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Prenatal Screening

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California Department of Public Health

Genetic Disease Screening Program

Prenatal Diagnosis Screening Standards and Definitions 2018

California Department of Public Health
Genetic Disease Screening Program

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**PRENATAL DIAGNOSIS CENTER
STANDARDS AND DEFINITIONS
2018**

I. COMPREHENSIVE PRENATAL DIAGNOSIS CENTER

A Comprehensive Prenatal Diagnosis Center is an established State-approved center with a complete range of prenatal diagnosis services and full-time multidisciplinary medical staff as follows:

- A. Has a Director who is certified in Clinical Genetics by the American Board of Medical Genetics and Genomics (ABMGG). The Director is responsible for such administrative duties as:
1. The supervision and the quality of testing, counseling, and medical care provided by all clinical members of the Prenatal Diagnosis Center (PDC) staff, including Satellites;
 2. Assurance that participation in prenatal diagnosis procedures by any pregnant woman is voluntary;
 3. Notifying the Genetic Disease Screening Program (GDSP) within ten working days of:
 - a. Any changes in locations where services are provided or in staffing of locations, including a plan to meet the Standards on an interim and permanent basis; and
 - b. Any case of maternal mortality that could possibly be related to or associated with prenatal diagnosis;
 4. The acceptance for prenatal diagnosis of all pregnant women referred from State funded or administered programs;
 5. The timely submission of required reports including reports on each patient with abnormal results, quarterly Prenatal Diagnosis Center reports, and all practitioners' Adverse Outcome Studies;
 6. The timely submission of required annual reports, including annual statistics on procedures performed and tests ordered through GDSP approved cytogenomics and cytogenetics laboratories;
 7. The acceptance of site visits by State staff or designated State agents and to make available confidential patient reporting systems, billing and medical records needed to monitor compliance with the PDC Standards and California Prenatal Screening Program Guidelines. PDC sites are

required to retain paper charts on-site for one year for chart audit. The retention of paper charts does not apply to institutions using electronic charting, as long as GDSP can access the necessary elements in the electronic chart.

- B. An approved Clinical Geneticist(s) certified in Clinical Genetics by ABMGG, or having Active Candidate status for the next ABMGG certification examination, must:
1. Be available to provide consultation in person within three working days to all families with abnormal or questionable results. The consultation offer must be documented in the patient's chart; and
 2. Supervise all professional services and be responsible for the evaluation of work performance by reviewing and signing off on all patient charts. The Clinical Geneticist must sign the chart within 30 days of the final date of service. The signature indicates a review of the family history; ultrasound findings; and cell-free DNA (cfDNA) screening, amniocentesis and/or Chorionic Villus Sampling (CVS) consent forms or documentation of declines to ensure appropriate services meeting State Standards have been provided. The chart must also be reviewed for the cfDNA screening, amniocentesis, and/or CVS results and documentation that the results and all significant clinical information have been sent to the referring physician. If the cfDNA screening, amniocentesis or CVS results are normal, this last review may be performed by an approved California licensed Genetic Counselor. If the results are abnormal, this review must be performed by a Clinical Geneticist and there must also be documentation of appropriate consultation offered to the patient. A Clinical Geneticist may be responsible for supervision of services to no more than 200 prenatal patients per week.

In Sections C, K, and L, the number of procedures excludes repeat insertions.

- C. Has ultrasound-guided amniocentesis available at greater than/equal to 15 weeks gestation (standard amniocentesis). This is performed by physicians who:
1. Have approval as Amniocentesis Practitioners, are certified by the American Board of Obstetrics and Gynecology or have Active Candidate status for the next certification exam, and after previously completing 25 second trimester procedures on women planning to continue their pregnancies with on-site supervision in the procedure room by an OB/GYN experienced in ultrasound-guided amniocentesis. Each of the physicians performing or supervising the procedures must have specific knowledge and experience with:
 - a. Obstetrical ultrasonography; and
 - b. Basic genetic information and appropriate counseling procedures for chromosomal, biochemical and neural tube defects; or
 2. Have interim approval to perform amniocentesis under supervision as

Interim Approval Amniocentesis Practitioners. Each Interim Approval Amniocentesis Practitioner must:

