The survey instrument is short and poses minimal burden on the time of respondents. Estimates of time required to complete the survey during the pilot phase range from 7 to 20 minutes. The annual hour burden calculation assumes each survey will last 15 minutes, therefore the total of annualized hourly costs to participants is estimated to be $30,040.

John M. Eisenbert,

Director.

[FR Doc. 00–10983 Filed 5–3–00; 8:45 am]

BILLING CODE 4160–90–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control And Prevention

[60Day–00–36]

Proposed Data Collections Submitted for Public Comment and Recommendations

In compliance with the requirement of section 3506 (c)(2)(A) of the Paperwork Reduction Act of 1995, the Centers for Disease Control and Prevention is providing opportunity for public comment on proposed data collection projects. To request more information on the proposed projects or to obtain a copy of the data collection plans and instruments, call the CDC Reports Clearance Officer on (404) 639–7090.

Comments are invited on: (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) ways to enhance the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques for other forms of information technology. Send comments to Seleda Perryman, CDC Assistant Reports Clearance Officer, 1600 Clifton Road, MS–D24, Atlanta, GA 30333. Written comments should be received within 60 days of this notice.

Proposed Projects

Youth Risk Behavior Survey—(0920–0258)—Renewal—National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP). The proposed project is the 2001 national school-based Youth Risk Behavior Survey. The purpose of this request is to renew OMB clearance to continue an ongoing biennial survey among high school students attending regular public, private, and Catholic schools in grades 9–12. The survey assesses priority heath risk behaviors related to the major preventable causes of mortality, morbidity, and social problems among both youth and adults in the U.S. OMB clearance for the 1999 survey expired January 2000 (OMB No. 0920–0258, expiration 01/00). Data on the health risk behaviors of adolescents is the focus of approximately 40 national health objectives in Healthy People 2010. The Youth Risk Behavior Survey provides data to measure at least 10 of these health objectives and 3 of the 10 Leading Health Indicators. In addition, the Youth Risk Behavior Survey can identify racial and ethnic disparities in health risk behaviors. No other national source of data measures as many of the 2010 objectives that address behaviors of adolescents. The data also will have significant implications for policy and program development for school health programs nationwide.

The total estimated cost to student respondents is $47,250, which is calculated in terms of their time spent in responding to the survey and is based on an assumed minimum wage of $5.25/hour for the 1999–2000 school year. The total estimated cost to school administrators is $5,882 which is calculated in terms of their time spent in recruitment and is based on an assumed average hourly rate of $34. Thus, the total costs to respondents, based on the costs of their time, are $53,132.

Respondents	Number of respondents	Number of responses per respondent	Burden per response (in hours)	Total burden hours.
High school students	12,000	1	0.75	9,000
School administrators	345	1	0.50	173
Total	12,345			9,173

Dated: April 28, 2000.

Charles W. Gollmar,

Acting Associate Director for Policy Planning and Evaluation, Centers for Disease Control and Prevention.

[FR Doc. 00–11095 Filed 5–3–00; 8:45 am]

BILLING CODE 4163–18–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

Notice of Intent; Genetic Testing Under the Clinical Laboratory Improvement Amendments

SUMMARY: The Centers for Disease Control and Prevention (CDC) acts as a scientific advisor to the Health Care Financing Administration (HCFA) in development of requirements for clinical laboratories under the Clinical Laboratory Improvement Amendments (CLIA). The CDC is issuing this notice to advise the public that the Department of Health and Human Services (HHS) will be preparing a Notice of Proposed Rule Making (NPRM) to revise the CLIA regulations applicable to laboratories performing human genetic testing. Before issuing the NPRM, comments are being solicited on the recommendations of the Clinical Laboratory Improvement Advisory Committee (CLIAC) to change current CLIA requirements to specifically recognize a genetic testing specialty. This new speciality area will address unique testing issues in the pre-analytic, analytic, and post-analytic phases of testing that could affect the accuracy and reliability of test results, and related issues such as informed consent, confidentiality, counseling, and the clinical appropriateness of a genetic test. To ensure that a full range of issues relating to this proposed action are addressed and potential impacts are identified, comments and suggestions are invited from all interested parties. Comments or questions regarding this proposed action should be directed to CDC at the address below.

