

# Health Research Priorities

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All health research projects funded under Chapter 9 of Act 77 of 2001 must be consistent with research priorities established by the Pennsylvania Department of Health in conjunction with the Health Research Advisory Committee. The research priorities are reviewed and revised as necessary. Separate health research priorities are established for formula and nonformula (competitive) funds.

- The **health research priorities for formula funds** (listed below) have remained unchanged since 2001. The formula funded research projects are non-competitive with funds allocated to those institutions that are eligible to receive the funds based on a formula established by Act 2001-77. Each year, the Department of Health sends the formula fund application, which contains additional requirements, to eligible institutions so they can apply for funding when the funds become available.
- The **health research priorities for nonformula funds** are revised every year that nonformula funds are available. Nonformula funds were not available during the 2012-13 fiscal year. The priorities for nonformula priorities are listed below, after the formula priorities. The nonformula funds are awarded competitively to institutions submitting research proposals solicited by a Request for Applications (RFA). To be placed on a mailing list to receive a copy of the RFA when it is released, please email: ra-healthresearch@state.pa.us.

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## Health Research Priorities by State Fiscal Year

### FORMULA Health Research Priorities for 2001-02 through 2015-16 fiscal years

Research priorities shall include the identification of critical research areas, disparities in health status among various Commonwealth populations, expected research outcomes and benefits and disease prevention and treatment methodologies.

The research priorities are clinical, health services, and/or biomedical research as defined in Act 2001-77. The ultimate goal of the research should be to improve health status and access. The Department should encourage, through the application process and accountability requirements, research that:

- emphasizes collaboration
- promotes business and community involvement
- increases infrastructure and research capacity
- increases the number of new investigators, new grants, new discoveries and new products
- leverages new and existing research funds, and
- leads to population-based applications that address disparities in health status among various Commonwealth populations.

An institution that receives \$400,000 or more in formula funds shall also comply with the requirements of Section 908 (c) of Act 2001-77.

Institutions receiving grants under Section 909 of Act 2001-77 shall also comply with the requirements of Section 910 of Act 2001-77.

### **NONFORMULA Health Research Priorities for 2001-02 FY**

Research priorities shall include the identification of critical research areas, disparities in health status among various Commonwealth populations, expected research outcomes and benefits and disease prevention and treatment methodologies.

For the purpose of priority setting and funding, the committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priority is:

- research on bioinformatics, as applied to cancer and/or infectious diseases, as a model for other diseases or processes.

Nonformula funded research shall be collaborative across research institutions or organizations, and, to the extent practicable, result in a regional or statewide resource. The Department should encourage applicants to include partners that are smaller colleges and universities and other institutions or organizations that are not academic medical centers. The Department should encourage research that leads to population-based applications that address disparities in health status among various Commonwealth populations.

In future years, other research priorities may be established.

### **NONFORMULA Health Research Priorities for 2002-03 FY**

The research priorities for nonformula funded research are:

- Regional/population differences in the incidence of cardiovascular disease and in the efficacy of prevention and treatment strategies. Why do these differences exist? What are the barriers to eliminating these differences? Apply and evaluate an intervention that, if successful, will lead to the cost effective elimination or reduction of these disparities and improvement in outcomes.
- Regional/population differences in the incidence of schizophrenia, bipolar disorder, major depressive disorders, and childhood autism spectrum disorders, and in the efficacy of prevention and treatment strategies. Why do these differences exist? What are the barriers to eliminating these differences? Apply and evaluate an intervention that, if successful, will lead to the cost effective elimination or reduction of these disparities and improvement in outcomes.

## NONFORMULA Health Research Priorities for 2003-04 FY

For the purpose of priority setting and funding, the committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities for nonformula funded research are:

- Research to improve the prevention, diagnosis, and treatment of certain lung disorders that may result from environmental exposures. Research must focus on one or more of the following lung disorders: bronchial asthma, occupational lung diseases, chronic obstructive pulmonary diseases (emphysema and chronic bronchitis), bronchiectasis, and interstitial lung diseases such as idiopathic pulmonary fibrosis, pulmonary vascular disease, and different forms of lung cancer. Research on cystic fibrosis or other lung disorders and interventions designed to modify tobacco use patterns will not be considered. The research must be focused on underserved populations or populations that are at high risk for lung disease. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are smaller colleges and universities and other institutions that are not academic medical centers in addition to the major research institutions. The research should lead to population-based applications that address disparities in health status among underserved populations including rural, urban, and other high-risk Commonwealth populations.
- Research to improve pregnancy outcomes for mothers and their children. Research may include but is not limited to one or more of the following areas: toxemia; intrauterine effects and prenatal factors related to autism; the effect of infectious diseases on pregnancy outcomes; factors related to endothelial function such as arginine, Vitamin E, and aspirin; factors related to premature labor; gestational diabetes; and detection of risks and causes of developmental abnormalities. The research must be focused on underserved populations or populations that are at high risk for experiencing adverse pregnancy outcomes. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are smaller colleges and universities and other institutions that are not academic medical centers in addition to the major research institutions. The research should lead to population-based applications that address disparities in health status among underserved populations including rural, urban, and other high-risk Commonwealth populations.

## NONFORMULA Health Research Priorities for 2004-05 FY

For the purpose of priority setting and funding, the committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities for nonformula funded research are:

### Neurodegenerative Diseases

- Research which develops or employs new technologies (e.g., imaging, biotechnology, nanotechnology, robotics, bioengineering) that leads to etiologic insights and/or early intervention approaches with the goal of preventing, ameliorating, treating, and/or curing Alzheimer's disease, Parkinson's disease, Amyotrophic Lateral Sclerosis, multiple

sclerosis or related neurodegenerative diseases (excluding stroke) and providing insight into these conditions. Research may include but is not limited to the development of new cost-effective techniques of imaging and cognitive tests for the early detection of Alzheimer's disease and the identification of specific markers that will improve understanding of the etiology of neurodegenerative diseases. The research must include but is not limited to the testing of a clinical application designed to improve the early detection, amelioration or treatment of persons with neurodegenerative diseases. Research should place emphasis on underserved populations that are at high risk for and disproportionately impacted by neurodegenerative diseases. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are smaller colleges and universities, biotechnology and bioengineering companies, and other institutions that are not academic medical centers in addition to the major research institutions. The research should hold the potential for population-based applications that address disparities in health status among vulnerable segments of the population, including rural, urban, or other high-risk Commonwealth populations. At least 50 percent of each grant's funds must be spent on health services and/or clinical research as defined in Act 77 of 2001; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 77 of 2001.\*

### **Tobacco Use and Cessation**

- Research into the underlying causes as well as the prevention and treatment of tobacco use. Research may include but is not limited to one or more of the following areas:
  - (1) novel approaches to understanding the etiologic mechanisms of tobacco use and addiction, especially among high-risk youth and other high risk populations such as long term 1+pack a day smokers and those with co-morbidities such as cardiovascular disease, pulmonary disease and depression;
  - (2) testing of new medications to reduce tobacco addiction; and
  - (3) the development and testing of prevention and treatment strategies to reach African Americans, Latinos or other racial/ethnic populations, persons with low education or income, or other special populations.

