Personalized medicine, the use of new methods of molecular analysis and bioinformatics to better manage a patient’s disease or predisposition to disease, is likely to change the way drugs are discovered and medicines are prescribed. This type of innovation is associated with considerable scientific uncertainty and financial risk. However, the political and financial systems that will support personalized medicine are not yet aligned to allow these advances. As with any paradigm shift, systemic changes in policy and reimbursement must be made to accommodate the new paradigm.

In this spirit, a series of proposed legislative incentives for personalized medicine have been developed and vetted within the Personalized Medicine Coalition. If enacted legislatively, it is anticipated that these incentives will help usher in a new, more efficient era of health care that improves quality and reduces cost. These incentives are designed for products subject to FDA regulation as these processes add risk, time and expense to the product development cycle. These incentives do not apply to laboratory-developed tests (LDTs). LDTs are conducted by the laboratory that develops the test and are thus a service, not a product for the purposes of this document.

There are several reasons for incenting personalized medicine through the legislative process:

1. Congress has a history of authorizing tax credits to stimulate scientific innovation that promises societal benefit. Without such incentives companies may be unable or unwilling to invest in promising lines of research because of the uncertainties about their costs and return on investment. Thus, policy makers in government believe that taxes credits foster technological advances that will lead to long-term economic growth.

2. For health plan coverage, personalized medicine style diagnostics and therapeutics targeted to an individual’s molecular structure must still require randomized clinical trials that cost the same regardless of market size for the resulting products. Federal incentives such as R&D grants or tax credits can reduce this burden.

3. Changes to the regulatory environment for personalized medicine products currently being considered by the FDA may increase the cost of developing such products. Federal incentives such as having an expedited clearance process for personalized medicine products can reduce this burden and increase the attractiveness of developing these types of products.

4. Reimbursement levels for diagnostics are currently often too low to produce a return on investment for the developer. For example, Genomic Health has developed a test and has successfully achieved a value-based price for their diagnostic test since 2004. However, even with the test being covered at the cost of about $3500, the company has yet to see a return on its investment. The cost to develop the test, conduct the appropriate clinical trials necessary to produce clinical utility information, and market the test, has yet to be recovered by the company. Grants or tax credits for R&D would help reduce the burden of development and allow innovative companies to enter the market in a stronger position.

Personalized medicine is at an inflection point. Many leaders in the field believe that we will not see the launch of many personalized medicine products in our current regulatory and reimbursement environments or that these products will be severely delayed. Given the changing nature of the environment for personalized medicine products, and the ever increasing cost of traditional drug development, legislative incentives could go a long way to moving personalized medicine forward at a rapid pace.
Definitions: The definitions that follow apply to all incentives

**CLIA:** The Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 263a).

**Eligible taxpayer:** A taxpayer who has developed and received FDA marketing approval or clearance for a companion diagnostic product or companion therapeutic product.

**Genetics:** The study of heredity and variation in living organisms.

**Genomics:** The study of an organism’s entire genome.

**Laboratory Developed Genetic Test:** A genetic test that is designed, validated, conducted, and offered as a service by a clinical lab subject to CLIA using either commercially available analyte specific reagents (FDA regulated) or reagents prepared by the laboratory (not FDA regulated) or some combination thereof (from S.976, 110th Congress).

**Personalized Medicine:** Personalized medicine is the application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, and help determine a patient's predisposition to a particular disease or condition (from S.976, 110th Congress).

**Pharmacogenomics (PGx):** Pharmacogenomics is the study of how genes affect a person's response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and dosing regimens that will be tailored to an individual's genetic makeup (from S.976, 110th Congress).

**Qualified companion diagnostic:** A diagnostic product cleared or approved by the Secretary of HHS under section 510 (k) or section 515 of the Federal Food, Drug, and Cosmetic Act for use in conjunction with a therapeutic product to inform treatment selection, initiation, dose customization, or avoidance.

**Qualified companion therapeutic:** A therapeutic product approved by the Secretary of HHS under 510(b)(1) of the Federal Food, Drug, and Cosmetic Act or under section 262 of the Public Health Service Act for which a companion diagnostic product is available.
Category: Research and Development

Title: Research, Development, and Experimentation Tax Credit for Therapeutic and Molecular Diagnostic Combinations.

Rationale: Because FDA review creates additional costs for diagnostic test developers and many qualified companion diagnostic products for personalized medicine are new to FDA review, the FDA review process should be incented. Not every diagnostic product will undergo FDA review but this incentive is for those qualified companion diagnostic products for personalized medicine that do undergo FDA review and therapeutics developed with them. Historically, diagnostics and therapeutics have been developed separately. Incenting the development of these two products together will motivate partnerships that might otherwise not develop.

