



September 26, 2011

Genetic Testing Registry Staff  
National Institutes of Health

**Re:** Comments on the practical utility of the proposed collection of information for the Genetic Testing Registry

The American Clinical Laboratory Association (ACLA) appreciates the opportunity to provide additional comments on the practical utility of the proposed collection of information for the Genetic Testing Registry (GTR). ACLA represents national, regional, and local laboratories across the country. Members of ACLA are proud to be at the forefront of delivering innovative genetic tests in partnership with healthcare providers and the patients they serve. As a result, we have a direct interest in the development of the registry.

NIH asked specifically for comment on the proposed estimate of time and cost for laboratories to submit data to the registry. Any comment in this area will be laboratory specific due to the voluntary nature of the registry, the size of the laboratory test menu and the degree to which the submitting labs provide information beyond the 31 required data fields. In general; however, for many ACLA laboratories, the stated average of 12.2 submissions per respondent, 3.0 hours to provide information for all data fields (i.e., minimal and optional fields) per submission, and a mean hourly wage of \$22.85 for a laboratory technician is underestimated. As an example, using cystic fibrosis data submission, there are different test codes for different indications: common mutations, fetal testing, sequencing, familial mutation for sequencing, duplications/deletions. The GTR will require each of these to be submitted individually. This is more likely an estimate of 12 hours for this one submission - cystic fibrosis. The cost estimate based on a laboratory technician salary is also underestimated for many ACLA member laboratories. Many of the data submission fields require the submission of complex data that will require the expertise of a genetic counselor or a laboratory director rather than a laboratory technician. ACLA will be pleased to meet with NIH to help work toward a more realistic estimate of paperwork burden.

Following are general comments on the overall design of the GTR and more specific comments on the practical utility of the proposed collection of information.

## **I. General Comments**

We remain concerned that the GTR Design Considerations and Field Definitions do not provide a definition of "genetic test." While NIH provides that "a Test is any separately orderable test offered by a laboratory," it does not provide guidance on which tests should be included in the GTR. We recommend that NIH provide clear instruction on which tests should be submitted.

A number of the requested data elements lend themselves to links to external databases or consensus statements, rather than submissions by individual laboratories. As discussed below, this includes information related to FDA-approved or cleared kits and fields addressing clinical validity and clinical utility where a consensus statement could be drafted by either professional associations or the NIH.

In general, we suggest that the NIH narrow the scope of the data requested through the GTR to better serve the needs of the intended audience. Our understanding is that the GTR is being developed to help practitioners and patients understand what tests are available and basic information about these tests. It appears that the level of detail and complexity of information proposed in these data fields is so involved that it may cause more confusion than increased understanding. Much of the information being requested is likely too technical to be readily understood by the general public or even the intended provider audience. ACLA believes that NIH review the information requested and attempt to pare down the amount of required information. We think requesting significant amounts of "optional" information will further complicate this task, as those reviewing the information will simply not understand why certain information was not included. As a result, ACLA believes that many of the optional fields should simply be excluded. The required information should be minimal, including the following suggested fields:

- Laboratory name
- Mailing address
- Primary laboratory contact name
- Contact information (i.e. phone number, email address)
- Laboratory director name
- Name of test
- Where test performed (internal, external) (please note additional comments on this issue below)
- Indications for use/clinical validity (pulled from a central source if available)
- Primary/alternate specimen source
- Analyte information
- What the test measures
- Mutation(s)/analytes tested
- Test development/regulatory status (see comments below regarding appropriate options to list)

Recommendations related to specific fields are included in the comments below. If a data element is optional, laboratories may wish to explain why no information is provided, and it may be helpful to include that language in the GTR, itself. We believe that NIH should consider this as an option.

Finally, as the GTR platform is developed, we hope that it will allow for general laboratory information to auto-populate for a laboratory that has previously entered such information for another test.

## **II. Comments on Specific Fields**

Proposed data fields on which we are providing comments are listed below and underlined, with our comments or concerns following.

Name of Laboratory (pages 2 and 3): NIH should clarify that this is the name of the laboratory on the CLIA license.

Laboratory Types of Service: Pick from List Plus Ability to Suggest New – Optional (page 3): This field appears to be included to provide general information on the types of services a laboratory offers. NIH should clarify whether services selected in this field are intended to represent all services offered by the laboratory or just those services involved in the specific test being submitted. Note there are state-specific laws regarding genetic counseling services.