The research shall focus on identification of new scientific technologies and approaches at the community level designed to reach a defined high risk population or populations and to address tobacco use and cessation in such populations. Overall, the research should place emphasis on underserved populations or populations that are at high risk for tobacco use and addiction. Applicants must establish a regional Center of Excellence to conduct research that is collaborative across research institutions or organizations. The Center of Excellence should, to the extent practicable, include partners that are smaller colleges, universities, industry, and other institutions that are not academic medical centers in addition to the major research institutions, including the Commonwealth's ongoing tobacco prevention and cessation programs. These funds shall support research and shall not duplicate the activities of the Commonwealth's tobacco prevention and cessation programs. The research should lead to population-based applications that address disparities in tobacco use among underserved populations including rural, urban, or other high-risk Commonwealth populations. At least 50 percent of a grant's funds must be spent on health services and/or clinical research as defined in Act 77 of 2001; no more than 50 percent of each grant's funds may be spent on biomedical research as defined in Act 77 of 2001.\*

\*Biomedical research is “comprehensive research pertaining to the application of the natural sciences to the study and clinical practice of medicine at an institution, including biobehavioral research related to tobacco use.” As stated in Act 77, biomedical research focuses on the application of the natural sciences and is distinguished from clinical and health services research as defined in Act 77.

### **NONFORMULA Health Research Priority for 2005-06 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priority is:

Research into the prevention and treatment of obesity and its complications. Research may include, but is not limited to, research in the following areas:

- Prevention-related health services research applicable to community-, school- and employer-based interventions using techniques that promote and sustain changes in behavior, physical activity, and nutrition; practical approaches for the implementation of effective strategies with applications to underserved populations; and community participatory research and studies that test and evaluate the cost effectiveness of interventions conducted in community, neighborhood and nontraditional settings. School-based approaches should be targeted to all students, not only to obese or overweight children. Research to document disparities will not be considered unless it is part of the research effort to understand, develop and evaluate an intervention to eliminate the disparity.
- Obesity-related health services research to evaluate methods to improve management of obesity and its consequences; novel restructuring of health care delivery, including attention to obesity in primary care; and broad population approaches to address the rising prevalence of obesity.
- Clinical research to test novel treatments for obesity including drugs that affect appetite and metabolism. Intervention studies should include novel approaches to weight loss and further understanding of pathophysiology that may improve maintenance of long-term weight loss and decreased morbidity due to obesity. Studies to evaluate the efficacy of bariatric surgery and other existing obesity therapies will not be considered.
- Translational research that would apply knowledge gained from basic research on obesity to the citizens of Pennsylvania, with an emphasis on comparing high- and low-risk populations. Particular emphasis should be placed on biomarkers and other novel research approaches to the mechanisms of obesity and of obesity-related diseases (for example, diabetes, cardiovascular disease, cancer and osteoarthritis).
- Basic research to gain greater insight into the fundamental mechanisms of obesity, appetite, satiety, metabolic control, and other relevant physiological mechanisms; studies related to adipocyte biology and the molecular and genetic factors leading to obesity, including novel hormones, proteins, and genes related to diabetes and metabolic disorders; and studies aimed at understanding the regulation of energy metabolism and the interrelationships between obesity and disease especially type II diabetes and the metabolic syndrome.

Research should emphasize populations that are at high risk for and/or disproportionately affected by obesity. Research may be focused on children, adults or all age groups. Outcomes, i.e., prevention of weight gain or amount of weight loss, must be measured at various intervals, and there must be a clear indication of how they are to be measured and anticipated effects. Applicants must establish a regional Center of Excellence to conduct

research in collaboration with other research institutions and organizations. The Center of Excellence must include partners that are from smaller colleges and universities. The Center of Excellence should also include biotechnology and bioengineering companies, or other institutions that are not academic medical centers, in addition to major research institutions. The research may include participation by behavioral scientists, exercise scientists, dietitians and nutritionists with expertise in obesity prevention or treatment. The research should hold the potential for population-based applications that address disparities in obesity among underserved segments of the population, including rural, urban, racial/ethnic minorities, or other high-risk Commonwealth populations. The Center of Excellence must build research capacity for health disparities research related to obesity through the mentoring and training of students and collaboration with predominantly minority-serving academic institutions in Pennsylvania. At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **NONFORMULA Health Research Priorities for 2006-07 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities shall involve collaborative Center of Excellence efforts across research institutions and organizations. The research priorities for nonformula-funded research are:

### **Vaccine Development**

Research into the development and/or evaluation of vaccines for viruses, bacteria, and other infectious agents, including cancer vaccines for cancers that are caused by infectious agents, with an emphasis on those vaccines that pose a serious health risk to a significant proportion of the population, including children. All such research must be focused on, and preparatory to, the development of one or more specific vaccines. Research may include, but is not limited to, studies in the following areas:

- Population-based studies of vaccine preventable diseases; predictive modeling of the spread of infections; identification and evaluation of strategies to contain and control the spread of infection.
- Prevention-related health services research aimed at improving the use of newly developed vaccines of proven efficacy among the populations at greatest risk; research to test the delivery and efficacy of relatively new vaccines such as the human papillomavirus (HPV) or new uses of vaccines such as pneumococcal and influenza vaccines for children; practical approaches for the implementation of effective vaccination strategies with applications to underserved populations; community participatory research and studies that test and evaluate the cost-effectiveness of vaccine-based interventions conducted in community, neighborhood, and nontraditional settings; and evaluation of the effectiveness of various outreach methods for improving immunization rates among populations such as Hispanics, rural and urban residents and immigrants.
- Investigations into the basic biology of viral, bacterial, and other infectious agents and how these agents cause disease, including their interactions within the host organism and mechanisms of transmission; studies of how the agent under study relates to other human and animal infectious agents; research on basic human immunology, with an emphasis on the contribution and role of various components of the immune response against the agent being studied; basic research to establish mechanisms of inducing long-lasting protective immunity

against viral and other pathogens; the development of platform vaccine technologies that can be applied to a broad spectrum of disease targets; the conception, design, and preparation of candidate vaccines, ideally agents that are stable, require only one dose, and remain at least partially effective despite mutation in the agent's genome. Relate this to the immunization coverage rate necessary to provide herd immunity for a vaccine.

- Translational research, including clinical trials of candidate vaccines; research on vaccine delivery systems, including DNA vaccines; proof of concept of new platform vaccine technologies; development and testing of adjuvants that would improve vaccine efficacy; development of new methods for large-scale vaccine production.
- Phased clinical trials to test the safety and efficacy of candidate vaccines in human subjects, once appropriate studies have been completed.

Research in the following areas will not be considered:

- Research related to the human immunodeficiency virus (HIV);
- Research addressing tropical diseases, like malaria, that are not highly prevalent in Pennsylvania and are not spread by aerosol transmission;
- Research related to the development of antibiotics; and
- Research related to animal vaccines to prevent zoonotic transmission to humans.

Research should emphasize populations that are at high risk for and/or disproportionately affected by the vaccine-related issue under study. The proposed research should hold the potential for population-based applications that address disparities among underserved segments of the population, including rural and urban residents, racial/ethnic minorities or other high-risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, health care providers and public agencies should be included in addition to major research institutions. To increase research capacity in Pennsylvania, the proposed research must include collaboration with a predominantly minority-serving academic institution in Pennsylvania and should encourage the mentoring and training of students, fellows and junior faculty. Research in health services must include objective evidence of outcomes, including the use of vaccines in a defined community or clinical setting.

At least 50% of each grant's funds must be spent on health services and/or clinical research as defined in Act 2001-77 (Act 77); no more than 50% of each grant's funds may be spent on biomedical research, as defined in Act 77.

