

Amy Patterson, MD
Acting Director, Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Room 750
Bethesda, MD 20892

July 12, 2010

RE: Request for Information (RFI) on the National Institutes of Health Plan to Develop the Genetic Testing Registry

Dear Dr. Patterson,

Boehringer Ingelheim Pharmaceuticals, Inc. appreciates the opportunity to comment on the Request for Information (RFI) published in the Federal Register on June 11, 2010, regarding the Genetic Test Registry proposed by the National Institutes of Health (NIH). Over the past several years, many prominent stakeholders have emphasized the need for increased information on personalized medicine and specifically on genetic testing. Increasing knowledge about the availability and utility of genetic tests will allow stakeholders to use them appropriately for diagnosis and treatment of patients. Genetic testing should be performed when clinically indicated. For example, mutational analysis of tumor tissue in clinically indicated patients would personalize cancer treatment and contribute to improving patient care.

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Boehringer Ingelheim (BI) supports the creation of the Genetic Test Registry as it represents an important step forward. Our comments focus on three broad points: the Genetic Test Registry should I) focus on improving clinical decision-making, II) be clear and user-friendly, and III) include a broad range of tests.

I. The primary goal of the Genetic Test Registry should be to encourage the generation of information and tools that improve patient and physician shared decision-making in an area in which information is often unavailable or may be unreliable.

Stakeholders across the healthcare spectrum would benefit from more information on the types of genetic tests and their clinical utility. A registry may be useful for enabling:

- Providers to make stronger positive/negative recommendations about tests;
- Patients to make better-informed clinical decisions; and,
- Researchers and policymakers to understand gaps in knowledge and support and/or design future research.

In addition to these factors, a well-developed and properly designed database would serve to increase general public confidence in genetic testing. A catalogue showing the number of tests that exist and the breadth of diagnostic and treatment challenges they address will provide a clearer sense of the availability and, hopefully, the utility of this type of technology. NIH's involvement in the registry alone could improve end-user confidence. As a neutral, science-driven entity (i.e., no commercial or regulatory

objectives), we believe that NIH is well positioned to engender public trust by ensuring sound inputs (data gathered from disparate private sources) and outputs (data points communicated to the broader public).

II. The Genetic Test Registry should contain well-defined yet user-friendly data, recognizing that there will be a fine balance between these two aims.

Although NIH has no plans to adjudicate the genetic test data, there must be a process in place to ensure that captured data is of high quality. Ideally, all quantifiable metrics (including clinical utility, clinical validity, sensitivity, and specificity) will need to be controlled using minimal integrity standards. For example, information proposed for inclusion in the registry should be supported by references. We see two main avenues through which to facilitate collection of reliable information: providing clear standards and definitions for i) data elements and ii) information entry.

- i. *Data Elements.* NIH will need standard definitions of any data elements that users will enter into the registry. Standards must account for the viewpoints of the scientific, test developer, and user communities. We recommend that NIH draw from widely-recognized general standards, such as the Center for Disease Control and Prevention's Alytic validity; Clinical validity; Clinical utility; and Ethical, legal, and social implications (ACCE) methodology, elaborating on definitions as needed. NIH should pay particular attention to utility metrics, as these have been among the most diversely defined and, arguably, ill-supported descriptive parameters of genetic tests.
- ii. *Information Entry.* NIH should clearly define the method for entering information and the particulars of entry, including the choice of data fields. If means for promoting participation in the registry can include interface with other repositories of needed information, these should be evaluated in the design process. BI suggests clarifying the mechanisms for submitting new and supplementary information prior to initial entry of a test in the registry, the frequency with which information can be updated, and the parties that are eligible or responsible for submitting these updates.

The clarity and comparability of concepts and data fields will be critical for consumer use. With this in mind, NIH should develop output specifics with ongoing contribution or feedback from stakeholders, emphasizing end-user ease and understanding. NIH should ensure that any outputs provided (based on highly technical input) are comprehensible, facilitating the average consumer's use of the registry. For instance, definitions of outputs can be expressed in simple language (e.g., expressing sensitivity as "how often a test is positive when genetic mutation X is present").