Purpose: Authorize a tax credit for the cost of research, development, and experimentation, including post-market studies, of qualified companion diagnostics to improve the personalization and effectiveness of medical therapies. Such activities are expected to improve patient’s response to treatments and/or decrease adverse events, which are a major contributor to patient’s morbidity and mortality and very costly. Improving the effectiveness, responsiveness, and safety of drugs will have the long-term benefit of reducing healthcare costs associated with morbidity and treating adverse events.

Intended for:
1. Diagnostic and therapeutic developers.
2. Research, development, and experimentation expenses paid or incurred in connection with the development of a qualified companion diagnostic product.
3. Research and experimentation of a qualified companion diagnostic product with the intent of improving the safety, efficacy or responsiveness of a pharmaceutical compound or class of compounds after they have entered the marketplace.

Tax credit should:
1. provide tax credits to offset the market segmentation that results from personalizing medicine in that companion diagnostics potentially segment the market in such a way that populations served by targeted therapeutics are smaller than the universe of patients that might be available to a pharmaceutical compound otherwise;
2. carry forward so that small and/or not profitable companies can take advantage of this tax credit when it is helpful to them;
3. transfer to a partner company if one company is unable to take advantage of the credit during the tax-credit-window;
4. be available for clinical validation and utility research studies up to five years after product launch; and
5. be good for up to five consecutive tax years starting with the first year that the credit is used.

Sample language:
Adapted from S. 3822, the “Genomics and Personalized Medicine Act of 2006,” 109th Congress. Original text altered.

(1) TAX CREDIT FOR RESEARCH AND DEVELOPMENT RELATED TO COMPANION DIAGNOSTIC TESTS OR COMPANION THERAPEUTICS-
(A) IN GENERAL.—Subpart D of part IV of subchapter A of chapter 1 of the Internal Revenue Code of 1986 is amended by adding at the end the following new section:

`SEC. 45N. COMPANION DIAGNOSTIC TEST CREDIT.

(a) Allowance of Credit.—For purposes of section 38, in the case of an eligible taxpayer—

(1) the companion diagnostic test credit for any taxable year is an amount equal to the qualified research expenses paid or incurred by the taxpayer during the taxable year in connection with the development of a qualified companion diagnostic test; and

(2) the companion therapeutic credit for any taxable year is an amount equal to the qualified research expenses paid or incurred by the taxpayer during the taxable year in connection with the development of a qualified companion therapeutic.

(b) Eligible Taxpayer.—For purposes of this section, the term `eligible taxpayer' means a taxpayer—

(1) who has been requested by the Secretary of Health and Human Services to develop a qualified companion diagnostic test;

(2) who has entered into a formal partnership with a company developing a qualified companion therapeutic if such taxpayer has entered into such partnership for the purpose of developing a qualified companion diagnostic test to provide information with respect to such therapeutic; or

(3) who—

(A) is developing a qualified companion therapeutic with respect to which a partnership agreement is entered under paragraph (2); or

(B) has developed a qualified companion therapeutic with respect to which a qualified companion diagnostic test is available.

(c) Qualified Companion Diagnostic Test.—For purposes of this section, the term `qualified companion diagnostic test' means a diagnostic product—

(1) that is required to be cleared or approved by the Secretary of Health and Human Services under section 510(k) or section 515 of the Federal Food, Drug, and Cosmetic Act; and

(2) that is intended to provide information on treatment selection or dosing with respect to a qualified companion therapeutic.

(d) Qualified Companion Therapeutic.—For purposes of this section, the term `qualified companion therapeutic' means a therapeutic product required to be approved by the Secretary of Health and Human Services under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act or under section 262 of the Public Health Service Act.

(e) Qualified Research Expenses.—For purposes of this section, the term `qualified research expenses' has the meaning given to such term under section 41(b).

(f) No Double Benefit—
Category: Research and Development

Title: Expansion and Acceleration of Genetic and Genomics Research.

Rationale: Expanded and accelerated research programs that collect genetic and genomic data are needed to advance the adoption of personalized medicine concepts and products for the benefits of patients.

Purpose: Appropriate federal funds for research related to personalized medicine.

Intended:

1. for diagnostic and therapeutics developers;
2. to provide funds for data generation, clinical studies, product development, clinical validation, and clinical utility studies;
3. to spur production of new PGx for additional drugs; and
4. to inspire novel approaches in PGx.

Sample language:
Taken from S. 3822, the “Genomics and Personalized Medicine Act of 2006,” 109th Congress, unaltered.