### **Gene-Environment Interactions**

Research on gene-environment interactions related to etiology and outcomes of chronic disease including, but not limited to, cardiovascular disease, asthma, serious mental disorders and cancer. Research shall focus on potentially modifiable environmental exposures, or behaviors including nutrition, which are hypothesized to affect disease etiology or outcomes in humans and genes that modify these associations. Research shall include, but not be limited to:

- Several integrated research studies around a common theme to identify: 1) genetic and environmental determinants of disease etiology or outcomes; and 2) biological mechanisms that underlie associations of genes and/or the environment with disease.
- Studies that use a statewide or regional cohort for research on gene-environment interactions in chronic disease etiology and outcomes and health disparities.



- Research involving haplotype and SNP analysis, as well as family studies with major gene effects and candidate genes.

Health services research that will improve the identification of “high risk families” that are disproportionately affected by the interaction of genetics and lifestyles, i.e. environmental agents, and will benefit from specific interventions to reduce risk can be supported by this proposal.

Research should emphasize populations that are at high risk for and/or disproportionately affected by the chronic disease under study. Because of the very large sample sizes required for identifying relatively small, relative risk <2, gene-environment effects, collaborations across institutions in Pennsylvania are strongly encouraged as well as collaborations with the Pennsylvania Cancer Registry or other appropriate state health resources. The proposed research should hold the potential for population-based applications that address disparities among underserved segments of the population, including rural and urban residents, racial/ethnic minorities or other high-risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, health care providers and public agencies should be included in addition to major research institutions. To increase research capacity in Pennsylvania, the proposed research must include collaboration with a predominantly minority-serving academic institution in Pennsylvania and should encourage the mentoring and training for students, fellows, and/or junior faculty. Additionally, resources to identify genetic and environmental contributions to chronic disease etiology and outcomes should be developed for use in future grants and contracts.

Research in the following areas will not be considered:

- Genetic screening without inclusion of specific defined environmental and lifestyle interactions; and
- Gene therapy.

At least 50% of each grant’s funds must be spent on health services and/or clinical research as defined in Act 2001-77 (Act 77); no more than 50% of each grant’s funds may be spent on biomedical research, as defined in Act 77.

## **NONFORMULA Health Research Priorities for 2007-08 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities shall involve collaborative Center of Excellence efforts integrating research efforts from several disciplines. The research priorities for nonformula-funded research are:

### **Regenerative Medicine and Post-Natal Stem Cell Biology**

Research on regenerative medicine including tissue maintenance and repair via repopulation from adult stem cells, with the goal of better understanding health and disease including, but not limited to, cancer, diabetes, stroke, heart disease, vascular disease and age-related disabilities.



Research may include, but is not limited to, studies in the following areas:

- Basic, translational and clinical research into regenerative medicine and its applications.
- Interdisciplinary, collaborative research projects that would support multiple investigators working in diverse research fields. Such fields may include, but are not limited to, cell and developmental biology, engineering (including bioengineering, tissue engineering and nanotechnology), cancer biology and cancer stem cells, veterinary medicine, and dental medicine.
- Development of core research technologies that would be of use to multiple research investigators and teams, such as xenogeneic stem cell transplantation, post-natal stem cell preparation, the development of assays, e.g., identification of stem cell markers, and transduction of genes that modify stem cell behavior, and in vivo imaging.
- Preclinical research projects proposed by individual investigators and groups of investigators.
- Phased clinical trials to test the safety and efficacy of adult stem cells in human subjects, once appropriate studies have been completed.
- New investigator awards to support young physician scientists and basic research investigators to build careers in regenerative medicine, including studies of cancer stem cells, tissue engineering, nanotechnology, and stem cell developmental biology, stem cells in veterinary medicine, and translational medicine.

Applications to establish a regional Center of Excellence for Research on Regenerative Medicine that will integrate core technology resources, multidisciplinary basic, translational and clinical research projects, and career development awards are encouraged.

Research involving studies of or using human embryonic stem cells will not be considered.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or other high-risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology companies, health care providers and public agencies, should be included in addition to major research institutions. The proposed research must include collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania, and should encourage the mentoring and training of students, fellows and junior faculty. Research in health services must include objective evidence of outcomes.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

### **Violence Prevention**

Research on violence prevention that addresses both of the following goals: (1) research to improve the identification of specific high-risk individuals likely to engage in violent behavior in order to further understand the interrelationship between genetic, i.e., host susceptibility, and specific environmental (both social and physical) risk factors, biochemical parameters and both structural and functional brain measurements and (2) research to evaluate, through clinical trials

with these high-risk individuals, the efficacy of interventions that have initially been demonstrated in other studies to reduce violence.

Goal (1): The first goal is to identify very high-risk individuals likely to express violent behavior years before these events. Research may include, but is not limited to, studies that would address the research question of whether or not such behavior is strictly a function of their social and physical environmental exposures early in life, or also a function of exposure to neurotoxic agents among genetically susceptible individuals, or both. Newer brain imaging techniques, including both structural and functional MRI and PET, etc., as well as better measures of identifying neuroendocrine metabolic parameters and prior environmental exposures, offer a unique opportunity to greatly improve the identification of very high-risk genotypes and phenotypes that would make it possible to focus on more intensive primary and secondary prevention approaches.

These studies should include multidisciplinary expertise in psychiatry, psychology, genetics, neuroimaging, biochemistry, epidemiology, social work and community studies.

Goal (2): The second goal is to conduct clinical trials with these high-risk individuals in order to evaluate the efficacy of interventions that have initially been shown in other studies to reduce violence, or interventions that are novel and innovative for which there are preliminary data of potential efficacy. Because it is unlikely that a definitive reduction in violence can be measured in the four-year grant period, these trials should focus on intermediate outcomes that can be evaluated within the four-year period. The intermediate outcomes should be clearly defined, and evidence should be presented to support the outcomes. It is important to note that these trials do not require a placebo control group; researchers may compare alternate therapies or even current intervention programs within the community.

In developing these clinical trials, collaboration with community groups, schools, legal authorities, social service agencies, etc. is strongly encouraged. It is also important that these trials clearly define the sample size, the estimated benefits expected and the power of the trial. It is expected that such studies should include heterogeneous populations at high risk, such as minorities, urban, low SES, rural populations as well as both males and females.

Research in the following areas will not be considered:

- Research that is limited only to the identification of high-risk communities.
- Research that is limited to the identification of high-risk individuals only by age, race, ethnicity, geography or socioeconomic characteristics.
- Research that does not address both goals (1) and (2).
- Ecological studies that compare rates of violent behavior across communities, i.e., an intervention versus control community only.
- Suicide and intentional self-harm.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or other high-risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology companies, health care providers and public agencies should be included in addition to major research institutions. The proposed research must include collaboration with a

minority-serving academic institution or a minority-serving community-based organization in Pennsylvania, and should encourage the mentoring and training of students, fellows and junior faculty. Research in health services must include objective evidence of outcomes.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **NONFORMULA Health Research Priorities for 2008-09 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities shall involve collaborative Center of Excellence efforts integrating research efforts from several disciplines. The research priorities for nonformula-funded research are:

### **Autism Spectrum Disorders**

Research to identify underlying causes of, determine the nature of the brain alterations in, better understand the genetic, metabolic, immunologic or environmental influences on, or improve early diagnosis and treatment of autism spectrum disorders. Research shall be limited to those disorders classified as pervasive developmental disorders (PDD) in the "Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)": Autistic Disorder, Rett's Disorder, Childhood Disintegrative Disorder, Asperger's Disorder, and Pervasive Developmental Disorder Not Otherwise Specified; research on other diagnoses will not be considered. Research may include, but is not limited to, the following areas:

- Studies of genetic and environmental epidemiology to determine risk and protective processes in the etiology of autism spectrum disorders.
- Studies of brain mechanisms underlying the development and regulation of behaviors characterizing autism spectrum disorders.
- Studies of brain maturation during vulnerable developmental periods for the appearance or worsening of specific signs or symptoms of autism spectrum disorders.
- Studies that unravel the complex circuitry of the central nervous system to understand the changes in neural structure and network connections associated with the disorder.
- Studies into the pathogenesis of autism spectrum disorders including research to identify specific autism susceptibility genes, studies that combine imaging and genetic techniques, and studies that examine behavioral and cognitive-genetic variability in autism.
- Studies of the pathology of autism spectrum disorders to identify novel molecular targets for drug development.
- Studies of the pathophysiology of specific components of the clinical syndrome of autism in order to develop novel biomarkers that can be used to monitor new treatment interventions.
- Studies of the correlation between key developmental factors and the valid diagnosis of autism spectrum disorders, including genetic, environmental and epi-genetic studies of families in which more than one child has been diagnosed with an autism spectrum disorder. Such studies should incorporate expertise in genetics, environmental measures and brain neurobiology and imaging.
- Studies to develop new treatments or compare and validate treatment of autism spectrum disorders.
- Studies aimed at developing and testing the efficacy and safety of pharmacologic agents to target the most common and impairing features of autism spectrum disorders.

- Studies to improve practices of healthcare providers and the quality, coordination or delivery of diagnostic and treatment services.
- Studies to establish methods for validated, population based registries of autism that can be utilized for public health research and service evaluation, especially in underserved regions of the Commonwealth.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or other high-risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology companies, health care providers and public agencies should be included in addition to major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students, fellows and junior faculty. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research in health services must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

### **Antibiotic Resistance**

Research to better understand and test approaches to reduce the prevalence of infections caused by antibiotic resistant bacteria in health care settings and in the community and to reduce associated morbidity and mortality of these infections. Research must be focused on bacteria that are resistant to all or most of the commonly-prescribed antibiotics. Research must include one or more of the following approaches: (1) studying the transmission of antibiotic-resistant organisms within community and/or healthcare settings, (2) studying the overuse of antibiotics within community and/or healthcare settings as a risk factor for emerging resistance, (3) evaluating novel approaches to reduce the transmission of antibiotic resistant organisms within community and/or healthcare settings and (4) applied research and clinical trials for products for which proof-of-concept has been demonstrated.

Research may include, but is not limited to, studies in the following areas:

- Development and/or evaluation of rapid, inexpensive, diagnostic tests capable of accurately guiding directed antimicrobial drug therapy, limiting broad spectrum use when unnecessary. Tests may be directed at single or multiple pathogens or biochemical pathways distinguishing infectious etiologies.
- New computational tools in systems biology and metabolomics to identify complex biochemical pathways that can uncover novel mechanism of action compounds.
- New approaches to antibacterial resistance using in vivo analysis of bacterial and host transcriptomes and metabolomes.
- Development of new therapeutic antibiotic drugs and bactericidal biomaterials.
- Clinical trials to determine the safety and efficacy of new drugs and biologics that can be used to treat and control drug-resistant bacterial infections.

- Evaluation of existing and/or novel surveillance systems for usefulness in detecting transmission of antibiotic resistance in the community and health care settings, including determinants of differences in prevalence and type of antibiotic resistance among regions of the Commonwealth, racial and ethnic groups, children and the elderly.
- Development and testing of novel control policies and interventions with healthcare professionals and the public to improve the use of antibacterial agents in humans and preserve the effectiveness of existing antibiotics.

Research in the following areas will not be considered:

- Research related to antimicrobial resistance other than bacterial drug-resistance
- Research to improve the use of antibacterial agents in veterinary medicine
- Research related to the prevention of healthcare infections associated with transplants
- Research related to tuberculosis

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or older adults and other populations that are at high risk for diseases caused by antibiotic resistant agents. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students, fellows and junior faculty. Research should collaborate with the Bureau of Epidemiology in the Department of Health and focus on the identification of areas and subregions of the state with an unusually high prevalence of antibiotic resistant organisms and clinical disease so as to identify the causal pathways and potential remedial actions. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research in health services must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **NONFORMULA Health Research Priorities for 2009-10 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priorities shall involve collaborative Center of Excellence efforts integrating research efforts from several disciplines. The research priorities for nonformula-funded research are:

### **Blindness and Visual Impairment**

Research to understand the underlying etiology of blindness and visual impairment and to evaluate promising new medical, surgical and genetic therapies to prevent and/or treat blindness and visual impairment as well as interventions to reduce disparities in access to care. Priority will be given to projects that emphasize the population aged 40 or older, given Pennsylvania's

disproportionate share of older individuals as well as the over-representation of blinding eye diseases in older individuals.

Research may include, but is not limited to, the following areas:

- Studies of the molecular and genetic bases of common blinding eye diseases, such as macular degeneration, glaucoma, diabetic retinopathy, and cataract.
- Studies to develop new therapies, including molecular, genetic, cellular, or nanotechnologies for retinal regeneration or transplant; optic nerve regeneration; prevention or reversal of cataract; and definitive therapy for diabetes and diabetic retinopathy.
- Studies to determine the extent and degree of cortical plasticity in the adult visual system.
- Studies to improve the quality, coordination or delivery of early detection and treatment services to the aging population.
- Studies of methods to restore vision by leveraging the non-visual senses.
- Studies of novel interventions for reducing barriers to vision care.
- Studies to determine the most efficient and effective approaches to providing vision care to underserved populations.

Research must include, as one component, a demonstration project in a defined population. The demonstration project must include one or more of the following studies: (1) studies to improve the quality, coordination or delivery of early detection and treatment services to the aging population, (2) studies of methods to restore vision by leveraging the non-visual senses, (3) studies of novel interventions for reducing barriers to vision care, (4) studies to determine the most efficient and effective approaches to providing vision care to underserved populations, and/or (5) another demonstration project closely aligned with the proposed research program.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or older adults and other populations that are at high risk for eye diseases. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **Cancer Vaccines**

Research on the development, use and evaluation of vaccines for cancer prevention and treatment. Research in protective or therapeutic cancer vaccines may include, but is not limited to, the following areas:

- Studies to identify novel tumor antigens, particularly those on premalignant lesions, precursors to cancer, and/or cancer stem cells, and to develop vaccines against such antigens.
- Research on strategies to effectively co-deliver antigens and adjuvants to generate tumor-specific cellular immunity.
- Studies to identify novel viral antigens associated with or causatively linked to cancer.
- Studies to identify tumor microenvironment antigens that can be targeted to inhibit angiogenesis or tumor invasion.
- Research on novel adjuvants with potent and specific immunostimulatory function and reduced systemic toxicity such as defensins, cathelicidins, and neurokinins.
- Research on vaccine technologies designed to target dendritic cells and enhance dendritic cell-mediated tumor antigen presentation.
- Studies on epigenetic modulation of known cancer antigens.
- Research on the blockade of immunoinhibitory pathways through receptor antagonists.
- Studies to enhance viral and cancer vaccine effectiveness through immuno-augmentation adjuvant therapies.
- Studies to stimulate immunity to tumor antigens released by dead or dying tumor cells as an adjunct to traditional cancer therapies, including those based on chemotherapy or antibody-dependent cellular toxicity.
- Prevention-related health services research aimed at improving the use of the human papillomavirus (HPV) or hepatitis B vaccine among the populations at greatest risk.
- Analysis of the antigens of tumors in patients treated with immunomodulators that demonstrate antitumor efficacy, such as IL-2, IFN, and anti-CTLA4 blocking antibodies.

