Technology graduate program at Brown University's Department of Molecular Pharmacology, Physiology & Biotechnology. She is also the founder of Spherics, the editor of The Encyclopedia of Controlled Drug Delivery Systems (1999), serves as an editorial board member for five journals, and was a 2005 co-chair of the Controlled Release Society, an international society dealing with drug delivery. To date, Dr. Mathiowitz has made 91 publications, issued 38 patents, 1 book; her work has been published in 95 conference proceedings and abstracts. She has experience with Polymers, drug delivery oral delivery vascular grafts, microencapsulation, nanoencapsulation and bioadhesion. Before joining Brown University, Dr. Mathiowitz worked at Enzytech (now Alkermes) and was one of the developers of the Prolease® drug delivery technology. Dr. Mathiowitz received her Ph.D. in Polymer Chemistry from the Weizmann Institute of Science in Israel and did her post-doctoral fellowship in drug delivery with Professor Robert Langer at MIT.

Laura T. Mazzola, Ph.D., has seventeen years of experience in the biotechnology industry, from research and development to the commercialization of platform technologies. Most recently she was CEO of Excellin Life Sciences, a company enabling cell-specific genetic engineering, guiding the enterprise from spin-out through corporate collaborations and Series A funding. She also founded NanoBioConvergence, a non-profit seminar series for nanotechnology and has been an invited lecturer at the UC Berkeley Haas School of Business. Dr. Mazzola was an early employee at Affymax and Affymetrix, developing the high-density array technology that became the revolutionary GeneChip(TM) product line. She then helped reorient business development at Symyx Technologies through pharmaceutical industry collaborations and licensed their first commercial product, earning the Frost & Sullivan 2002 Market Engineering Technology Innovation Award. Dr. Mazzola has been a technology analyst for Nature Biotechnology, California State Senate, NIH, and National Academy of Sciences. She received a B.A. from Kalamazoo College and a M.S. and Ph.D. in Physical Chemistry from Stanford University.

Linda K. McLoon, Ph.D., is a tenured Professor at the University of Minnesota in the Departments of Ophthalmology and Neuroscience. Her research focuses on diseases of the eye and orbit, and she has published over 70 peer-reviewed scientific articles. Specifically, her laboratory is developing new drugs to treat eye motility disorders, studying why eye muscles are spared in muscular dystrophy, and using a novel drug delivery method develop a clinically relevant method to treat optic nerve and retinal ischemia. Her research is primarily funded by the National Institutes of Health, and in 2006 she received a mid-career merit award from Research to Prevent Blindness. Dr. McLoon is currently chair of the program committee for her section of the Association for Research in Vision and Ophthalmology, serves on the editorial board of Investigative Ophthalmology and Visual Sciences, reviews manuscripts for 28 scientific publications, as well as reviews grant applications for NIH, the NMRC of Singapore and for a number of private foundations. She is an active member of the Graduate Program in Neuroscience (GPN) as Admissions Committee Chair and serves on the Steering Committees of the GPN and Muscular Dystrophy Center. She teaches Human Anatomy to both medical and dental students. She currently has 2 graduate students and has mentored 40 medical students, 12 fellows, and 35 undergraduates.

Michael S. Paul, Ph.D., is the President and CEO of LineaGen, Inc., a biotechnology company focused on the discovery and commercialization of biomarker-based molecular diagnostics for the improved diagnosis and treatment of common diseases. Dr. Paul also works closely with vSpring Capital and Mesa Verde Venture Partners as a Venture Partner in the evaluation of life science investment opportunities. Prior to founding LineaGen, Inc., he was the Chief Operating Officer and President at LineaGen Research Corporation, a Utah non-profit organization from which LineaGen, Inc. was founded. Prior to LineaGen, Dr. Paul worked for Huntsman Biotechnology Corporation as Vice President of Business Development, and for the publicly-traded biopharmaceutical company, NPS Pharmaceuticals as Director of Strategic Development. Dr. Paul serves on the Board of Trustees for the Utah Technology Council (UTC), serves as Chair of UTC's Life Science Advisory Board, and was an Appointee of the Governor of Utah to the Steering Committee for the Utah Technology Industry Commission. Dr. Paul has also worked at the University of Utah Technology Transfer Office in the marketing of University inventions to the pharmaceutical and biotechnology industries. Dr. Paul is a licensed patent agent of the United States Patent and Trademark Office and received his B.A. in Biology from Colby College and his Ph.D. in Biochemistry and Molecular Biology from the University of Utah.

Franklyn G. Prendergast, M.D., Ph.D., is Edmond and Marion Guggenheim Professor of Molecular Pharmacology and Experimental Therapeutics and Director of the Center for Individualized Medicine at the Mayo Clinic College of Medicine. In a prior position at the Mayo Clinic, Dr. Prendergast served as Director of the Mayo Clinic Comprehensive Cancer Center. Dr. Prendergast also serves on the Board of Trustees of the Mayo Foundation and the Board of Directors of Eli Lilly and Company. His research focuses on structural protein biology and bioimaging and has earned him numerous accolades, including an E.E. Just Award from the American Society of Experimental Biology and the Musgrave Gold Medal of the Institute of Jamaica. He earned his BA and MA in physiology as a Rhodes Scholar at Oxford University, his PhD in biochemistry from the University of Minnesota and his MD from the University of the West Indies.

Krishnendu (Krish) Roy, Ph.D., is an Associate Professor in Biomedical Engineering and chair of the BME graduate studies committee at The University of Texas at Austin. He received his bachelor's degree from the Indian Institute of Technology, followed by his M.S. in Biomedical Engineering from Boston University and his Ph.D. in Biomedical Engineering from Johns Hopkins University School of Medicine. Dr. Roy then joined Zycos, a start-up biotechnology company, where he served first as a Scientist and then as a Senior Scientist in the Drug Delivery Research group. He left his industrial position to join The University of Texas at Austin in 2002. Dr. Roy's research interests are in biomaterials, controlled release technologies and biomedical polymers, especially for engineering immunotherapy. His research in drug delivery focuses on developing novel delivery systems for gene-based vaccines and adjuvants specifically for cancer and infectious diseases. He is also developing new nanofabrication technologies to fabricate physiologically responsive drug delivery vehicles. In the area of stem cell engineering his work focuses on both embryonic and adult stem cell cultures to generate blood cells, especially cells of the immune

system including dendritic cells and T cells for immunotherapeutic applications. His work is funded extensively by NIH, NSF, The Coulter Foundation, The Whitaker Foundation, etc. His work has resulted in two issued US patents and 4 pending patent applications. Dr. Roy has received numerous awards and honors including an NSF CAREER award, the 2007 Young Investigator Award from the Society for Biomaterials, the 2007 Young Investigator Award from the Houston Society for Engineering in Medicine and Biology, the 2006 Coulter Foundation Translational research Award, the 2005 Global Indus Technovator Award from MIT, and the 2003 Whitaker Foundation Bioengineering Research Award. He was also twice the recipient of outstanding researcher awards from the Controlled Release Society Inc. Dr. Roy is a member of the editorial board of The Journal of Controlled Release and has served a guest editor for the special issue on Stem Cells and Biomaterials for the journal Biomaterials. He serves as the Chair of the Cell and Organ Therapy Special Interest Group of the Society for Biomaterials and a member of the Advisor Board of the US Chapter of Society for Biomaterials & Artificial Organs of India.

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