A. Genetics and Genomics Research-
   (1) IN GENERAL- The Secretary shall expand and accelerate research and programs to collect genetic and genomic data that will advance the field of genomics and personalized medicine, with prioritized focus on--
      (a) studies of diseases and health conditions with substantial public health impact;
      (b) population-based studies of genotype prevalence, gene-disease association, gene-drug response association, and gene-environment interactions;
      (c) systematic review and synthesis of the results of population-based studies using methods of human genome epidemiology;
      (d) translation of genomic information into molecular genetic screening tools, diagnostics, and therapeutics, through well-conducted clinical trials and studies;
      (e) translation of genomic information into tools for public health investigations and ongoing biosurveillance and monitoring;
      (f) systematic review of data on analytic validity and clinical validity of molecular genetic tests;
      (g) comprehensive studies of clinical utility, including cost-effectiveness and cost-benefit analyses, of molecular genetic tests and therapeutics;
      (h) population based studies to assess the awareness, knowledge, and use of genetic tests and their impact on the population health and health disparities; and
      (i) methods to enhance provider uptake or adoption of pharmacogenomic products into practice.
Category: Regulation

Title: Expedited FDA Approval for Personalized Medicines: Therapeutics and Diagnostics Developed Together.

Rationale: FDA regulates products to protect consumers and to assure consumers that the drugs that they take are safe, effective, and will treat the condition for which it was developed without unpleasant and unintended effects. Personalized medicine therapeutics and diagnostics developed together may enhance consumer protection because they take into account an individual’s genetic and biological makeup and how that will impact their response to a therapeutic agent. Pairing a diagnostic and therapeutic may allow some pre-selection of patients for which a drug is more likely to be effective because likely non-responders or patients more likely to have adverse effects are pre-selected out.

Purpose: To facilitate the development and marketing of personalized medicines, companion diagnostics and related technologies thereby improving the efficacy and safety of pharmaceuticals through streamlined FDA review and approval procedures.

Intended for:

1. Medical technology companies or laboratories that develop diagnostic products designed to test the dosing or applicability of a specified pharmaceutical product.

2. Pharmaceutical companies that develop drug therapies whose usage is targeted by companion diagnostics and associated technologies used to determine the dosing or appropriateness of that pharmaceutical.

This incentive should:

1. speed the time to market for these products;

2. reduce industry concerns that a combination Rx/Dx submission could slow down product review due to complexity; and

3. reduce the development costs to industry thus making these products economically viable.

Sample language: (designed to specify those products for which this incentive is to apply)

"For companion diagnostic products under its purview, the Food and Drug Administration shall develop and apply expedited review and approval procedures for submissions covering technologies that potentially act to define the marketability of identified pharmaceuticals to specified sub-populations, groups of individuals, or individual, as well as pharmaceuticals and diagnostics developed using these technologies. The streamlined and expedited review processes shall apply to, but not be limited to, pharmaceuticals and associated diagnostics whose design incorporates an understanding of the human genome, pharmaceuticals whose appropriate selection or use is potentially defined by specified diagnostic tests, and diagnostic tests that help define the appropriate selection or use of identified pharmaceuticals."
Category: Regulation

Title: Expedited FDA Approval for Personalized Medicines: Therapeutics and Diagnostics Developed Separately.

Rationale: Personalized medicine has the ability to improve the treatment outcomes for currently-marketed therapeutics. For example, traditionally, when a patient is put on the drug warfarin, blood-levels of the drug are carefully monitored over a number of doctors visits. Too much of the drug could cause a bleeding incident; too little, the drug will not work as designed, that is prevent the blood clots that can lead to stroke. Currently, laboratories can conduct a test to determine what level of the drug should be optimal for a given individual. These types of diagnostic developments increase the efficacy and efficiency of medical treatments.

Purpose: To support the development of diagnostics for therapeutic selection and dosing decisions.

Intended for: Medical technology companies or laboratories that develop diagnostic products designed to test the dosing or applicability of a specified therapeutic product.

Incentive should:

1. encourage companion diagnostic development for drugs that are currently on the market;

2. allow peer-reviewed scientific and clinical research, and previously submitted drug trial results, to be used in fulfilling FDA regulatory requirements for companion diagnostics developed for drugs that are currently on the market;

3. reduce the time and costs of development to industry, thus making these products economically viable by eliminating redundancy and using the least burdensome approach possible; and

4. create a stable and predictable regulatory environment for the review and approval of companion diagnostics (e.g. harmonization of the FDA and CLIA roles).
Category: Reimbursement

PMC members agree that incenting reimbursement will drive the development of personalized medicine. Below is a list of ideas that have been considered by PMC but have not been adopted at this time as official policy suggestions. During 2008 the PMC will be addressing both public and private reimbursement systems and we expect a number of incentives related to reimbursement to come from that effort. Some of the ideas that have been mentioned so far are:

**Prevention category in CMS:** Many personalized medicine products are designed to determine an individual’s predisposition to disease. Knowing, for example, one’s chances of getting diabetes based on genetic markers may motivate an individual to take preventative action. Preventative action leads to better and less expensive health care.

**CMS Coverage of FDA cleared products:** All products cleared by the FDA should be covered by CMS. Private insurers are encouraged to follow suit.

**Value-based pricing:** Some members argue for value-based reimbursement for diagnostic products for personalized medicine is an appropriate incentive as the current reimbursement levels do not support the development of these products.