Research in the following areas will not be considered:

- Biomedical and clinical research to develop or improve prophylactic vaccines against hepatitis B and HPV.
- Clinical trials on the direct effects of therapeutic cancer antibodies currently approved and on the market (including but not limited to Rituxan, Herceptin, Erbitux, and Avastin).
- Research on cancer vaccines in veterinary medicine.

Research should hold the potential to address the health needs of underserved segments of the population including rural, urban, racial/ethnic minorities or older patients and other populations that are at high risk for cancer. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not traditional academic medical centers such as smaller colleges and universities as well as businesses, biotechnology and pharmaceutical companies, healthcare providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with minority serving academic institutions or minority serving community-based organizations in Pennsylvania are strongly encouraged and should include the mentoring and training of students. All research collaborators must play a substantial and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. In addition to the clinical and basic science projects proposed, the



research must either include an active clinical trial or result in a proposal for an approvable clinical trial at the completion of this body of research. Health services research may include research on any aspect of the selected cancer vaccine including studies of dissemination, patient adherence, behavioral science focused on cancer vaccines, and cost effectiveness research related to hepatitis B and HPV. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **NONFORMULA Health Research Priority for 2010-11 FY**

For the purpose of priority setting and funding, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. The research priority shall involve collaborative research integrating efforts from several disciplines and institutions. The research priority for nonformula-funded research is:

### **Substance Abuse**

Research to understand the biological basis of addiction and the neural changes that can lead to addiction and to evaluate interventions to prevent and treat addictions. The research should focus primarily on addiction to illicit drugs, but should not exclude research on alcohol or tobacco use as co-morbidities to illicit drug use or research on polydrug use. Illicit drugs include, but are not limited to, marijuana or hashish, opium, heroin, cocaine (including crack), inhalants, hallucinogens (including phencyclidine [PCP], lysergic acid diethylamide [LSD], and Ecstasy [MDMA]), or prescription-type psychotherapeutics used nonmedically, which include stimulants, sedatives, tranquilizers, and pain relievers (including opioid analgesics). Opioid analgesics include methadone, other opioids such as oxycodone and hydrocodone, and synthetic narcotics such as fentanyl and propoxyphene.

Research may include, but is not limited to, the following areas:

- Research to investigate why certain substances are addictive and what happens to cells in the brain to cause craving; which neural circuits, cells, and mediators in the brain are involved in substance abuse and how can they be modulated to break the cycle of addiction; how various substances of abuse affect brain cells, targets in the brain (receptors and transporters), communication between brain cells, and pathways that are important in behavior; how the brain changes with substance use, whether the effects are dose-dependent, when brain changes become irreversible, how brain changes alter behavior, and how people vary in their adaptive changes in brain function with substance use.
- Research on the mechanisms of drug interactions and co-drug dependency, how multiple drugs interact with each other and the brain to potentiate each other in terms of addiction risk, and how this cycle can be “short-circuited.”
- Research on animal models to elucidate the functional brain impairments associated with substance use and addiction.
- Research on the use of noninvasive brain imaging to identify brain regions and neural pathways that are differentially activated during drug addiction.

- Research to determine whether potential therapeutics for the management of substance use disorders can be identified by their ability to alter addiction-associated patterns of brain activity.
- Research on how host susceptibility, genetic factors, and environmental factors interact to contribute to addiction susceptibility, particularly early life environmental exposures and their effects on the brain.
- Research on the genetic and epigenetic factors that influence life-time risk of substance abuse.
- Research on risk factors that influence the initiation of substance use, addiction to substances and relapse from substance abuse treatment.
- Research on the use of genetic and genomic information to tailor individualized approaches to substance abuse prevention and treatment.
- Research on the measurement of risks for and severity of addiction.
- Research on disorders and risky behaviors that co-occur with substance abuse disorders and how these co-morbidities can be managed effectively.
- Research on the genetic, neurological, social, and contextual factors that influence the effectiveness of programs aimed at preventing substance use and abuse in late adolescence and early adulthood.
- Research on the impact of a chronic, continuing care versus acute care addictions treatment model on the costs of treatment and health outcomes.
- Research to determine which program delivery approaches maximize program sustainability, barriers to the implementation of evidence-based practices, and how evidence-based practices can be implemented most effectively through all phases of prevention and treatment, including diagnosis, intervention, and long-term follow-up.
- Research on interventions for individuals for whom current approaches are ineffective.
- Research on the barriers to the implementation of substance abuse screening in primary care settings, effective approaches to expand screening for substance use disorders in health care settings, and tools and technologies to better identify which patients will respond to various types of treatment approaches for use in substance abuse screening.
- Research to determine the efficacy of new therapies to prevent or treat addiction. Testing of such interventions should include objective evidence of prevention or treatment in defined cohorts.

Research in the following areas will not be considered:

- Research focused primarily or exclusively on addictions other than illicit drugs. Research focused primarily or exclusively on gambling, addictive sexual behavior, obesity and food addiction, tobacco use and alcohol abuse will not be considered.
- Research on the benefits of any substance of abuse.
- Research on the abuse or misuse of antibiotics.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, and other populations that are at high risk for substance abuse. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is

strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.

At least 50 percent of each grant's funds must be spent on clinical and/or health services research as defined in Act 2001-77; no more than 50 percent of each grant's funds may be spent on biomedical research, as defined in Act 2001-77.

## **NONFORMULA Health Research Priorities for 2011-12 FY**

For the purpose of priority setting, the Health Research Advisory Committee recommends keeping the *clinical and health services research* nonformula funding category separate from the *other research* funding category. Funding for the commercialization priority must be spent on biomedical research and/or clinical research and/or health services research. Funding for the translational genomics priority must be spent on clinical research and/or health services research; none of the funding for the translational genomics priority can be spent on biomedical research. The research priorities for nonformula funded research are:

The research priority for 50 percent of nonformula funds is:

### **Commercialization of Research Related to Cancer Diagnostics and Therapeutics**

The primary purpose of this priority is to support research activities that commercialize and bring to market new cancer diagnostics and therapeutics for which proof of concept has previously been demonstrated, that is, preliminary data confirm that the product, technology or approach is capable of solving or diminishing a specific problem related to the diagnosis or treatment of one or more malignant diseases. Research activities should lead to a better understanding of the biology and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability, ultimately leading to improvements in the health of all Pennsylvanians. A goal of this initiative is commercialization of innovations derived from prior research endeavors.

Research may include, but is not limited to, the following areas:

- Research to reduce health disparities through the development of medical technologies that are affordable, accessible and acceptable to the targeted populations
- Research to develop technologies, reagents, instrumentation, and methodologies to improve cancer diagnosis or treatment or to predict or assess response to therapy
- Research on new therapeutics and monitoring technologies for cancer
- Research on medical imaging systems for cancer screening and early cancer detection or image-guided cancer interventions
- Research aimed at the discovery or development of health-related nanoscale and nanostructured technologies, devices and systems for the diagnosis or treatment of cancer

Research in the following areas will not be considered:

- Research related to cancer vaccines
- Research on cancer diagnostics and therapeutics that are currently approved by the Food and Drug Administration for commercial use.