- a. Currently be in a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME or have completed a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME; and
- b. Apply to and be approved by GDSP as an Interim Approval Amniocentesis Practitioner. Part of the application process is to identify each on-site supervisor who must be in the procedure room immediately adjacent to the practitioner during the procedure. The supervisor must be a State-approved Amniocentesis Practitioner who is an OB/GYN experienced in ultrasound-guided amniocentesis. Each supervisor must provide a written acknowledgment that they shall be in the room and immediately adjacent to the performing Interim Approval Amniocentesis Practitioner during the supervised procedure(s). After approval, Interim Approval Amniocentesis Practitioners may then perform second trimester amniocentesis procedures on California Prenatal Screening Program patients; and
- c. Perform at least 25 second trimester amniocentesis procedures on women planning to continue their pregnancies with on-site supervision by the supervising State-approved Amniocentesis Practitioner who shall be in the room and immediately adjacent to the performing Interim Approval Amniocentesis practitioner performing the procedure. The Interim Approval Amniocentesis Practitioner must perform a minimum of 5 amniocentesis procedures annually or they will have approval withdrawn; and
- d. Submit a log for review every six months with the following parameters of the 25 supervised procedures to GDSP. The practitioner is required to provide:
 - i. A patient identifier;
 - ii. The indication for performing the procedure;
 - iii. The date the procedure was performed;
 - iv. The gestational age at the time of the procedure;
 - v. The name of the in-room Supervisor;
 - vi. The number of fetuses;
 - vii. The number of insertion attempts;
 - viii. Whether an inadequate volume of amniotic fluid (less than 10 cc's) was obtained, with a reason for inadequate sample size;
 - ix. Whether fetal anomalies were observed on ultrasound, with details of any fetal anomalies;

- x. Whether the cytogenetic or cytogenomic results were normal or abnormal, with details for any abnormal result;
 - xi. Whether the procedure was followed by failure to obtain a test result, with reason for any failure;
 - xii. Whether the procedure was followed by normal fetal loss, with gestational age at fetal loss;
 - xiii. Name of person reporting the cytogenetic or cytogenomic results, and the date results were reported; and
 - xiv. Whether an elective termination occurred prior to reporting of results.
- e. Upon completion of the required 25 supervised amniocentesis procedures and submission of the log(s), the Interim Approval Amniocentesis Practitioner may be granted full approval as an Amniocentesis Practitioner and then they must begin collecting Adverse Outcome data on consecutive second trimester amniocentesis procedures under the conditions outlined in Section N.
3. The following volume requirements apply to State-approved Amniocentesis Practitioners:
- a. Each State-Approved Amniocentesis Practitioner must perform at least 15 successful second trimester amniocentesis procedures per year for cell culture and analysis, or they may be placed on provisional approval status or have approval withdrawn.
 - b. Any State-approved Amniocentesis Practitioner that provides direct supervision over a Fellow in an ABOG/ACGME recognized Fellowship Program or another amniocentesis practitioner may include supervised second trimester amniocentesis procedure(s) referred to in Section C.2.c. toward their annual volume requirement.
 - c. If an Amniocentesis Practitioner performs less than 5 second trimester amniocentesis procedures annually, the Amniocentesis Practitioner's approval will be withdrawn.
- D. Has consultative ultrasonography available which is performed by a physician on site who:
- 1. Is Board certified in Radiology by the American Board of Radiology or OB/GYN by ABOG, or has Active Candidate status for the next Board examination, and
 - 2. Has completed a fellowship recognized by the American Board of Radiology, ABOG and/or ACGME and had supplemental subspecialty training in:
 - a. maternal/fetal medicine; or
 - b. clinical genetics, with an emphasis upon fetal medicine; or

- c. diagnostic radiology, body imaging or the equivalent with an emphasis upon fetal medicine.

The supplemental training must be at a facility that performs at least 2,000 second trimester fetal ultrasound exams a year that meet the anatomical guidelines of the American Institute of Ultrasound in Medicine/American College of Radiology (AIUM/ACR) for complete fetal examinations. The supplemental training must include at least three months of targeted fetal ultrasound examinations that involve high-risk obstetric imaging and must include basic physics, techniques, performance, and interpretation followed by three months of proctoring, i.e., co-reading, by a qualified consultative sonologist; and

- 3. Has previously performed 500 detailed second trimester ultrasound exams on patients referred specifically for the detection of fetal abnormalities. Indications would include:

twins, early growth delay, oligohydramnios, polyhydramnios, abnormality observed at another facility, history of genetically transmitted disease, insulin dependent diabetes, family history of malformation and advanced maternal age.