The Department has also established a Secretary's Advisory Committee on Genetic Testing (SACGT) to advise the Department on the medical, scientific, ethical, legal, and social issues raised by the development and use of genetic

testing. The SACGT is currently addressing, in consultation with the public, broad questions related to the adequacy of oversight of genetic testing. If, after public consultation and analysis, SACGT finds that further oversight measures are warranted, it will recommend options for such oversight. The public comment for the SACGT issues is being conducted separately (See the December 1, 1999 **Federal Register**, 64 FR 67273). The reason for independent solicitations is that the SACGT is addressing more general aspects of genetic testing, such as the criteria that should be used to assess the benefits and risks of genetic tests. That purpose differs from this solicitation that deals specifically with the application of CLIA to genetic laboratory testing. The two requests for public comments thus solicit complementary information: the SACGT comments will guide development of recommendations to the Secretary on policy and oversight issues, whereas comments on the CLIAC recommendations will guide development of appropriate genetic testing laboratory requirements for revision of the CLIA regulations.

DATES: Written comments received by July 3, 2000, will be incorporated into the record.

ADDRESSES: Send comments to D. Joe Boone, Ph.D., Assistant Director for Science, Division of Laboratory Systems, Public Health Practice Program Office, Centers for Disease Control and Prevention, 4770 Buford Highway., N.E., Mailstop G25, Atlanta, Georgia 30341, at telephone (770) 488–8080.

SUPPLEMENTARY INFORMATION:

Background

A. Human Genetic Testing

Human genetic testing involves the analysis of chromosomes, dioxyribonucleic acids (DNA), ribonucleic acids (RNA), and genes and gene products (*e.g.* proteins and enzymes) to detect heritable or acquired disease-related disorders or conditions. Federal and private-sector human genome projects will soon decipher the structure for the 100,000 to 140,000 genes residing on the 23 pairs of human chromosomes. It is expected that along with this definition of structure will come associations between the variations in gene structure and a variety of conditions and diseases. Once associations have been delineated, the use of genetic testing is expected to expand significantly to determine whether an individual has a condition or disease or might develop a condition or disease in the future.

Human genetic testing is expected to lead to a whole new era in health care. Some tests may determine not only whether an individual has a particular disease or condition, but also may determine their risk of developing a disease or condition in the future. However, along with the tremendous potential for improving health and preventing disease, genetic testing can also do great harm if errors occur in: (1) The selection of an appropriate test, (2) the performance of the test, (3) the interpretation of the tests results, or (4) the clinical application of the test results. False-positive or false-negative results can be especially troublesome when the test is being used to predict future risk of disease in an individual without any current symptoms of disease.

The process of performing a genetic test can be broken into three distinct phases: (1) The pre-analytic phase, which encompasses such events as determining which genetic test, if any, is appropriate to answer the clinical question being asked and collecting an appropriate sample and transporting it to the test site; (2) the analytical phase, which involves steps taken to perform the analysis and analyze the results; and (3) the post-analytic phase, which includes reporting and interpretation of the results. It is important to recognize that the laboratory may need to be involved in carrying out or assisting with all three phases of testing and that errors can occur either within the laboratory or at the interface between the laboratory and the care provider.

In the pre-analytic phase, one recent study found that 20 percent of adenomatous polyposis coli (APC) genetic tests were ordered for inappropriate indications and 19 percent of patients received genetic counseling before testing occurred (Giardiello FM, *et al.* The use and interpretation of commercial APC gene testing for familial adenomatous polyposis. N Engl J Med 1997;336:823–827). Another recent survey of 245 molecular genetic testing laboratories found that 55 percent of the laboratories did not require informed consent prior to testing and 31 percent did not have a written policy on confidentiality (McGovern MM, *et al.* Quality assurance in molecular genetic testing laboratories. JAMA 1999;835–840). This same study found what the authors considered to be substandard laboratory practice, which could lead to adverse clinical outcomes, in 15 percent of the laboratories. In the post-analytic phase of testing, the Giardiello study reported that 31 percent of the cases were misinterpreted by the physician. The McGovern study found that 30 percent of laboratories did not provide access to genetic counseling.

These and other studies point to the need for improvements in laboratory practice and better coordination between the care provider, laboratory, genetic counselor, and the patient to ensure quality in genetic testing. The HHS has sought the advice of experts in laboratory medicine and genetic testing to help identify places in the testing process where testing problems are most likely to occur, and to determine what modifications to current CLIA regulations could provide greater assurance of accurate and reliable testing. Issues for which the laboratory might provide additional assistance to the laboratory user such as informed consent, counseling, and protecting confidentiality were also considered. The recommendations below were developed during a series of public meetings of the Clinical Laboratory Improvement Advisory Committee (CLIAC).

B. Current Roles of Government and Professional Organizations in Genetic Testing

In considering whether to create a genetic specialty under CLIA and whether to include the provisions recommended by the CLIAC, it is important to understand the current roles of government and professional organizations in genetic testing, and to note that no single agency or organization is likely to be able to address all of the issues raised by genetic testing.