Funds shall be used for biomedical research and/or clinical research and/or health services research, as defined in Act 2001-77. Activities that are not biomedical, clinical or health services research as defined by Act 2001-77 will not be considered. Collaboration between business and academic institutions is encouraged. The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, and other populations that are at high risk for the health condition addressed by the proposed research project. Research proposals should include a reasonable sustainability plan including but not limited to how the project will contribute to the growth or maintenance of a sustainable business entity; how the innovation will be produced and marketed; how revenues will be generated to commercialize the innovation and other funding sources; and the organization's prior commercialization experience. No more than 50% of the funds may be used for research infrastructure as defined in the Act, as amended. Research infrastructure is defined as including the following items: office equipment, office supplies, nonprofessional personnel, and laboratory or building construction or renovations, used to conduct research.

The research priority for 50 percent of nonformula funds is:

### **Translational Genomics**

Research to evaluate the clinical utility of genomic information for improving patient outcomes and clinical decision making.

Advances in genomics have the potential to improve the delivery of health care by targeting interventions to individuals who, due to genetic factors, will receive the greatest benefit and experience the lowest risk of adverse events. The promise of personalized medicine for improving health outcomes has led to investment in research to sequence the human genome and identify genetic markers for disease and disease outcomes. The success of this investment depends on the ability to translate these discoveries into clinical practice. Although a number of associations linking genetic variants with disease susceptibility or drug metabolism profiling have been identified, there are few rigorous, prospective studies demonstrating the presence or absence of specific variants with specific outcomes, such as improved therapeutic response or reduction in adverse events. Clinical studies integrating genomic findings into clinical trials and population-based studies are necessary to justify the increased costs of testing.

While advances in genomics have the potential to improve clinical decision making by identifying who will and will not benefit from an intervention, comparative effectiveness has the potential to improve health care outcomes and reduce health care costs by determining the relative clinical and economic impact of alternative interventions. Comparative effectiveness research examines differences in outcomes across populations of patients, focusing on whether the "average" patient would benefit from a given intervention. However, even for interventions found to be effective, the benefit often accrues to only a minority of patients in the population. The ability to identify which patients will and will not benefit from an intervention based on genetic factors could greatly increase the impact of comparative effectiveness research and the utility of personalized medicine.

There is a critical need to generate the evidence necessary to ensure the effective translation of genomic tests into improved health and health care. This research falls into the gap between comparative effectiveness research and basic research to identify novel genetic factors that are associated with response to therapy or risk of disease. The focus of this research is on evaluating

and maximizing the clinical utility of genomic information, including the impact of genomic information on clinical decision making and patient outcomes, the ability for genomic information to predict who will and will not benefit in a comparative effectiveness study, and the dissemination and utilization of evidence based strategies for the use of personalized medicine to improve health care value.

Research may include, but is not limited to, the following areas:

- Research to evaluate how therapies tailored to genomic information compare to standard therapies in prevention, screening and treatment in terms of health care cost and outcomes
- Research to evaluate the impact of genomic information compared to existing methods of individualizing health care services including methods which use family history of disease or individual behavioral risks to tailor prevention, screening and treatment.
- Research to determine how well genomic information can predict individual outcomes in comparative effectiveness studies, including clinical trials and prospective cohort studies
- Research to determine how the use of genomic information influences clinical decision making and patient outcomes
- Research to evaluate the effects of incorporating genomic risk prediction into electronic medical records
- Research to identify patient, provider and system barriers and interventions to overcome barriers to the implementation of personalized strategies for prevention, screening and treatment

Research in the following areas will not be considered:

- Identification of novel genomic markers for disease and disease outcomes
- Comparative effectiveness research that does not include the evaluation of genomics strategies for personalized medicine.
- Use of Genome Wide Association Studies (GWAS) or similar techniques to develop risk scores based on multiple SNPs alone. However, such approaches could be used to select high risk subjects for preventive or clinical therapeutic studies which are focused on evaluating the utility of genomics.
- Studies that include only investigation of somatic mutations.
- Gene therapy.

Funds must be used for clinical research and/or health services research, as defined in Act 2001-77. None of the funds can be used for biomedical research as defined as defined in Act 2001-77.

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or older adults and other high risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather

than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating. No more than 50% of the funds may be used for research infrastructure as defined in the Act, as amended. Research infrastructure is defined as including the following items: office equipment, office supplies, nonprofessional personnel, and laboratory or building construction or renovations, used to conduct research.

## **NONFORMULA Health Research Priorities for 2013-14FY and 2014-15 FY**

The nonformula research priorities for 2014-15 are big data in health research and an expanded access study on the effect of pharmaceutical grade Cannabidiol (CBD) in children with intractable epilepsy. The 2013-14 FY funds, which were put on hold due to the master settlement arbitration, were released during the 2014-15 FY and were combined with the 2014-15 FY funds.

For the purpose of priority setting, the Health Research Advisory Committee recommended combining the two nonformula funding categories of clinical and health services research and other research. At least 50 percent of the funds must be spent on clinical research and/or health services research. The research priorities for nonformula-funded research are:

### **Big Data in Health Research**

The priority is research to develop methods, software, and other technologies designed to analyze vast data sets at the level of molecules, proteins, organelles, cells, tissues, organs, physiological systems, organisms, populations, health care systems, and ecosystems.

With the rapid expansion of high-throughput laboratory technologies and electronically integrated health care systems, biomedical researchers have access to more and more complex data than ever before. Vast data sets exist at the level of molecule, protein, organelle, cell, tissue, organ, physiological system, organism, population, health care system, and ecosystem. Health care systems now electronically record an ever-increasing volume and variety of variables from patient monitoring systems, imaging, and “omics” technologies as well as data in electronic health records (EHRs). The major challenge now is to manage these large and growing data sets and discover within them insights that can guide future research, education, and clinical care.

Pennsylvania institutions are currently well represented in major national health research initiatives focused on big data, including the National Institutes of Health (NIH) Big Data to Knowledge (BD2K) and the Patient-Centered Outcomes Research Institute (PCORI) Clinical Data Research Networks (CDRN). The Commonwealth is well positioned to take a leadership role in advancing the field and exploiting its expertise and resources for significant advances in biomedical research and health care. The goal moving forward is to embrace the size and complexity of available data through the transfer, merging, storage, visualization, and processing of disparate data and the use of new algorithms and software tools to computationally discover predictive and causal relationships.

Research activities should lead to improved design, implementation, and utilization of data systems, both research and clinical, to enhance the exploitation of data from the molecular to the population level to improve the health and well being of Pennsylvanians.

Funding for the big data priority must be spent on biomedical research and/or clinical research and/or health services research as defined in Act 2001-77. Activities that are not biomedical, clinical, or health services research as defined by Act 2001-77 will not be considered.