The emphasis of these examinations is a detailed and targeted survey of fetal anatomy for malformations and must include:

fetal number, fetal presentation, documentation of fetal life, placental localization, amniotic fluid volume, gestational dating, detection and evaluation of maternal pelvic mass, and a survey of fetal anatomy for malformations; and

- 4. Performs, as a solo practice Consultative Sonologist, a minimum of 200 detailed second trimester prenatal ultrasound exams annually on pregnancies at risk for fetal abnormalities. Each group practice Consultative Sonologist shall perform at least 150 detailed second trimester prenatal ultrasound exams annually on pregnancies at risk for fetal abnormalities. A group practice is defined as a situation where all Consultative Sonologists practice at the same location.

If these minimum requirements are not met for two consecutive years, the Consultative Sonologist would become provisional and GDSP will notify the practitioner that if the practitioner's ultrasound volume continues to be low after the third year, the Consultative Sonologist's approval status may be withdrawn.

- 5. Is part of an ultrasound practice at a State-approved Prenatal Diagnosis Center that is accredited by the American College of Radiology (ACR) or the American Institute of Ultrasound in Medicine (AIUM).

- E. Provides all clients choosing to terminate the pregnancy referral to a facility with assured access to second trimester abortions by a method which usually allows confirmation of diagnosis unless medically contraindicated.

F. Has genetic counseling services which are performed by an approved California licensed Genetic Counselor or Clinical Geneticist. Each approved Center must have at least one California licensed Genetic Counselor or one Genetic Counselor with a temporary California license, and:

1. Prior to cfDNA screening, Chorionic Villus Sampling (CVS), and/or amniocentesis procedures, each woman must be offered genetic counseling under the supervision of a Clinical Geneticist and provide informed consent.
2. Genetic Counselors with a temporary Genetic Counselor License must attend continuing education courses and/or conferences for 15 hours within a year of being given approval at a PDC.

At least ten of the hours must be from continuing education courses and/or conferences that are approved as Category 1 continuing education units (CEUs) by the National Society of Genetic Counselors (NSGC). Only 5 hours of the 15 hours may be from events relevant to a genetic counselor's continuing education that is approved by NSGC as Category 2 CEUs.

3. All patients seen for genetic counseling must have a genetic risk assessment that includes the minimal elements contained in the Prenatal Genetic Screening Questionnaire and/or Pedigree. A pedigree is required if the patient, partner or fetus is at increased risk for a genetic disorder due to a significant family history indicated on the questionnaire.

G. Utilizes GDSP approved cytogenetics and/or cytogenomics laboratories. A cytogenomics laboratory is defined by GDSP as a laboratory that meets all State and federal requirements to perform prenatal karyotyping and prenatal chromosomal microarray tests. A cytogenetics laboratory is defined by GDSP as a laboratory that meets all State and federal requirements to perform prenatal karyotyping but does not perform prenatal chromosomal microarray tests. Cytogenetics laboratories performing only karyotyping must submit evidence of a collaborative agreement with a GDSP approved cytogenomics laboratory performing chromosomal microarray tests for initial and continued GDSP approval. All laboratories performing chromosomal microarray tests must also meet all State and federal requirements for performing karyotypes from amniotic fluid and CVS samples in order to be approved as cytogenomics laboratories. Initial and continued GDSP approval as a cytogenomics or cytogenetics laboratory is contingent on the following criteria:

1. Holding a Clinical Laboratory Improvement Amendments (CLIA) Certificate of Compliance or Certificate of Accreditation and being licensed as a Clinical Laboratory by the State of California.
2. Direction by a clinical cytogeneticist certified by the American Board of Medical Genetics and Genomics (ABMGG) or Canadian College of Medical Genetics (CCMG) and licensed by the State of California to direct a clinical cytogenetics laboratory. Laboratories must also meet the

Technical Supervisor requirements of CLIA. The director of a laboratory performing high complexity testing may function as the technical supervisor provided he or she meets the qualifications specified in CLIA.