Genetic tests are currently regulated at the Federal level through three mechanisms: (1) The Clinical Laboratory Improvement Amendments (CLIA); (2) the Federal Food, Drug, and Cosmetic Act; and (3) during investigational phases of test development, under applicable regulations for the Protection of Human Subjects (45 CFR 46, 21 CFR 50, and 21 CFR 56). In addition, some States regulate and private-sector organizations monitor genetic testing laboratories.

On October 31, 1988, Public Law 100–578, Clinical Laboratory Improvement Amendments of 1988 (CLIA), Section 353 of the Public Health Service Act, (42 U.S.C. 263a) was enacted. On February 28, 1992 (57 FR 7002), HHS published a final rule applicable to all laboratories that examine human specimens to provide information for the diagnosis, prevention, or treatment of any disease or impairment of, or assessment of the health of, human beings. (Note: Facilities that only perform testing for forensic purposes and research

laboratories that test human specimens but do not report patient specific results are exempt from the CLIA regulations.)

Under CLIA, laboratories are required to meet specific requirements before they can become CLIA-certified. Regulated tests are categorized according to their level of complexity: waived, moderate, and high complexity, with the regulatory requirements increasing in stringency with the complexity of the tests performed. Under CLIA, the Health Care Financing Administration (HCFA) in partnership with CDC develops standards for laboratory certification. The advice of the HHS Clinical Laboratory Improvement Advisory Committee (CLIAC) may also be sought. Laboratories performing non-waived tests receive on-site inspections conducted by HCFA or by designated organizations or State-operated CLIA programs.

Overall monitoring includes a comprehensive evaluation of the laboratory's operating environment, personnel, proficiency testing, quality control, and quality assurance. Laboratory directors are required to take specific actions to establish a comprehensive ongoing quality assurance program, which ensures that the performance of all steps in the testing process is accurate. Although laboratories under CLIA are responsible for all aspects of the testing process (from specimen collection through specimen analysis and reporting of the results), CLIA oversight emphasizes intralaboratory processes as opposed to the clinical uses of test results.

All laboratory testing devices, kits and their components are subject to FDA oversight under the Federal Food, Drug, and Cosmetic Act. Testing devices and tests that are packaged and sold as kits to multiple laboratories require premarket approval or clearance by the FDA. This premarket review involves an analysis of the device's accuracy as well as its analytical sensitivity and specificity. Premarket review is performed based on data submitted to FDA's scientific reviewers. In addition, for devices for which the link between clinical performance and analytical performance has not been well established, FDA requires additional analyses to determine the test's clinical characteristics, or its clinical sensitivity and specificity. In some cases, FDA requires that the predictive value of the test be analyzed.

The majority of new genetic tests are being developed by laboratories for their own use, that is, in-house tests. The FDA established a measure of regulation of in-house tests by instituting controls over the active ingredients (analyte-specific reagents) used by laboratories to perform tests. This regulation subjects reagent manufacturers to certain general controls, such as good manufacturing practices; however, with few exceptions, the current regulatory process does not require a premarket review of these reagents. The regulation requires that the sale of reagents be only to laboratories capable of performing high-complexity tests and requires that certain information accompany both the reagents and the test results. The labels for the reagents must also state that ''analytical and performance characteristics are not established.'' Also, the test results must identify the laboratory that developed the test and its performance characteristics and must include a statement that the test ''has not been cleared or approved by the U.S. FDA.'' In addition, the regulation prohibits direct marketing of in-house developed tests to consumers.

Human subjects participating in the research phase of development of a genetic test are under the protection of human research subjects regulations administered by the National Institutes of Health (NIH) and the FDA. NIH oversees the protection of human research subjects in HHS-funded research, while the FDA oversees the protection of human research subjects in trials of investigational (unapproved) devices, drugs, or biologics being developed for eventual commercial use. Fundamental requirements of these regulations are that experimental protocols involving human subjects be reviewed by an organization's Institutional Review Board (IRB) to assure the safety of the subjects and that risks do not outweigh potential benefits.

Some State agencies may monitor laboratories performing genetic testing, including licensure of personnel and facilities. In some instances, the State Public Health Laboratory and State-operated CLIA program are responsible for quality assurance activities. A few States, such as New York, have promulgated regulations that go beyond the requirements of CLIA. States also administer newborn screening programs and provide other genetic services through maternal and child health programs.

Private-sector organizations, in partnership with HCFA and CDC may also develop laboratory and clinical guidelines and standards. A number of organizations are involved in helping to assure the quality of laboratory practices and in developing clinical practice guidelines to ensure the appropriate use of genetic tests. These organizations include the College of American Pathologists (CAP), which develops standards for its membership and establishes and operates proficiency testing programs; the NCCLS (formerly called the National Committee on Clinical Laboratory Standards), which develops consensus recommendations for the standardization of test methodologies; and the American College of Medical Genetics (ACMG), which develops guidelines for the use of particular tests and test methodologies and works with the CAP to provide proficiency tests for certain genetic tests. Other organizations, such as the American Academy of Pediatrics, American College of Obstetrics and Gynecology, American Society of Human Genetics, and National Society of Genetic Counselors, are also involved in the development of guidelines and recommendations regarding the appropriate use of genetic tests.