Research may include, but is not limited to, the following areas:

- Research to develop algorithms and software/application programming interfaces to discover causality in big data from multiple sources. Some examples of driving biomedical projects on which to focus these efforts include cancer metastases, neurodegenerative disorders, and autoimmune diseases.
- Research that integrates uni- or multimodal, multiplatform, and/or multiscale data across diverse data types and sources (e.g., omics, imaging, laboratory, clinical, socioeconomic, environmental, social media, wearable or mobile devices, company loyalty programs, self-reported data) to create single or multiscale models of molecular, cellular, organ, system, organism, or population processes or behaviors. Some examples of driving biomedical projects on which to focus these efforts include obesity, chronic obstructive pulmonary disease, non-alcoholic fatty liver disease, and infectious disease outbreaks/epidemics.
- Research focused on the integration and mining of the EHR systems of multiple health care providers and systems across the Commonwealth for comparative effectiveness research or modeling. Some examples of driving clinical projects on which to focus these efforts include atrial fibrillation, diabetes mellitus and otitis media.
- Research to develop and test in community-based health care systems analytics software to identify linkages at the patient level (e.g., clinical flags raised through comparison with hundreds to millions of other patients in the database with similar data) and at the system level (e.g., quality assurance flags raised when trends are detected). Some examples of driving clinical projects include post-surgical complications, preventive screening, rare diseases, and pharmacogenomic testing indicators.
- Clinical and/or health services research that integrates multiple data sources through cloud computing in a way that addresses issues related to security, confidentiality, and consent.
- Research to model statewide health behaviors, trends, and needs prediction through the merging of multiple large data sets, including the integration of statewide datasets (e.g., Pennsylvania Health Care Cost Containment Council [PHC4], Pennsylvania Cancer Registry, Epidemiologic Query and Mapping System [EpiQMS], Behavioral Risk Factor Surveillance System [BRFSS], Pennsylvania Statewide Immunization Information System [PA-SIIS]).

Research in the following areas will not be considered:

- Focus on enhancing computing infrastructure
- Focus on data collection/generation or the development of technology to generate data
- Secondary statistical or epidemiological analysis of single large data sets (or multiple comparable data sets of the same type of data)
- Narrow focus on a single disease without demonstration of generalizability of the selected approach to health research or clinical care more broadly
- Genome-wide association studies or other research focused on identifying disease risk or cause rather than on developing methods for using large omic or other data sets to identify disease risk or cause
- Design and development of registries, tissue banks, and other health data systems

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, older adults, and/or other high-risk constituencies in the Commonwealth. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in



collaboration with other research institutions and organizations. Collaboration between academic institutions, health care systems, health care insurers, public health agencies, and/or business is encouraged. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities and local public health agencies, should be included in addition to major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must include clear objectives and targeted outcomes. No more than 50% of the funds may be used for research infrastructure as defined in the Act, as amended (e.g., equipment, supplies, nonprofessional personnel, and laboratory or building construction or renovation).

### **Expanded Access Study on the Effect of Pharmaceutical Grade Cannabidiol (CBD) in Children with Intractable Epilepsy**

The purpose of this priority is to implement an expanded access study using pharmaceutical grade Cannabidiol (CBD) compound for the treatment of medication-resistant forms of pediatric intractable epilepsy. The study will provide both compassionate care to children with intractable epilepsy and contribute scientifically valuable safety and efficacy data to existing research on the use and effect of CBD on seizure frequency in pediatric intractable epilepsy.

In preparation for the release of this research priority, the Pennsylvania Department of Health (DOH) entered into an agreement with a manufacturer of pharmaceutical grade CBD. This manufacturer will provide a course of treatment for fifty pediatric patients at no cost to the awardee. The drug, in turn, must be provided to the study participant at no cost. The awardees will work directly with the manufacturer to secure, manage and distribute the drug in accordance with its United States Food and Drug Administration's (FDA) approved expanded access drug status.

The scope of this priority is statewide to ensure eligible patients from across the Commonwealth an opportunity to participate. Interested applicants must demonstrate a capacity to provide statewide patient access. Though all applications must designate a lead institution or health care provider, applicants are encouraged to partner with fellow research institutions and health care providers to ensure convenient access sites for patients. Partnership applications must outline planned roles of all named partners and the lead organization's plan for the management of those partners. Special consideration will be given to applicants who provide local access sites in areas not currently served by existing pharmaceutical grade CBD distribution programs.

Proposed studies, to meet FDA's Expanded Access to Investigational Drugs for Treatment Use requirements, must enable access to an investigational drug for the treatment of patients with serious or immediately life threatening conditions that lack therapeutic alternatives but do not meet the requirements for inclusion in clinical trial. The protocol included in this research priority serves as a model protocol template to ensure FDA approval of expanded use of CBD. The awardee must at minimum adhere to and use the template. Applicants are able to tailor the protocol template to meet their studies' needs as long as they adhere to these essential elements. An FDA consultant has been appointed to provide regulatory services for the submission of the protocol to the FDA as an Expanded Access Investigational New Drug (IND), free of charge to the investigator.

CBD is currently considered a Schedule I drug. In order to dispense the product the physician investigator will need to obtain the appropriate Schedule I licensing. The services of a Drug Enforcement Administration (DEA) consultant will be provided free of charge to the investigator. The costs associated with licenses will be the responsibility of the awardee. CBD will need to be stored in a safe in accordance with the Federal and state regulations. The awardee will be responsible for the cost associated with that storage.

Additionally, the awardee will be required to phenotype seizures in a way that is compatible and repeatable, and can be compared to national data. An example of this is the Epilepsy Drug Consortium. Any costs associated with this requirement are the responsibility of the awardee.

## **NONFORMULA Health Research Priorities for 2015-16FY**

For the purpose of priority setting, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. At least 50 percent of the funds must be spent on clinical research or health services research or both clinical research and health services research. The research priorities for SFY 2015-16 nonformula funded research are:

### **Health Care Innovation**

This research priority focuses on the comparative effectiveness and implementation of strategies to improve cost-effective population health management and health outcomes. These strategies could include innovative service delivery models, remote monitoring technologies, decision support tools, staffing models, behavior change strategies, communication techniques, and data analytics, among others.

Decades of fee-for-service payment has led to a health care delivery system focused on the volume of services provided. The increasing adoption of value-based payment methodologies over the past several years has put health care providers at financial risk for the value they provide to patients and populations. This evolution in health care financing is largely driven by concerns that despite spending far more than any other country on health care, the United States ranks relatively poorly on metrics of population health. Health care innovation has largely focused on patient care within hospitals or outpatient clinical offices and has been slower to focus on improving health outcomes in communities where people live, learn, work, and play. Many studies have shown that patients' health behaviors (for example, smoking, eating, physical activity, medication adherence, and / or substance use) are responsible for a large portion of patients' morbidity and premature mortality. Advances in the use of big data to identify populations at risk with modifiable risk factors can help with better targeting, but targeting is not a solution by itself. New interventions are needed to improve the health of populations.

Research in this area will link clinical experts with social scientists and operations researchers to design the health care delivery system of tomorrow: one that focuses on keeping people healthy and not just on treating them once they get sick. This priority will emphasize the use of technology and new means of remote monitoring and chronic disease management to identify best practices that are implementable across a variety of health care delivery settings in Pennsylvania.

Research may include, but is not limited to, the following areas and questions:

- Research to determine the most effective population health management strategies

- Research to determine best approaches for patient engagement in improving health outcomes
- Research to determine right balances of personnel and technology to achieve population health management goals in economically sustainable ways
- Research to determine how best to engage health care providers in value-based payment methodologies, including pay-for-performance, patient-centered medical homes, and accountable care organizations
- Research to ascertain methods to pre-identify patients or patient subgroups most likely to respond to different population health management or clinical approaches

Research in the following areas will not be considered:

- Testing of specific drugs, devices, or diagnostic tools in isolation
- Research in nursing homes or other long-term care facilities

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, or older adults and other high risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating. No more than 50 percent of the funds may be used for research infrastructure as defined in the Act, as amended. Research infrastructure is defined as including the following items: office equipment, office supplies, nonprofessional personnel, and laboratory or building construction or renovations, used to conduct research. Any proposals submitted under this initiative must include explicitly defined outcomes of clinical or economic relevance or both that can be objectively evaluated against reasonable comparators.