3. Karyotyping performed by personnel licensed by the State of California to perform prenatal karyotyping. Each person performing such high complexity tests or examinations, as defined under CLIA, shall possess a valid clinical cytogenetic scientist license except for persons licensed by the State of California as a clinical cytogeneticist licensed to direct a clinical cytogenetics laboratory; a clinical laboratory bioanalyst; or a clinical laboratory scientist. Karyotype test interpretation should be performed by an ABMGG-certified or CCMG-certified clinical cytogeneticist of the facility where karyotyping is performed.
4. For cytogenomics laboratories, microarray testing performed by personnel licensed by the State of California to perform chromosomal microarray testing. Each person performing such high complexity tests or examinations, as defined under CLIA, shall be licensed by the State of California as a clinical cytogeneticist; a clinical cytogenetic scientist; a clinical laboratory bioanalyst; a clinical genetic molecular biologist licensed to direct a genetic laboratory; a clinical laboratory scientist; or a clinical genetic molecular biologist scientist. Microarray test interpretation should be performed by an ABMGG-certified or CCMG-certified clinical cytogeneticist, or by an ABMGG-certified or CCMG-certified molecular geneticist in conjunction with an ABMGG-certified or CCMG-certified clinical cytogeneticist, of the facility where microarray testing is performed.
5. Laboratory personnel must have training, competency assessments, and continuing education as required by appropriate regulatory bodies, e.g., College of American Pathologists (CAP), CLIA, Centers for Medicare & Medicaid Services.
6. Compliance with the American College of Medical Genetics and Genomics (ACMG) Standards and Guidelines for Clinical Genetics Laboratories (revised 2018), and, for cytogenomics laboratories, the ACMG Standards and Guidelines for Constitutional Cytogenomic Microarray Analysis, including Postnatal and Prenatal Applications (2013).
7. Prior to independent prenatal amniotic fluid cell culture and analysis, a new applicant cytogenetics or cytogenomics laboratory must meet criteria 1-6 above as appropriate and provide evidence of quality assurance and quality control policies for the implementation of prenatal karyotyping. A laboratory seeking approval to conduct amniotic fluid karyotyping must:
 - a. Establish a consultative affiliation with an approved laboratory which is financially independent of the applicant agency to split and proficiently analyze 50 consecutive amniocentesis samples from viable pregnancies for clinical diagnosis, meeting the analytical standards of ACMG's Standards and Guidelines for Clinical Genetics Laboratories (revised 2018) for cell culture, count, analysis, and karyotyping. If the samples are from California Prenatal Screening Program patients,

PDCs shall inform patients that samples are being split. Either the applicant laboratory or the approved laboratory may be responsible for splitting the 50 consecutive samples prior to analysis by each respective laboratory. During this period, samples that are too small to split shall remain at the laboratory receiving the sample for culture and analysis. Test results from the samples analyzed shall be reported for clinical purposes by the laboratory receiving and splitting the samples, if the laboratory is appropriately certified, licensed, and accredited under federal and state law and regulation. The applicant laboratory must submit a review of the 50 results of the test, and ongoing quality assurance/quality control indicators once the test is validated. Review of the 50 samples by both applicant and consultative affiliate laboratories must be documented in a letter itemizing the cases and including a general overview of the quality assurance/quality control policies enacted for the ongoing monitoring of amniotic fluid karyotyping. A record of this review must be kept for ten years in an easily retrievable form. The successful analysis of at least 98 percent of the split samples by the applicant laboratory shall be deemed proficient; and

- b. Submit results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys); and
 - c. Submit a copy of the applicant laboratory's CLIA Certificate; and
 - d. Submit a copy of the applicant laboratory's California Laboratory License; or
 - e. If an applicant laboratory holds a license or permit as a clinical laboratory, with approval to perform prenatal karyotyping, issued by a state in which the clinical laboratory standards, including standards for validation studies for prenatal karyotyping approval, are equal to or exceed GDSP standards (as determined by GDSP), the applicant laboratory may submit these validation studies to GDSP as evidence of quality assurance and quality control policies, together with results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys), a copy of the applicant laboratory's CLIA Certificate, and a copy of the applicant laboratory's California Laboratory License, to meet the requirements of this subsection.
8. A new applicant cytogenomics or cytogenetics laboratory seeking approval to conduct CVS karyotyping must:
- a. Establish a consultative affiliation with an approved laboratory which is financially independent of the applicant agency to split and proficiently dissect, culture, and analyze 50 consecutive CVS samples from viable pregnancies for clinical diagnosis, meeting the analytical standards of ACMG's Standards and Guidelines for Clinical Genetics Laboratories (revised 2018) for cell culture, count, analysis, and karyotyping. If the