Presently, no federal agency has specifically addressed other aspects of oversight that are critical to the appropriate use of a genetic test, including the clinical validity and clinical utility of a given test. Also not addressed are other important issues such as informed consent and genetic counseling.

C. Proposed Changes to CLIA Laboratory Regulations

Currently, CLIA has very specific requirements for certification of laboratories in areas such as cytology, microbiology, and clinical cytogenetics; a specialty category of genetics does not currently exist even though genetic testing is covered under the general provisions of CLIA. If a genetics specialty category is created, genetic testing will need to be defined (see definitions under question 1).

Recommendations of Clinical Laboratory Improvement Advisory Committee (CLIAC)

On September 11, 1997, January 29, 1998, May 28–29, 1998, September 17–18, 1998, and September 22–23, 1999 the CLIAC met to develop recommendations on how the CLIA regulation might be modified to address genetic testing. Summary accounts of the meetings at which these recommendations were developed can be found at the CDC website at *http://www.phppo.cdc.gov/dls/cliac/default.asp*. The CLIAC's deliberations provide definitions for laboratories performing genetic testing; address issues in the pre-analytic, analytic, and post-analytic phases of testing; and describe how a laboratory's responsibilities and those of the care

provider, genetics counselor, and individual being tested are related.

While these recommendations were developed by experts in the field of genetics and laboratory aspects of genetic testing, we are interested in determining the impact of imposing the specific requirements recommended by CLIAC on the wide spectrum services offered by the nation's 170,000 clinical laboratories. We are interested in determining which, if any, of these recommendations might prove problematic to low volume laboratories, which may be the only source of a specific genetic test. Finally, we are interested in receiving comments about whether implementing these recommendations would increase, decrease, or have no effect on the quality of, access to, or cost of genetic testing services.

Please note that genetic testing laboratories are already subject to the current personnel, quality assurance, quality control, and patient test management provisions of CLIA (42 CFR Part 493). Also note that the recommendations have been divided into topics which apply globally to all phases of genetic testing, and those specific to the pre-analytic, analytic, and post-analytic phases of testing.

While this Notice of Intent requests comments on a range of laboratory issues related to potential regulation of genetic testing recommended by the CLIAC, the Department has not yet determined whether the scope of CLIA will allow regulation of all of these issues.

CLIA Questions on Which Comment Is Being Solicited

The CLIAC has made recommendations on the issues listed below. We are interested in receiving comments on the following questions which arise when considering the adoption of these recommendations under the regulatory provisions of CLIA.

General Requirements

Note: These issues apply to more than one phase of the testing process.

1. Are the Following Definitions for Categories of Genetic Testing To Be Covered Under a New CLIA Specialty of Genetics Appropriate (or Too Broad or Too Restrictive)?

A. *Current CLIA Requirement:* A specialty of genetic testing has not been defined under CLIA. However, CLIA already applies to genetic testing since it regulates any laboratory that examines human specimens to provide information for diagnosis, prevention, or treatment of any disease or impairment of, or assessment of the health of, human beings.

B. *CLIAC Recommendation:* The CLIAC suggested that the following definitions for the specialty of genetic testing be adopted.

Molecular genetic and cytogenetic test—An analysis performed on human DNA, RNA, and chromosomes to detect heritable or acquired disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes. Such purposes would include predicting risk of disease, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations.

Biochemical genetic test—The analysis of human proteins and certain metabolites, which is predominantly used to detect inborn errors of metabolism, heritable genotypes, or mutations for clinical purposes. Such purposes would include predicting risk of disease, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations. [Tests that are used primarily for other purposes, but may contribute to diagnosing a genetic disease (*e.g.* blood smear, certain serum chemistries), would not be covered by this definition.]

C. *Issue:* A genetic speciality will be linked to specific personnel qualifications and responsibility requirements, as well as proficiency testing and quality control provisions (see other recommendations which could also be implemented under the specialty). Therefore, inclusion or exclusion from the specialty could alter a laboratory's staffing plans, reimbursements, and overall costs.

2. What Is the Role of a Laboratory Director in Documenting the Clinical Validity of a Genetic Test Their Laboratory Plans To Offer? If There is a Role, How Should the Laboratory Director's Documentation of the Clinical Validity of a Genetic Test Be Monitored?