### **Traumatic Brain Injury**

Traumatic brain injury (TBI), including concussions, skull fractures, and other intracranial injuries, is a major cause of death and disability in the United States, contributing to about 30 percent of all injury-related deaths. In Pennsylvania alone, there were 2,225 deaths from injury involving TBI in 2010. Nationwide, about 2.5 million emergency department visits, hospitalizations, or deaths were associated with TBI—either alone or in combination with other injuries. These figures do not account for injuries sustained outside of the country by service members who are particularly vulnerable to TBI from blast-related injuries during training and combat.

TBI disproportionately affects certain Pennsylvania populations. From 2006-2010, rural citizens showed significantly higher age-adjusted TBI death rates than urban men and women, and black men showed significantly higher TBI death rates than white men for all age groups under 40 for

which there are data. Mortality rates for trauma victims in rural areas are twice those of urban victims. In 2010, 3.5 million people, or about 27 percent of the state's 12.7 million residents, lived in Pennsylvania's 48 rural counties, and this population is expected to increase another three percent by 2030.

TBI, caused by direct or indirect blows to the head or body, is most often caused by falls, which disproportionately affect the oldest and youngest populations; unintentional blunt trauma, including sports-related concussions and blasts experienced by miners; motor vehicle crashes; and assaults. Individuals who survive TBI can face anything from minor, short-term effects lasting a few days to disabilities and disorders that last a lifetime. It is well documented that progressive neurological dysfunction is observed after repetitive traumatic brain injury, including concussion, in high-impact sport athletes and in soldiers. Sequelae of TBI can include neurodegenerative syndromes like chronic traumatic encephalopathy and Alzheimer's disease (AD). The long-term disease burden of brain disorders is staggering—both in terms of human suffering and economic cost. For example, it is estimated that for AD and other dementias, care costs over the next several decades will exceed \$20 trillion nationwide.

Research may include, but is not limited to, the following areas and questions:

- Develop technologies that improve prevention or diagnosis or both of TBI and its long term consequences
- Research on eliminating barriers to diagnosis and treatment of TBI in rural and minority populations
- Research on improving outcomes for individuals after early detection of TBI and its long-term sequelae in vulnerable populations
- Research to determine risk factors (for example genetics, drug use, hypertension) that predispose individuals to increased risks of neurodegenerative disease following TBI
- Elucidate the fundamental molecular mechanisms that underlie post-TBI neurodegenerative disease pathologies to develop a new generation of preventive measures and treatments to mitigate these effects
- Research that explores the similarities between mechanisms of TBI-related neuronal death and neuronal damage that occurs in other neurodegenerative diseases.
- Research on developing candidate compounds that slow or halt progression of post-TBI neurodegenerative diseases
- Research on delineating the relationship between TBI and its sequelae through longitudinal studies
- Research to determine the differences between neurodegenerative pathologies in individuals who suffered and those who have not suffered TBIs through longitudinal studies

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial and ethnic minorities, or older adults and other high risk Commonwealth populations. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses, biotechnology and pharmaceutical companies, health care providers and local public health agencies should be included in addition to major research institutions. At least two of the collaborators must be major research institutions. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed

research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating. No more than 50 percent of the funds may be used for research infrastructure as defined in the Act, as amended. Research infrastructure is defined as including the following items: office equipment, office supplies, nonprofessional personnel, and laboratory or building construction or renovations, used to conduct research.

### **NONFORMULA Health Research Priorities for 2018-19FY**

For the purpose of priority setting, the Health Research Advisory Committee recommends combining the two nonformula funding categories of clinical and health services research and other research. At least 50 percent of the funds must be spent on clinical research or health services research or both clinical research and health services research. The research priority for SFY 2018-19 nonformula funded research is:

#### Collaborative Research on Opioid Abuse and the Overdose Crisis

One of the most devastating health crises to have emerged during the past decade has been the widespread prevalence of opioid and heroin abuse and addiction, contributing to a dramatic rise in overdose deaths across the United States. From 2000-2015, one-half million deaths nationwide have been due to overdose, with 60 percent of these emanating from opioid or heroin use. The opioid epidemic in Pennsylvania is especially problematic, registering the eighth highest overdose death rate in the country at nearly 22 deaths per 100,000 people in 2014. Nationwide in 2014, Pennsylvania had the third highest number of opioid deaths with 2,732 behind only California with 4,521 and Ohio with 2,744.

Pennsylvania's rural areas are overwhelmed with the challenges of meeting the needs of overdose victims. Rural communities face limited availability of mental health services and few options for dealing with dependency. Since 2014, the Center for Rural Pennsylvania has held 11 public hearings on confronting the heroin and opioid epidemic in Pennsylvania and on the impacts this epidemic is having on rural counties.

Pennsylvania's largest urban areas are also experiencing surges in overdoses. In Philadelphia, the number of opioid deaths increased by almost 30 percent from 2015 to 2016, with a total amount of 900 deaths. Allegheny County had a 44 percent increase in opioid overdose deaths from 2015-2016, with opioids factoring into over 60 percent of its 613 overdose deaths. Allegheny County emergency room visits for overdoses doubled during that year, to a total of 5,698 visits.

There are two overarching pathways to opioid addiction that are driving the surge in deaths. One relates to the prevalence of prescription use, evolving to addiction, overdose and death; the other relates to behavioral and mental health issues that result in drug dependency, also leading to overdoses and deaths. Further concerns relate to the challenges associated with treating individuals who have become dependent on opioids. There is currently no cure for opioid addiction; rather, the option available for treatment involves combining medication, counseling, and recovery meetings to support individuals to maintain sobriety. This approach necessitates a deepening of research to improve health care delivery systems, including the role that precision medicine, data analytics and telehealth may have on mitigating the impacts of the crisis.

Research for this priority may include, but is not limited to, the following areas:

- Research to investigate the use of precision medicine in the prevention, treatment and recovery from opioid use disorder;
- Research to identify the barriers and best practices needed to evaluate methods for improved pain management or opioid use disorder or both and its consequences;
- Research related to restructuring the health care delivery system, including attention to pain or opioid disorder in primary care or both; and
- Research related to broad population approaches to address the rising prevalence of opioid use disorder.

Research in the following areas will not be considered:

- Research focused on drug discovery to identify or develop new agents for treating pain or opioid addiction or both.
- Research focused on the benefit of opioids
- Research focused exclusively on any other substance of addiction, for example, other illicit drugs, cannabinoids, alcohol, tobacco and food

The research should hold the potential for addressing the health needs of underserved segments of the population, including rural, urban, racial/ethnic minorities, older adults and/or other high-risk constituencies in the Commonwealth. To foster cross-institutional collaborative research among organizations across the Commonwealth, an applicant must conduct research in collaboration with other research institutions and organizations. To the extent possible, organizations that are not academic medical centers, such as smaller colleges and universities, businesses and local public health agencies, should be included in addition to major research institutions. Collaborations with organizations already focused on the opioid epidemic are strongly encouraged. Collaboration with a minority-serving academic institution or a minority-serving community-based organization in Pennsylvania is strongly encouraged, and should include the mentoring and training of students. All research collaborators must play a substantive and meaningful role in multiple aspects of the proposed research. Research proposals must be organized around specific focused topics or issues rather than a wide range of unrelated projects. Health services research must include objective evidence of outcomes. Research must test at least one hypothesis, not be merely descriptive or hypothesis-generating.