samples are from California Prenatal Screening Program patients, PDCs shall inform patients that samples are being split. During this period, samples that are too small to split shall remain at the laboratory receiving the sample for culture and analysis. Test results from the samples analyzed shall be reported for clinical purposes by the laboratory receiving and splitting the samples, if the laboratory is appropriately certified, licensed, and accredited under federal and state law and regulation. The applicant laboratory must submit a review of the 50 results of the test, and ongoing quality assurance/quality control indicators once the test is validated. Review of the 50 samples by both applicant and consultative affiliate laboratories must be documented in a letter itemizing the cases and including a general overview of the quality assurance/quality control policies enacted for the ongoing monitoring of CVS karyotyping. A record of this review must be kept for ten years in an easily retrievable form. The successful analysis of at least 98 percent of the split samples by the applicant laboratory shall be deemed proficient; and

- b. Submit results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys); and
 - c. Submit a copy of the applicant laboratory's CLIA Certificate; and
 - d. Submit a copy of the applicant laboratory's California Laboratory License; or
 - e. If an applicant laboratory holds a license or permit as a clinical laboratory, with approval to perform prenatal karyotyping, issued by a state in which the clinical laboratory standards, including standards for validation studies for prenatal karyotyping approval, are equal to or exceed GDSP standards (as determined by GDSP), the applicant laboratory may submit these validation studies to GDSP as evidence of quality assurance and quality control policies, together with results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys), a copy of the applicant laboratory's CLIA Certificate, and a copy of the applicant laboratory's California Laboratory License, to meet the requirements of this subsection.
9. A laboratory that has obtained prior GDSP approval to conduct amniotic fluid karyotyping and is seeking approval to conduct CVS karyotyping must:
- a. Establish a consultative affiliation with an approved laboratory which is financially independent of the applicant agency to split and proficiently dissect, culture, and analyze 25 consecutive CVS samples from ongoing, continuing pregnancies for clinical diagnosis, meeting the analytical standards of ACMG's Standards and Guidelines for Clinical Genetics Laboratories (revised 2018) for cell culture, count, analysis, and karyotyping. If the samples are from California Prenatal Screening

Program patients, PDCs shall inform patients that samples are being split. During this period, samples that are too small to split shall remain at the laboratory receiving the sample for culture and analysis. Test results from the samples analyzed shall be reported for clinical purposes by the laboratory receiving and splitting the samples, if the laboratory is appropriately certified, licensed, and accredited under federal and state law and regulation. The applicant laboratory must submit a review of the 25 results of the test, and ongoing quality assurance/quality control indicators once the test is validated. Review of the 25 samples by both applicant and consultative affiliate laboratories must be documented in a letter itemizing the cases and including a general overview of the quality assurance/quality control policies enacted for the ongoing monitoring of CVS karyotyping. A record of this review must be kept for ten years in an easily retrievable form. The successful analysis of at least 96 percent of the split samples by the applicant laboratory shall be deemed proficient; and

- b. Submit results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys); and
 - c. Submit a copy of the applicant laboratory's CLIA Certificate; and
 - d. Submit a copy of the applicant laboratory's California Laboratory License; or
 - e. If an applicant laboratory holds a license or permit as a clinical laboratory, with approval to perform prenatal karyotyping, issued by a state in which the clinical laboratory standards, including standards for validation studies for prenatal karyotyping approval, are equal to or exceed GDSP standards (as determined by GDSP), the applicant laboratory may submit these validation studies to GDSP as evidence of quality assurance and quality control policies, together with results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys), a copy of the applicant laboratory's CLIA Certificate, and a copy of the applicant laboratory's California Laboratory License, to meet the requirements of this subsection.
10. Prior to independent microarray analysis, an applicant cytogenomics laboratory must provide evidence of quality assurance and quality control policies for the implementation of prenatal microarray testing. A laboratory seeking initial and continued approval to conduct prenatal microarray analysis must meet the following requirements:
- a. Submit an application documenting compliance with the ACMG Standards and Guidelines for Constitutional Cytogenomic Microarray Analysis, including Postnatal and Prenatal Applications (2013) for platform verification, accuracy testing, and precision testing. The application must include:

i) for Cytogenomics Laboratories with a microarray platform previously validated in accordance with ACMG Standards and Guidelines for Constitutional Cytogenomic Microarray Analysis, including Postnatal and Prenatal Applications (2013) on or prior to June 30, 2015:

(1) If the completed validation study on at least 30 postnatal and/or prenatal samples included at least five abnormal prenatal specimens, and meets ACMG precision testing requirements, this validation study may be submitted to meet the requirements of this section. The successful analysis of at least 95 percent of the samples shall be deemed proficient. The precision of the microarray platform should be established by running two abnormal samples twice in separate experiments, with the concordance of the repeated runs documented and submitted. All variants, including benign, should be documented and results should be unmasked for precision testing. The successful analysis of 100 percent of the samples in the precision testing shall be deemed proficient, recognizing that the size of copy number variants may not be identical in each run. Records of these studies must be kept for ten years in an easily retrievable form; or

(2) If the completed validation study did not include at least five abnormal prenatal specimens, an additional validation study on five prenatal samples previously characterized as abnormal must also be submitted to meet the requirements of this section. The microarray should confirm these results, and findings of reportable microarray copy number variants and absence of heterozygosity (AOH), loss of heterozygosity (LOH), regions of homozygosity (ROH), and long contiguous stretches of homozygosity (LCSH), if applicable, should be confirmed by another method if below levels detectable by karyotyping. Samples must comprise a representative distribution of the specimen types to be tested (uncultured cells from amniotic fluid; uncultured cells from CVS; cultured cells from amniotic fluid; and cultured cells from CVS, as applicable). DNA must be extracted by the laboratory from the relevant specimen type/s, and the DNA extraction process must be part of the validation process. If the original validation study did not include precision testing on two abnormal samples twice in separate experiments, an additional precision study on two abnormal samples, with the concordance of the repeated runs documented, must be submitted. All variants, including benign, should be documented and results should be unmasked, and the successful analysis of 100 percent of the samples in the

precision testing shall be deemed proficient, recognizing that the size of copy number variants may not be identical in each run. Records of these studies must be kept for ten years in an easily retrievable form; and

(3) The relevant contents from the Standard Operating Procedure specifying the criteria to classify aberrations as clinically relevant, benign, or of unknown clinical relevance (e.g. identifying gene content, databases utilized); and

(4) Sample reports for abnormal findings and variants of unknown significance; and

(5) Results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys); and

(6) A copy of the applicant laboratory's CLIA Certificate; and

(7) A copy of the applicant laboratory's California Laboratory License; and

(8) A copy of the applicant Director's California Laboratory License; or

ii) for Cytogenomics Laboratories that have not previously validated the microarray platform on or prior to June 30, 2015:

(1) A validation study in tabular form demonstrating an ability to proficiently test and analyze 30 previously characterized prenatal samples by microarray. At least five abnormal samples must be included. For samples previously characterized as abnormal from cytogenetic studies, the microarray should confirm these results, and findings of reportable microarray copy number variants and absence of heterozygosity (AOH), loss of heterozygosity (LOH), regions of homozygosity (ROH), and long contiguous stretches of homozygosity (LCSH), if applicable, should be confirmed by another method if below levels detectable by karyotyping. Samples must comprise a representative distribution of the specimen types to be tested (uncultured cells from amniotic fluid; uncultured cells from CVS; cultured cells from amniotic fluid; and cultured cells from CVS, as applicable). DNA must be extracted by the laboratory from the relevant specimen type/s, and the DNA extraction process must be part of the validation process. The successful analysis of at least 95 percent of the samples shall be deemed proficient. The precision of the microarray platform should be established by running two abnormal prenatal samples twice in separate experiments, with the concordance of the repeated runs documented and submitted. All variants, including benign, should be documented and results should be unmasked for

precision testing. The successful analysis of 100 percent of the samples in the precision testing shall be deemed proficient, recognizing that the size of copy number variants may not be identical in each run. Records of these studies must be kept for ten years in an easily retrievable form; and

(2) The relevant contents from the Standard Operating Procedure specifying criteria to classify aberrations as clinically relevant, benign, or of unknown clinical relevance (e.g. identifying gene content, databases utilized); and

(3) Sample reports for abnormal findings and variants of unknown significance; and

(4) Results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys); and

(5) A copy of the applicant laboratory's CLIA Certificate; and

(6) A copy of the applicant laboratory's California Laboratory License.

