

Worldwide Regulatory Strategy
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Global Research & Development

NIH GTR RFI Comments
National Institutes of Health, Office of Science Policy
6705 Rockledge Drive
Room 750
Bethesda, MD 20852

Submitted via email to GTR@od.nih.gov

To NIH, Office of Science Policy,

Pfizer appreciates the opportunity to comment on the National Institutes of Health (NIH) plan regarding the creation of a Genetic Test Registry (GTR). Pfizer applauds the NIH for working to develop a voluntary registry that will serve as a centralized public resource to provide information about the availability, scientific basis and usefulness of genetic tests.

Pfizer is a global biopharmaceutical company whose mission is to discover, develop and deliver safe and innovative medicines. Our diversified health care portfolio includes biologics, small molecule drugs, vaccines and over the counter therapies. At Pfizer, we set high standards for quality and safety in our discovery, development and manufacturing. We are committed to developing targeted medicines to fulfill unmet medical needs in areas such as cancer and infectious disease. As the science base accrues, information from genetic tests will become increasingly important for the optimal use of a growing number of our products. In some cases, a genetic test serves as an obligatory or companion diagnostic such that the need for testing to guide prescribing is indicated in the label of the product. Pfizer sees the value of a public repository of information about genetic tests as a resource for researchers, health practitioners and patients.

General comments:

Utilization of genetic tests to aid management of patient health and medical conditions is primarily driven by evidence of impact on outcomes. As such, a systematic approach such as the GTR can aid the diffusion of such knowledge and provide stakeholders with key information about the rapidly growing spectrum of tests being offered. Making test performance characteristics and reference information (analytical validity, clinical validity and utility) publicly available should increase confidence in these types of tests among healthcare providers and patients, and could help improve the proper utilization of genetic tests. Standard submission formats and standard definitions of data elements are critical. Therefore, we are pleased that the GTR will be housed within the National Library of Medicine and implemented by the National Center for Biotechnology Information (NCBI) with oversight by the NIH and scientific community. To ensure that the resource is as comprehensive as possible, submission of data should be a simple, standardized process and pilot-tested to ensure that it is not burdensome to data providers. Feedback from pilot testing of the GTR with diverse segments of the stakeholder community will also be critical to ensure that this database succeeds in providing clear and accessible information that is useful to its intended users. In addition, a genetic test registry could assist regulatory agencies in evaluating tests and developing appropriate pathways for oversight. We encourage the NIH to consult with both CMS and FDA throughout the process of developing the GTR.

Specific comments:

The section number refers to the number of the question in the RFI.

1. One of the points for clarification is whether the GTR will only include information on FDA-cleared/approved (510k/PMA) or FDA-reviewed Investigative Use Only (IUO) diagnostics, or whether it will include any and all tests including laboratory-developed or “home brew” tests (LDTs). While we recognize the value of including a broad range of available tests, we would propose the registry be split clearly into two sections: “FDA approved tests” and “Non-FDA approved and experimental tests.” The “FDA approved” section should be a mandatory registry controlled by the FDA and modeled on the [Drugs@FDA](#) site while the other section would be voluntary and more similar to [ClinicalTrials.gov](#). Our recommendation is based on concern that the quality of analytical and clinical validity and clinical utility data submitted for the latter category of tests should not be viewed as necessarily comparable to data for products that have undergone FDA review and approval. If the proposed registry treats all submitted tests equally and there is no vetting of data or information to support these validity and utility claims, users could be misled into thinking a test is more robust than it actually is. Companies that have made the investment to develop their test through a rigorous FDA approval process would be at a disadvantage because they would effectively be forced, for reasons of legal liability, to restrict their analytical & clinical validity and clinical utility claims to what is in their FDA-approved labeling. On the other hand, companies with tests that have not undergone FDA scrutiny are not subject to the same constraints.
2. The GTR has potential to provide value for different categories of genetic tests as described below.
 - **FDA-reviewed/approved diagnostics.** Currently, there is no [Drugs@FDA](#) site equivalent for diagnostics, with approved current labeling available, so the value of this registry is high. If listing in the GTR was automatic with approval of a test through the 510K or PMA process, then this registry could serve as a clearinghouse for information on tests that are subject to FDA oversight.
 - **IUO diagnostics.** There are several potential benefits for inclusion of information on IUO-level diagnostics that companies like Pfizer are developing in conjunction with our partners (e.g. DxS/Qiagen & Abbott). This would allow patients who may want to participate in pivotal clinical trials to know which test they should request. This would avoid the inefficiency and inconvenience of duplicative testing and consumption of precious patient samples such as tumor biopsies prior to a patient being enrolled in molecularly targeted therapeutic clinical trials. One possibility would be to cross reference information on IUO tests on [ClinicalTrials.gov](#) or otherwise linking the two databases.
 - **LDTs.** If the GTR decides to include both FDA-reviewed tests and other marketed tests such as Oncotype Dx that are not FDA-endorsed, it will be useful as a single source of information for all genetic diagnostics since it is relatively easy to get labeling information for FDA-regulated diagnostics from public sources, but difficult or impossible to get comparable information on many LDTs. However, if the registry does include both FDA reviewed/approved and non-FDA reviewed tests, this raises the issue that information for these two categories is unlikely to be directly comparable due to the differences in regulatory oversight. Recognition of this difference could be highlighted by segmenting the registry based on regulatory clearance status of the test. We would also suggest inclusion or linkage of tests in the registry to additional sources of information such as peer-reviewed studies that address analytical validation, clinical validation and clinical utility.