A. *Current CLIA Requirement:* Under 493.1407 Standard; Laboratory director responsibilities, (e) the laboratory director must ensure that testing systems developed and used for each of the tests performed in the laboratory provide quality laboratory services for all aspects of test performance, which includes the pre-analytic, analytic, and post-analytic phases of testing, ensure that the test methodologies selected have the capability of providing the quality of results required for patient care, and ensure that verification procedures used are adequate. Under 493.1213 Standard; establishment and verification of method performance specifications, prior to reporting patient test results the laboratory must verify or establish for each method, the performance specifications for: accuracy; precision; analytical sensitivity and specificity, if applicable; the reportable range of patient test results; the reference range; and any other applicable performance characteristics.

B. *CLIAC Recommendation:* Although the CLIAC considered the scope of the current laboratory director responsibilities to be adequate, they were concerned about how to monitor the laboratory director's documentation of the clinical validity for the tests performed. The CLIAC recommended adding specific requirements for analytical and clinical validation of tests (see question 7 below).

C. *Issue:* Although there are specific requirements for analytic validation, no specific requirements for clinical validation have been included under CLIA. Clinical validation of all tests, such as cholesterol, has been assumed to have been documented before tests are offered. Concerns about requiring specific documentation of the clinical validity of genetic tests have been expressed, with some expressing the view that establishing the clinical validity and documenting it for the tests offered are outside of the laboratory's purview.

3. Who Should Be Authorized To Order a Genetic Test?

A. *Current CLIA Requirement:* Under 493.1105 Standard; Test requisition—the laboratory must perform tests only at the written or electronic request of an authorized person.

Note: Under 493.2 Definitions—An authorized person means an individual authorized under State law to order tests or receive results, or both.

B. *CLIAC Concern:* The CLIAC raised the issue that some States provide no guidance on this issue.

C. *Issue:* Is genetic testing sufficiently different from other types of laboratory testing to warrant a new Federal requirement to define who is authorized to order a genetic test?

4. Should the Laboratory Be Required to Document That Informed Consent Has Been Obtained by an Authorized Person From the Person Being Tested Before Performing Certain Genetic Tests or Types of Tests (Screening, Diagnostic, Carrier, Presymptomatic, Susceptibility)?

A. *Current CLIA Requirement:* CLIA, at present, does not specifically require a laboratory to document that an informed consent has been obtained by

an authorized person before testing is performed.

B. *CLIAC Recommendation:* The CLIAC recommended the following guidance on this issue.

• Because of the sensitive nature of certain genetic tests, the laboratory must have assurance that the ''authorized'' person has obtained informed consent.

• At the request of the ''authorized'' person, the laboratory shall assist in developing appropriate informed consent for the particular test, including the limitations and consequences of the test results.

Note: The National Bioethics Advisory Commission in its August 1999 report on ''Research Involving Human Biological Materials: Ethical Issues and Policy Guidance'' provides guidance to *research laboratories,* which are exempt from CLIA if they do not report patient specific results. These recommendations do not apply to clinical interventions, quality control, or teaching, but only to ''a systematic investigation designed to develop or contribute to generalizable knowledge.''

C. *Issue:* Imposition of this requirement on laboratories could serve to protect patients from inappropriate testing, but increases the laboratory burden of documentation and could also delay obtaining genetic testing results. Are the CLIA regulations an appropriate place for regulating informed consent related to genetic testing? Also, how do current State medical consent laws factor into this?

5. Should Additional Processes Be in Place to Enhance the Confidentiality of Certain Genetic Test Information and Results?

A. *Current CLIA Requirement:* Under 493.1109 Standard; Test report, (a)—the laboratory must have adequate systems in place to report results in a timely, accurate, reliable, and confidential manner, and, ensure patient confidentiality throughout those parts of the testing process that are under the laboratory's control.

B. *CLIAC recommendation:* The CLIAC recommended the following guidance on this issue.

• Due to the sensitive nature of certain genetic test results, the laboratory must have a policy in place to protect the confidentiality of test result reporting.

• All requests for additional tests must follow confidentiality and informed consent requirements (see above).

Note: HHS under the Health Insurance and Portability and Accountability Act (HIPAA) published in the **Federal Register** on November 3, 1999 a proposed rule Standards for Privacy of Individually Identifiable Health Information. This rule applies to individually-identifiable health information that has been electronically transmitted or maintained. The NPRM is accessible at (http://www.aspe.hhs.gov/admnsimp/).

C. *Potential implication of the CLIAC issue:* This would not impose an additional requirement on laboratories, but would clarify that a policy must be in place for the genetic specialty. Is being this explicit for genetic testing necessary?