(7) A copy of the applicant Director's California Laboratory License.

- b. If an applicant laboratory holds a license or permit as a clinical laboratory, with approval to perform prenatal microarray, issued by a state in which the clinical laboratory standards, including standards for validation studies for prenatal microarray approval, are equal to or exceed GDSP standards (as determined by GDSP), the applicant laboratory may submit these validation studies to GDSP as evidence of quality assurance and quality control policies, together with sample reports for abnormal findings and variants of unknown significance and results from participation in four consecutive external proficiency testing assays (College of American Pathologists Surveys), a copy of the applicant laboratory's CLIA Certificate, and a copy of the applicant laboratory's California Laboratory License, to meet the requirements of this subsection.
- c. If an applicant laboratory seeking approval for microarray analysis is not currently approved by GDSP to perform karyotyping, the applicant laboratory must concurrently apply for GDSP approval to perform amniotic fluid and CVS karyotyping.
- d. At a minimum, for whole-genome microarray platforms, the design must allow for detection of clinically-significant gains and losses as determined by the ACMG Standards and Guidelines for Constitutional Cytogenomic Microarray Analysis, including Postnatal and Prenatal Applications (2013). It is also desirable to have enrichment of probes targeting dosage-sensitive regions or genes well associated with congenital anomalies or neurocognitive impairments.

- e. Back-up cultures of all prenatal samples undergoing array analysis must be established and maintained for the purposes of (i) possible array failures on direct extractions, (ii) evaluation of possible mosaicism on an independent culture, and (iii) the need to perform metaphase chromosome or fluorescence in situ hybridization analysis to investigate CNVs. Microarray test results should be verified before results are reported.
 - f. For new lots of arrays, a known positive sample should be run for quality control purposes. A new lot may be considered validated if the same result is obtained from the sample tested.
 - g. An assessment of day-to-day, run-to-run, and within-run variation is required to demonstrate reproducibility.
11. For prenatal samples undergoing analysis, maternal cell contamination (MCC) analysis should be performed on all samples if contamination is suspected.
 12. For microarray testing, if applicable, continuing analyses of not less than 100 constitutional microarrays per year, of which a minimum of twenty should be on prenatal samples, with at least 90 percent of final results completed and reported to the Prenatal Diagnosis Center within 21 calendar days from the date the test was ordered.
 13. For karyotyping, continuing analyses of not less than 100 prenatal cell cultures (CVS, amniocentesis, fetal blood/tissue) per year with final results to meet turnaround times as outlined in ACMG's Standards and Guidelines for Clinical Genetics Laboratories (revised 2018).
 14. Submission of details of any changes in microarray test platform or array design to GDSP, when applicable.
 15. Participation in and successful completion of any State of California provided or approved laboratory inspection, proficiency testing and/or quality control program including submission of appropriate documentation of participation and results.
 16. Participation in the relevant external proficiency testing programs through the College of American Pathologists. Proficiency testing should be performed according to 1988 CLIA guidelines.
 17. Assured access to resources for the determination of alpha fetoprotein and acetylcholinesterase concentrations in amniotic fluid for diagnosis of neural tube defects.
 18. Quality assurance issues (e.g. accuracy of diagnoses, culture failure rates), complaints, or other factors deemed pertinent regarding applicant and approved laboratories may be referred by GDSP to the Cytogenetics Subcommittee of GDSP's Continuous Quality Improvement Committee for recommendations. Final decisions are made by GDSP.
- H. Any trainee performing genetic services in a Prenatal Diagnosis Center must be under the direct, constant and on-site supervision of an appropriate

specialist on the staff of an approved Comprehensive Prenatal Diagnosis Center.