- 6.c. We strongly suggest that companies be asked to provide a full copy of their labeling, that is, Instructions for Use – similar to the drug labels or product inserts on the Drugs@FDA site.
- 6.d. For 510k tests, it should be required to name the predicate device and its 510k number. For tests that may not be FDA approved, it would be helpful to note if they are qualified for RUO or IUO.
- 6.e. "Intended use for the test" has a clear meaning to regulators and payers, so this is an important element to include and to define with input from FDA and CMS. This should be linked to the risk category for the test consistent with regulatory classifications.
- 6.m./n. We support inclusion of this type of information in the GTR; however, there is wide variance in what can be classified as analytical or clinical validity data. Even the FDA has acknowledged problems with the wide differences in the quality or strength of such data for previously FDA approved products, highlighting the challenge of interpreting these data, particularly in the absence of regulatory scrutiny or peer review.
- 6.o. For FDA-approved tests, this information will presumably come from the product label and be supported by published scientific studies. For non-FDA reviewed and experimental tests, it will be critical to include not only the evidence for utility, but the primary sources of information, preferably peer-reviewed publications.
7. We envision challenges for submission of certain types of information depending on the format and guidelines for relative data elements. Submissions for analytical validity, clinical validity and clinical utility may be subjective unless clear and consistent definitions are in place and information quality assurance safeguards are applied. For many potential data elements, key questions include how to ensure that content is accurate and kept up to date and who has the responsibility to do so? Many kinds of information can easily get out of date, ranging from the practical (e.g., test provider(s) to the scientific (e.g., latest findings related to clinical validity or utility) and technical (procedural modifications that impact performance.) To facilitate maintenance of the registry, NIH needs to ensure a mechanism for updating entries and ensuring their accuracy in addition to the ongoing submission of new entries.
11. As a consequence of regulatory oversight, we are concerned that there could be inappropriate comparison of data from FDA regulated versus non-FDA regulated tests, and that makers of FDA-approved tests might even be discouraged from submitting their tests if they felt disadvantaged in how they could portray their products due to labeling constraints. Low participation by makers of FDA-approved tests would create an unfortunate gap in the database. We therefore feel it is important that a distinction be made between data elements relating to analytical validity, clinical validity and clinical utility that have undergone FDA scrutiny and those that have not be addressed in the development of the GTR. See our comments in response to question 1.

The creation of a resource such as the NIH GTR for comprehensive and transparent access to information about available genetic tests has the potential to serve as an important catalyst for the integration of these new molecular diagnostic tools into medical research and medical care. We hope that the NIH will find our comments on the GTR to be helpful and will not hesitate to call upon Pfizer to provide further input or feedback as development of the GTR gets underway.

Respectfully submitted,



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