Laboratory Affiliations – Text Field – (page 3): The description of this field asks whether a laboratory is “linked to” other entities. The types of relationships that should be reported here are unclear. NIH should clarify whether this is the appropriate place to identify parent companies of fully owned subsidiaries.

Laboratory Participation in External Programs: – Select from List – (page 3): “CETT Program” should be deleted as an option, as this program no longer exists.

Data Exchange Programs (page 3): NIH should define and provide further examples of the types of programs it is interested in for these fields. “CETT Program” should be deleted as an option, as this program no longer exists.

Primary Laboratory Contact: Yes/No Check Box – Required (page 4): In most cases, the Laboratory Director as defined by CLIA will not be the most appropriate point of contact for purposes of questions arising from the GTR. In fact, in a large laboratory, the individual who is the CLIA Laboratory Director will not have sufficient time or resources to triage these calls, so it may not be useful to include that individual’s contact information. Laboratories should assign a more appropriate individual such as the CLIA technical supervisor (commonly known as the technical director) or other designated person to triage questions and direct them to appropriate personnel within the laboratory, and we believe that this is the individual who should be listed here.

Default Parameters – Pull-Down List – (page 8): This field appears to be part of the set of default values that will automatically populate unless a laboratory overrides them. Laboratories should also be able to define the containers acceptable for specimen collection. It is unclear into where this information will populate. Further clarification would be helpful. In this field, laboratories should be able to select more than one option, with an instruction for laboratories to “pick all that apply.” This is also redundant with “Adding a Test”.

Default Sample Negative Report – Optional (page 8) and Default Sample Positive Report – Optional (page 8): Because laboratory reports are frequently updated, inclusion of a sample may not be useful and it may be difficult for laboratories to keep this field up to date. Moreover, the value of this criterion is somewhat difficult to understand. We recommend that this field be removed, given that similar fields (Sample Negative Report: Upload Document – Manual Entry – Optional and Sample Positive Report: Upload Document – Manual Entry – Optional) are also listed later in the draft document. We believe it is more useful for laboratories

to include test-specific sample reports, as appropriate, than to maintain generic default sample reports in the GTR.

Lab unique code (page 10) – We have concerns that multiple codes are used for the same test with different methodologies or indications for testing (eg, CF whole gene sequencing, duplication/deletion, targeted mutation analysis). It is unclear how the GTR will handle this and if requiring laboratories to have a unique submission for each type of testing. In a manner this is creating a directory of service. If so, there should be an ability to electronically upload all information (ie, eDOS).

FDA category designation (page 10) – a LDT is not a FDA category designation. Consider revising to “Category Designation”.

FDA Review (page 10) – We need clarification if this is for manufacturers or clinical laboratories. The GTR should have different views depending on whether a manufacturer or laboratory is completing the information.

Test-Specific License(s) (page 10) – The example provided was NYSDOH. While NYSDOH provides individual Test Approval of LDTs, it does not review unmodified FDA-cleared/approved assays, nor does NYSDOH license a test. NYSDOH provides instead individual test approval after review of the laboratory’s validation package for the test. We recommend that name be changed to NYSDOH Approved with “yes” or “no” as an option.

Test Orderable By: – Pull-Down List – Optional (pages 11): Who can order a test is generally determined by state and federal law. Because of this, we recommend that this field be removed. NIH may have been trying to address whether a patient can order a specific test, which would depend on where the patient is located and the applicable law in that state.

Disease: (page 12): This field and those immediately following should automatically populate for common diseases or markers, as it would be burdensome for laboratories to fill in each of these fields.

TEST METHODOLOGY (page 14): In general, we feel that too much detail is being requested within this category of fields. Information provided here should parallel what laboratories provide in their directories of services.

Primary Test Methodology: Pull-Down List with Ability to Suggest New – (pages 14): This field should be made optional, with the pull down list expanded.

Platforms: Laboratory-Specific Pull-Down List – (page 14): The usefulness of this field is not readily apparent, even if providing such information is optional.

Instrument(s) Used During Testing: Laboratory-Specific Pull-Down List – (page 14): This field is not useful. The specific instruments used to perform a test may vary day to day or change when equipment is updated or replaced. Ordering physicians and patients do not need this level of detail regarding how a test is performed.

Test Targets: (page 15): This field and those immediately following should automatically populate for common diseases or markers, as it would be burdensome for laboratories to fill in each of these fields.