To support consumer understanding, BI recommends that the registry be equipped with an objective "user's guide." This will help patients interpret complex data appropriately. In addition to clear definitions, the user's guide should comprise consensus benchmarks for data elements whenever appropriate. Benchmarks will provide patients with a point of reference so that they can evaluate and compare tests. For the more sophisticated consumer, the user's guide could also include a function to link the summary genetic data provided in the registry to additional information on the test and its uses. This information could include publications, studies, guidelines, and any other supporting material that will provide helpful information or context for consumers or other end-users.

One key consideration from a 'consumer protection' lens is the stage of test development. Without knowing the test's stage of development, any user of the registry might have an incomplete or inappropriate understanding of the test's potential relevance to them. For this reason, BI recommends that NIH set standard definitions for a test's stage of development and include descriptive information only on those tests that exceed a predetermined development threshold. This would, however, require an adjudicative role for NIH, which it has not expressed an interest in taking. An alternative approach would be for NIH to establish

standard definitions of test development to be self-reported by manufacturers, and possibly factored into the “user’s guide” described above or into a separate evaluation algorithm.

As NIH notes in the RFI, transparency and stakeholder input on the registry’s design and functions are critical considerations. Clearly defined opportunities for stakeholder input will be an important foundation for both consumer and manufacturer confidence in the registry as a data source. It will also allow NIH to be responsive to evolving consumer needs (e.g., improved clarity). BI suggests that NIH offer stakeholders the opportunity to comment at multiple intervals during the life of the Genetic Test Registry, including but not limited to:

- After NIH has defined the goal of the registry;
- After NIH has created and launch-tested an initial version up of the registry, including data fields;
- Periodically after the registry’s launch (for comments on the registry’s rigor, success, issues, and how it is used by stakeholders); and
- Upon release of any research performed by a public-sector entity using the registry data. (This comment period is especially important if NIH does not take on a curator role. Stakeholders will desire the opportunity to comment on the strength of evidence in the registry and the interpretation and implications of the study findings.)

III. The Genetic Test Registry should include FDA-approved devices as well as locally- developed tests.

The NIH has specifically requested comments on the types of tests to include within the Genetic Test Registry. BI recommends that all genetic tests—those approved by the FDA as well as locally developed tests—be included.

While the FDA does have the prerogative to review, clear, and maintain data on genetic tests, it has not fully exercised that prerogative to date.¹ Rather, most genetic tests are locally developed in CLIA/state-certified labs that have some reporting requirements. These reporting requirements are generally less comprehensive and rigorous than the type being considered for the Genetic Test Registry. Even for tests that undergo FDA review, there is no centralized, easily accessible catalogue of tests and their characteristics. As such, data on both types of tests are not widely available. By gathering comprehensive data on the full range of these tests in a central repository, the Genetic Test Registry will be a valuable and often unique source of information to the public.

In the future, one can imagine adding more sophisticated functions to the Genetic Test Registry, should NIH choose to take a more active role in its upkeep and receive the necessary resources. For instance, NIH could link common genetic test data to other sources of consumer, provider, and patient information from a variety of public and private sources. Another consumer-oriented step would be to interpret the relative value of multiple tests of the same type, as consumers would benefit from expert comparative analysis of their options. We do, however, recognize the degree of technical difficulty in developing and utilizing a common algorithm for gauging the relative merits of diverse tests applied to a single condition or treatment.

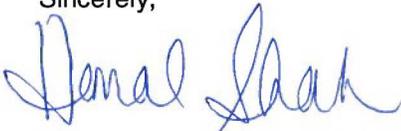
As another, perhaps simpler, means of making the registry more user-friendly, NIH could consider enabling patients to view lists of the therapies of a particular type that have associated genetic tests. This would allow patients, in consultation with their care providers, to choose an appropriate test-therapy or to select a drug class for which there is an associated test. Alternatively, NIH could develop a list of questions that patients could ask providers, which would be a resource to help patients initiate a discussion about the utility

¹ FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests (LDTs), Date July 19-20, 2010. Accessed at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm>

of genetic testing for their health conditions. Of course, any new applications for the Genetic Test Registry would need to be developed with continual, resolute, and explicit attention to the ethical issues attending genetic testing.

In closing, we anticipate that the Genetic Test Registry will be a very valuable tool for many different actors in the healthcare space, and we appreciate the opportunity to submit comments.

Sincerely,



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