NEW YORK STATE | Department of Health | Wadsworth Center

ASSAY APPROVAL IN GENETIC TESTING - MOLECULAR

Please submit all information as outlined below.

Submit one hard copy of the entire package and one electronic copy (as a PDF file on a CD or flash drive) to:

US Postal Service: Clinical Laboratory Evaluation Program, Biggs Laboratory, Wadsworth Center, New York State Department of Health, Empire State Plaza, Albany, NY 12237; Attn: Assay Validation Review

UPS, FedEx, Courier: Clinical Laboratory Evaluation Program, Biggs Laboratory, Wadsworth Center, New York State Department of Health, Dock J - P1 Level, Empire State Plaza, Albany, NY 12237; Attn: Assay Validation Review

Materials submitted, including related data packages, cannot be returned to the laboratory. All materials are maintained under strict confidentiality. As relates to New York State's Freedom of Information Law (commonly called FOIL): The Department's Records Access Officer has advised Wadsworth Center that if documents are marked "proprietary"; "confidential"; or with any labeling indicative of the submitter's desire for an increased level of protection based on the submission content, such protection from immediate release based on a FOIL request is justified. Laboratories will be given an opportunity to block information release if a request for the material is filed under the FOIL, by presenting evidence that the materials contain trade secrets. Marking should minimally appear on the cover page of each unit of material. Documents not marked with such terms will not block release of the submission through a FOIL request.

SECTION 1: GENERAL INFORMATION

Laboratory Name: _____ NYS PFI: _____

Contact Person: _____

Phone: _____ Fax: _____ Contact E-mail: _____

Assay (Test) Name (e.g. *ABCD* mutation panel): _____

Methodology (e.g., PCR; sequencing, MPLA): _____

Gene/exons included (if different from Assay Name): _____

Validated Specimen Type(s) _____

Clinical Purpose: _____

_____

_____

Laboratory Director/Assistant Director (NYS Certificate of Qualification Holder for Genetic Testing – Molecular)

CQ Code_____ **Signature**_____

Laboratory Director (if not the responsible CQ Holder for Genetic Testing – Molecular)

CQ Code_____ **Signature**_____

SECTION 2: COMPLETE THIS PART ONLY FOR THOSE SUBMISSION TYPES LISTED BELOW. ALL OTHER SUBMISSIONS REQUIRE A COMPLETE PACKAGE AS DESCRIBED IN SECTION 3.

☐ FDA approved assays:
Provide the information described in Sections 3.6 and 3.7.

☐ Modified FDA or NYS-approved assay:
Describe the modification or change and attach a summary of the study performed to validate the modification.

☐ Addition of an assay under an approved exemption, provide the following:

- Completed Section 1 above;
- Provide a copy of your original exemption approval letter;
- A description of the condition being tested for, its incidence in the population and the proportion of affected individuals that will be identified by the test;
- An overview justifying the selection of genetic targets including a list of references which support the association of the gene(s) with the condition and a description of the database used in determining the significance of identified variants;
- The educational materials that will be provided to the patient and physician for the purpose of obtaining informed consent;
- Examples of reports for all possible outcomes (i.e., no mutation detected, positive for known mutation, heterozygous carrier, variant of unknown significance);
- A statement, signed by the director, that the validation was performed according to the laboratory's previously approved validation plan, indicating any deviations from the validation plan.

SECTION 3: COMPLETE THIS ENTIRE SECTION AND PROVIDE ALL REQUIRED ATTACHMENTS

Please submit the following information, organized as numbered or tabbed attachments as indicated below. If an item is not included, indicate the reason. Indicate the **page numbers and/or tabs where** the items and/or attachments can be found. **SUBMISSIONS THAT ARE NOT ORGANIZED AS DESCRIBED MAY BE RETURNED AND THE REVIEW SIGNIFICANTLY DELAYED.** Please refer to the **New York State Clinical Laboratory General Systems and Genetics Specialty Standards of Practice** in preparing your submissions.

Section 3.1: Overview

Page/Tab	
	Brief description of the disease, the gene (including structure and location of the alteration)
	Description of the test, principle of test, indications for testing
	Hard copies of pertinent references

Section 3.2: Specimen and Requisition Requirements

Page/Tab	
	Specimen collection and shipping requirements
	Specimen rejection criteria
	Sample requisition form meeting requirements in **Requisition Sustaining Standard of Practice 4 (Requisition S4): Request Form**.