How Does the Laboratory Deal with Variants of Unknown Significance (VUS) Results? (page 16): In general, we feel that too much detail is being requested under this heading. This field is only significant for sequencing and is not significant for other more routine genetic tests. This field should not be included for routine tests and should be eliminated from the GTR. Some of the specific fields under this heading, such as What Software is Used to Interpret Novel Variations? – Text Field – seems to be irrelevant to the purposes of the GTR and not useful for health care providers or for patients.

Will the Laboratory Re-Contact the Offering Physician if Variant Interpretation Changes? – Yes/No Checkbox –(page 16): This question addresses detailed issues of laboratory policy that are inappropriate for inclusion in the GTR and raise legal and liability concerns. This field should be removed.

Research Performed after clinical testing is complete – Text Field – Manual Entry – Optional (page 16): This question addresses detailed issues of laboratory policy that are inappropriate for inclusion in the GTR and raise legal and liability concerns. This field should be removed.

PERFORMANCE CHARACTERISTICS (page 17): In general, we feel that the information requested in this category is not relevant for the purposes of the GTR. NIH should consider what technical information is important to the intended audience and limit the requested data to a more targeted set of fields. Specific fields are discussed below.

Analytical Validity: Test + Citation – Required (page 17): Laboratories can provide this information, but it is unclear how useful it will be. In most cases, analytical validity is not of a concern with genetic tests, because there is little dispute about the ability of the test to accurately test for the genetic markers in question. Analytical Sensitivity (page 17): Again, laboratories can provide this information, but its usefulness is questionable. Analytical sensitivity is almost universally high for genetic tests, and differences in data reported in this field may have more to do with laboratory policy for how such figures are calculated than the true sensitivity of tests. Precision (page 17) and Accuracy (page 17): Both of these fields are of questionable importance in the GTR. Further, please note that the descriptions under these fields should be reversed: “Precision” generally refers to the reproducibility of results, or “how close repeated results match each other”; “Accuracy” generally refers to “how close the results match those from independent sources.” We note that none of the examples provided with NIH’s materials include responses to either of these fields and recommend that both be removed.

Assay Limitations: Text + Citation – Optional (page 17): This information may be better provided elsewhere in the GTR, such as the targeted population or the purpose of the test.

Proficiency Testing Performed on this Test: Yes/No Checkbox – (page 17): We recommend eliminating this field. Laboratories are required to perform Proficiency Testing under CLIA, and such testing is performed for all tests regardless of whether a formal program

Genetic Testing Registry Staff  
September 26, 2011

is available or the laboratory performs an alternative assessment. Note inter-laboratory exchange is a type of alternative assessment and should be removed.

Method used for Proficiency Testing: – Check Box – Optional (page 17): If this field is maintained, “Intra-Laboratory” should not be listed separately. Such testing is a type of “Alternative Assessment” and should be incorporated into this option.

Description of Proficiency Testing Method: Text + Citations – Optional (page 17): All laboratories perform Proficiency Testing, and the GTR is an inappropriate place to collect information on Proficiency Testing methods. Individuals seeking test information through the GTR will not understand information on Proficiency Testing provided in this format, and such information could easily be misconstrued.

Internal Test Validation Method Description: Text + Citation – Optional (page 17): Similar to the comment above on Proficiency Testing Method, we feel it is inappropriate to use the GTR to gather this information.

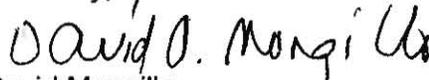
Clinical Validity: Text + Citation –(page 18): These fields are best documented through literature and are not laboratory-specific. For this reason, it would be better to gather this information in a centralized single document than from individual clinical laboratories. These fields are more appropriate for research laboratories than for clinical laboratories. We recommend that these fields and the related fields that follow be removed from the GTR.

CLINICAL UTILITY: TEXT + CITATION – OPTIONAL (page 18): We recommend removing this section from the GTR. At ACLA’s November 2010 meeting with NIH, all parties agreed that the best approach would be to address clinical utility in a centralized manner using materials from experts in the field. This information is not laboratory specific and is inappropriate to include as proposed.

\* \* \*

Thank you for the opportunity to comment. Please do not hesitate to contact me if you have any questions.

Sincerely,



David Mongillo  
V.P. Policy and Medical Affairs  
[dmongillo@clinical-labs.org](mailto:dmongillo@clinical-labs.org)  
(202) 637-9466