6. Assuming That a Genetic Specialty Under CLIA Is Defined and Recognized, Should a Laboratory Covered Under This Specialty Be Required To Provide Genetic Counseling to Their Clients (Including Medical Care Providers and Patients), for the Tests They Offer?

A. *Current CLIA Requirement:* Under 493.1419/493.1457 Standard; Clinical Consultant responsibilities—laboratories are required to have a qualified clinical consultant to provide consultation regarding the appropriateness of the testing ordered and interpretation of test results. The consultant must be available to provide consultation and to assist in ensuring that appropriate tests are ordered to meet clinical expectations, and ensure that reports of test results include pertinent information required for specific patient interpretation, and that matters related to the quality of test results are communicated.

B. *CLIAC Recommendation:* The CLIAC recommended that the qualifications and responsibilities of the clinical consultant be expanded to assure that someone associated with the laboratory be capable of providing genetic counseling to the laboratory's clients (care providers, patients, individuals, etc.).

Clinical Consultant—Be an M.D., D.O., and have two years experience in genetic testing.; or hold a Ph.D. in a relevant discipline, be Board certified, and have two years experience in genetic testing; or hold an MS in Genetic Counseling, be Board certified, and have two years experience in genetic testing (prospective).

Clinical Consultant—For genetic testing, require that the Clinical Consultant assist clients in ordering appropriate tests to meet clinical needs.

C. *Issues:* Will there be a sufficient number of qualified clinical consultants available and is the experience mentioned necessary for all types of genetic tests? Will care providers request/accept assistance in ordering genetic tests? What should the role of the laboratory be in counseling providers and/or patients. Does it extend to family members?

Requirements Related to Specific Phases of the Testing Process

These issues apply to one phase of the testing process.

7. Should the Following Requirements Be Added Under a Specialty of Genetics to CLIA To Address Unique Aspects of Laboratory Responsibility for Genetic Testing?

Pre-Analytic Phase

Obtaining Clinical Information on the Test Requisition and the Ordering of Additional Tests

A. *Current CLIA Requirement:* Under 493.1419/493.1457; Standard; Clinical Consultant responsibilities—laboratories are required to have a qualified clinical consultant to provide consultation regarding the appropriateness of the testing ordered and interpretation of test results. The consultant must be available to provide consultation and to assist in ensuring that appropriate tests are ordered to meet clinical expectations, and ensure that reports of test results include pertinent information required for specific patient interpretation, and that matters related to the quality of test results are communicated. Also under 493.1105, Standard; Test Requisition, (f)—the laboratory must assure that the requisition or test authorization includes any additional information relevant and necessary to a specific test to assure accurate and timely testing and reporting.

B. *CLIAC recommendation:* Test Requisition and ordering additional tests:

• Appropriate clinical information to ensure accurate and reliable genetic testing must be provided with the test request.

Note: In some instances very explicit information may be required to decide which test method to use and to appropriately interpret the results. Such information would include all that is relevant and necessary to ensure accurate and timely testing, interpretation and reporting of results and elements to ensure proper identification of the subject being tested. Relevant information for a genetic test may include date of birth, gender, ethnicity, and/or family history)

• When deemed necessary, the laboratory shall assist those ordering tests by suggesting follow-up tests, when appropriate, to expedite the function of obtaining relevant clinical information.

Re-Use of Tested Specimens.

• When patient identifiers are not removed from the specimens, informed consent must be obtained prior to re-use of previously tested specimens for quality control (QC) and quality assurance (QA) purposes.

• When the laboratory intends to re-use previously tested specimens without patient identifiers for QC and QA, it must have a procedure that permits patients with a personal objection to other uses of their specimen to be able to elect not to have their specimen used for these purposes.

• The use of a retained sample does not require informed consent if all identifiers are removed and the patient has had an opportunity to decline being tested.

C. *Issue.* The laboratory may require additional patient information in order to make decisions about which specific tests or additional tests would be most useful to provide the needed clinical information. However, this information may be difficult to obtain in every instance. With respect to additional testing, coverage or payment for testing may be an issue. The conditions under which testing specimen may be re-used for quality control is generally accepted as good laboratory practice, but not explicitly provided for under current requirements.

Analytic Phase

Personnel Qualifications

A. *Current CLIA Requirement:* Under Subpart M—Personnel for High Complexity Testing:

Laboratory Director—Be an M.D. or D.O. or DPM with certification in clinical and/or anatomic pathology; or be a Ph.D. and be certified by a board approved by HHS; or be an M.D. or D.O. and have two years directing or supervising high complexity testing; or hold a doctorate degree in a chemical, physical, biological, or clinical laboratory science, be certified, and have two years of supervisory experience in high complexity testing; or be grandfathered.