Section 3.3a: Materials and Methods (Newly Applying Laboratories)

This section should include ***all*** information relevant to the test if you are new to the program; for example, include DNA extraction, dilution, and quantitation protocols. Procedure manuals must contain all required elements as described in the **NYS General Systems Standards, Operating Procedures Sustaining Standard of Practice 2 (SOPM S2) Content (a-q)**. Also include:

Page/Tab	
	Reagent recipes (stock and working), final concentrations
	Vendor/catalog information for all required materials, reagents, equipment, instrumentation
	Reagent quality control (stability and storage requirements)
	Step-by-step protocol (clear enough for a technical staff person to follow)
	Primer list with sequences, reference (literature or database) from which they were derived. Include where they reside on the gene.
	Description of positive controls, describe source and how they were verified as positive controls (e.g., sequenced cell line from clinically diagnosed patient, etc.)
	Description of negative controls
	Description of how controls are used in the assay; if rotated, give algorithm
	Technical limitations and troubleshooting guide, protocol to deal with assay problems
	Description of assay interpretation and translation to the report
	Quality assurance (how is reliability demonstrated per **Quality Assessment Sustaining Standard of Practice 3 (QA S3): Ongoing Verification of Examination Accuracy)**
	Safety - Biohazard, chemical and radiation exposure

Section 3.3b: Materials and Methods (Laboratories with Previously-Approved Assays)

This section should include information to describe the specific test. Procedure manuals must contain all required elements as described in the **NYS General Systems Standards, Operating Procedures Sustaining Standard of Practice 2 (SOPM S2) Content (a-q)**. Also include:

Page/Tab	
	Reagent recipes (stock and working), final concentrations
	Vendor/catalog information for all required materials, reagents, equipment, instrumentation
	Reagent quality control (stability and storage requirements)
	Step-by-step protocol, (clear enough for a technical staff person to follow)
	Primer list with sequences, reference (literature or database) from which they were derived. Include where they reside on the gene.
	Description of positive controls, describe source and how they were verified as positive controls (e.g., sequenced cell line from clinically diagnosed patient, etc.)
	Description of negative controls
	Description of how controls are used in the assay; if rotated, give algorithm
	Technical limitations and troubleshooting guide, protocol to deal with assay problems
	Description of assay interpretation and translation to the report

Section 3.4: Validation

Page/Tab	
	Explanation/narrative describing how validation studies were performed
	Validation study results and interpretation; provide summary tables
	Reproducibility (intra- and inter-assay); typically 3-5 samples repeated 3 times in the same run for intra-assay variability and 3-5 samples repeated on 3 different days
	For sequence analysis submit color electropherograms showing one complete normal sequence and then electropherograms showing only those fragments in which a variation was detected.
	Sensitivity/specificity or positive predictive value; as applicable
	If the validation was completed by parallel testing with another laboratory, include a copy of the correspondence demonstrating concordance; if there is a discrepancy describe how it was resolved

Section 3.5: Results and Interpretations

Page/Tab	
	Describe expected results from controls and what an indeterminate result would look like (size of PCR fragments/gel/banding patterns etc.)
	Provide ***high quality original*** results of a sample of validation data or a run showing wild type, heterozygous and homozygous (if available) mutant results.
	If performing sequence analysis, include one complete "normal" control electropherogram, and electropherograms (both directions) of detected mutations or snps, clearly marked on the sequence (include base and amino acid changes, extent of deletion/insertion).
	Describe criteria to accept and reject results

Section 3.6: Consent Form

The consent form should comply with the Genetic Testing Confidentiality Law Article 7, Section 79-l. Each consent form should be "disease-specific", i.e, there should not be a blank line to fill in for the disease. If you have a general form, an information sheet covering material specific to the test should be attached to the consent and initialed by the patient to indicate they received/read the material. Laboratories should have a policy in place [i.e. a consent form available that adheres to these requirements for clients to use] to ensure the patient agrees to the test requested.

Check (√) to indicate that your consent form includes the following elements:

	Description of the disease
	Description of the test
	Principle of the test
	Meaning of a positive test result
	Meaning of a negative test result
	Statement regarding test limitations
	Who will receive this information, confidentiality
	Statement that genetic counseling be offered *prior to* signing the form and that it be available after the test. Also, include a statement that further testing or additional physician consults may be warranted.
	Statement regarding specimen retention [destroy sample after 60 days]. If you retain the blood/DNA [be clear which is being saved], there should be a separate check box or initial line for the patient to indicate they agree with usage and storage of the specimen after testing. This separates their consent for you to store/use their specimen from their consent for the test.
	Signature lines for client and for physician /counselor / health personnel administering the form.

Section 3.7: Sample Reports

Sample reports (in the laboratory's official report format) for all applicable findings including interpretive text, assay limitations (both diagnostic and technical limitations), compliant with **Reporting Sustaining Standard of Practice 1 (Reporting S1): Report Content**

Page/Tab

	Provide a sample report showing a negative result
	Provide sample reports showing positive results (heterozygous, compound heterozygous, homozygous as applicable)
	For sequence reports, submit one report of a known mutation, a likely deleterious result, a possibly deleterious result, and a variant of unknown significance.

Check (√) to indicate that your reports include the following elements:

	Test result
	Interpretive statement, which specifically explains the test results
	Method used
	Use of proper nomenclature (HGVS)
	Explanation of test limitations, any required disclaimer statements
	Specimen information, (date collected, received, reported, accession no., patient name and date of birth, indication for testing, sample type)
	Signature line for Laboratory Director or Assistant Director (Certificate of Qualification holder)