Technical Supervisor—Although no genetic specialty currently exists, the following technical supervisor requirements apply to the specialty of cytogenetics.—Be an M.D., D.O. or DPM with four years of training or experience in genetics, two of which have been in clinical cytogenetics; of Ph.D. with four years of training or experience in genetics, two of which have been in clinical cytogenetics.

General Supervisor—Be qualified as a laboratory director or technical supervisor; or be an M.D., D.O., DPM, or have a Doctorate, Masters or Baccalaureate degree in a chemical, physical, biological or clinical laboratory science, and have one year training or experience in high complexity testing; or have an Associate degree, or equivalent, in a chemical, physical, biological or clinical laboratory science and have two years training or experience in high complexity testing; or be grandfathered.

Clinical Consultant—Be qualified as a laboratory director or be an M.D., D.O., DPM and licensed to practice medicine in the State in which the laboratory is located.

B. *CLIAC recommendation:* To the current requirements listed above, add the following:

Laboratory Director—Be an M.D. or D.O. or DPM with certification in clinical and/or anatomic pathology; or be an M.D., D.O., or Ph.D. and be certified in medical genetics by a board approved by HHS; or be an M.D. or D.O. and have two years directing or supervising high complexity testing; or hold a doctorate degree in a chemical, physical, biological, or clinical laboratory science, be certified, and have two years of supervisory experience in high complexity testing; or be grandfathered

If a genetic specialty is developed, the CLIAC recommended the following personnel qualifications.

Technical Supervisor—Be an M.D. or D.O. with certification in clinical and/or anatomic pathology plus two years sub-specialty training in genetics and have two years supervisory experience in high complexity genetic testing, or have four years supervisory experience in high complexity genetic testing in the relevant subspecialty; or be an M.D., D.O. or Ph.D. and be certified in the appropriate medical genetics specialty and have two years experience directing or supervising high complexity genetic testing in the relevant subspecialty; or hold a doctorate degree in a chemical, physical, biological, or clinical laboratory science, and have four years of training or supervisory experience in high complexity genetic testing in the relevant subspecialty; or be grandfathered.

General Supervisor—Be qualified as a laboratory director or technical supervisor; or be an M.D., D.O., hold a Doctorate or Masters degree in a chemical, physical, biological or clinical laboratory science, and have two years experience in high complexity genetic testing; or hold a Baccalaureate degree in a chemical, physical, biological or clinical laboratory science and have three years experience in high complexity genetic testing; or be grandfathered.

Clinical Consultant—Be an M.D., D.O., and have two years experience in genetic testing.; or hold a Ph.D. in a relevant discipline, be Board certified, and have two years experience in genetic testing; or hold an MS in Genetic Counseling, be Board certified, and have two years experience in genetic testing (prospective).

C. *Issue:* Could assure higher quality in genetic testing, but could restrict who could serve in these personnel categories. The extent of the impact is dependent upon the tests included in the definition of the genetic specialty.

Personnel Responsibilities

A. *Current CLIA Requirements:* See Subpart M of 42 CFR Part 493.

B. *CLIAC Recommendations.* To the current requirements, add the following:

Technical Supervisor—The Technical Supervisor (in addition to the Laboratory Director and Clinical Consultant currently required under CLIA) must ensure that reports include pertinent information required for clinical interpretation that is meaningful to a non-geneticist health care provider.

Clinical Consultant—For genetic testing, require that the Clinical Consultant assist clients in ordering appropriate tests to meet clinical needs.

C. *Issue:* Could assure higher quality in genetic testing, but could be difficult for all laboratories to acquire the personnel with the skills needed.

Quality Control and Patient Test Management

A. *Current CLIA Requirement.* Under 493.1105 Standard; Test requisition and 493.1107 Standard; Test records a laboratory must ensure that the requisition or test records include patient's name or unique identifier and laboratory number; date of collection and receipt in the laboratory. Under 493.1213 Standard; establishment and verification of method performance specifications, prior to reporting patient test results the laboratory must verify or establish for each method, the performance specifications for: accuracy; precision; analytical sensitivity and specificity, if applicable; the reportable range of patient test results; the reference range; and any other applicable performance characteristics.

B. *CLIAC Recommendation.* The CLIAC recommended that the following new provisions be added:

Quality Control/Contamination

• A specimen should be stabilized until the clinical information for accurate testing is available.

• The laboratory must be designed to minimize contamination.

• Amplification procedures which are not in wholly closed systems must have separation between preparative and post-amplification steps.

• Work processes must minimize risk of mixing samples, and risk of

contamination of equipment, reagents, and/or supplies.

• RNA work areas must be separated from DNA work areas.

Specimen Integrity

• Requirements to ensure identification of the subject being testing include: date of birth; gender; ethnicity; patient or family number; specimen source; time of collection; and name of person obtaining sample

Validation of Tests

Analytic validation:

• Laboratories must verify or establish reproducibility for each method within and between runs, and between technologists.

• Methodology must be appropriate for conditions being evaluated.

• Quality control parameters must be applicable.

• Reagents must be validated.

Clinical Validation: Laboratories must consider the following clinical parameters for test validation:

• A positive confirmatory test must have a defined positive predictive value which can be communicated to the care giver.

• Where the disease prevalence is more frequent than 1/10,000, the validity must be documented in at least 10 positive probands (including cell lines or DNA/RNA) prior to offering the test.

• Predictive value should be defined in terms of ethnic populations, when applicable

C. *Issue:* These recommendations are based on what the CLIAC considers to be good laboratory practice in genetic testing. They represent extensions to existing requirements to specifically address some of the unique aspects of genetic testing. Are these sufficiently comprehensive, adequate, or are they not needed?

Proficiency Testing (PT)

A. *Current CLIA Requirement:* Under 493.801 Condition; Enrollment and testing of samples—a laboratory must enroll in an approved proficiency testing program for each specialty for which it seeks certification. Currently, no PT requirement exists, because there is no genetic specialty, therefore the following PT requirement applies. Under 493.1703 Standard; Comparison of test results—when a laboratory performs tests for which PT is unavailable, the laboratory must have a system for verifying the accuracy and reliability of its test results at least twice a year.

B. *CLIAC Recommendation:* The CLIAC recommended including the following new provision:

• When an approved PT program does not exist for the test, the regulations should require alternatives (to be performed three times per year, on five specimens per event). Examples include: Split samples sent to another laboratory; blinded test samples; test samples in duplicate by separate technologists, in a blinded manner; and other equivalent approaches

C. *Issue:* Requiring PT would provide a basis for evaluating the accuracy of genetic testing.

Post-Analytic Phase

Special Reporting Requirements

A. *Current CLIA Requirement:* Under 493.1109 Standard; Test report—a laboratory must, upon request, make available to clients a list of test methods and information that may affect the interpretation of test results, such as interferences.

B. *CLIAC Recommendation:* Laboratory reports must include the following, as applicable, as they relate to the interpretation of the test result:

—Interpretation.

—Comments.

—Recommendations for further testing or clinical consultation.

—Summary of the test method and its limitations.

• When individual interpretation of the test result is required, the signature of the Director or designee must appear on the report.

• A means to quickly contact the Laboratory Director/Technical Supervisor, in addition to address, must be indicated on the report.

• Any reference to family members in a test report must utilize standardized pedigree nomenclature or numeric indicators, instead of individual names.

• Specific requirements for reporting molecular genetic testing include:

—A list of the mutant alleles tested.

—The rate detection of the panel.

— A revised assessment of likelihood based on test results, as applicable.

—Important clinical implications for other family members should be provided, as applicable.

—Variables that affect test interpretation (*e.g.* ethnicity) must be specified in the report, and limitations of the testing must be defined.

C. *Issue:* Requiring laboratories to provide this information could increase the accuracy of interpretation of genetic testing reports, but may increase the laboratories' burden.

Record/Specimen Retention

A. *Current CLIA Requirement:* Under 493.1109 Standard; Test report—the laboratory must retain the original or an exact duplicate of each test report for a period of at least two years after the date of reporting.

B. *CLIAC Recommendation:*

• Copies of patient reports of genetic testing shall be retrievable for a minimum of 10 years, or longer if required by State law. Electronic reports are acceptable.

• The laboratory must have a policy defining specimen retention policies.

C. *Issue:* Maintaining reports for a longer period of time may be beneficial but this could be burdensome.

Dated: April 27, 2000.

Jeffrey Koplan,

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[Program Announcement 00107]

Population-Based Surveillance of Autism Spectrum Disorders and Other Developmental Disabilities; Notice of Availability of Funds

A. Purpose

The Centers for Disease Control and Prevention (CDC) announces the availability of fiscal year (FY) 2000 funds for a cooperative agreement program for Population-Based Surveillance of Autism Spectrum Disorders and other Developmental Disabilities. CDC is committed to achieving the health promotion and disease prevention objectives of ''Healthy People 2010.'' This announcement is related to the focus area of Maternal, Infant and Child Health. http://www.health.gov/healthypeople.

The purpose of the program is to: Enhance an existing system or develop and implement a new system to undertake a multiple source surveillance methodology, from existing data records, for determining the prevalence of autism and other developmental disabilities, such as mental retardation, cerebral palsy, and vision and hearing impairments, in 3–10 year-old children within a geographically-defined area (combination of States, Statewide, or regions within a State).

B. Eligible Applicants

Assistance will be provided only to the health departments of States or their