- I. An interdisciplinary meeting of the Comprehensive Prenatal Diagnosis Center staff including ultrasonography, amniocentesis practitioner, genetic counseling, and medical genetics staff must be held at least once every three months.
- J. If a staff change(s) results in an approved Center no longer meeting the requirements of these Standards or other provisions of California law, the Center Director must arrange for consultation and supervision of the appropriate areas by appropriately qualified, licensed, and credentialed outside personnel and notify GDSP of the consultation arrangement.
- K. All first trimester Transcervical Chorionic Villus Sampling (TC CVS) procedures must be performed by physicians who:
 1. Have approval as TC CVS Practitioners, are certified by the American Board of Obstetrics and Gynecology or have Active Candidate status for the next certification examination, and have had specific training and special expertise in prenatal diagnosis. This training must include detailed obstetrical ultrasonography, as well as basic genetic information and appropriate counseling procedures for chromosomal, biochemical, and neural tube defects. Such physicians shall have:
 - a. Performed a total of at least 25 first trimester TC CVS procedures. These may be performed on women who are not planning to continue their pregnancies or on women referred for prenatal genetic indications and planning to continue their pregnancies. However, a minimum of 5 first trimester TC CVS procedures must be performed on women referred for prenatal genetic indications and planning to continue their pregnancies. All first trimester TC CVS procedures performed on continuing pregnancies must have on-site supervision in the procedure room by an OB/GYN who is experienced in TC CVS. (Experienced is defined as having performed at least 25 TC CVS procedures on women continuing their pregnancies.); and
 - b. Been approved as TA CVS practitioners or meet the Standards for approval as a TA CVS practitioner; or
 2. Have interim approval to perform first trimester Transcervical Chorionic Villus Sampling procedures under supervision as Interim Approval TC CVS Practitioners. Each Interim Approval TC CVS Practitioner must:
 - a. Currently be in a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME or have completed a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME; and
 - b. Apply to and be approved by GDSP as an Interim Approval TC CVS Practitioner. Part of the application process is to identify each on-site supervisor who must be in the procedure room immediately adjacent to

the practitioner during the procedure. The supervisor must be a State-approved TC CVS Practitioner who is an OB/GYN experienced in first trimester TC CVS procedures. Each supervisor must provide a written acknowledgment that they shall be in the room and immediately adjacent to the performing Interim Approval TC CVS Practitioner during the supervised procedure(s). After approval, Interim Approval TC CVS Practitioners may then perform TC CVS procedures on California Prenatal Screening Program patients; and,

- c. Perform at least 25 first trimester TC CVS procedures on women planning to continue their pregnancies with on-site supervision by the supervising State-approved TC CVS Practitioner who shall be in the room and immediately adjacent to the practitioner performing the procedure. The Interim Approval TC CVS Practitioner must perform a minimum of 5 TC CVS procedures annually or they will have approval withdrawn; and
- d. Submit a log for review every six months with the following parameters of the 25 supervised procedures to GDSP. The practitioner is required to identify:
 - i. A patient identifier;
 - ii. The indication for performing the procedure;
 - iii. The date the procedure was performed;
 - iv. The gestational age at the time of the procedure;
 - v. The name of the in-room Supervisor;
 - vi. The type of CVS (TC or TA), if applicable;
 - vii. The number of fetuses;
 - viii. The number of insertion attempts;
 - ix. Whether an inadequate volume of chorionic villi (less than 5 milligrams) was obtained, with a reason for inadequate sample size;
 - x. Whether fetal anomalies were observed on ultrasound, with details of any fetal anomalies;
 - xi. Whether the cytogenetic or cytogenomic results were normal or abnormal, with details for any abnormal result;
 - xii. Whether the procedure was followed by failure to obtain a test result, with reason for any failure;
 - xiii. Whether the procedure was followed by normal fetal loss, with gestational age at fetal loss;
 - xiv. Name of person reporting the cytogenetic or cytogenomic results, and the date results were reported; and

- xv. Whether an elective termination occurred prior to reporting of results.
 - e. Upon completion of the required 25 supervised TC CVS procedures and submission of the log(s), the Interim Approval TC CVS Practitioner may be granted full approval as a TC CVS Practitioner and then they must begin collecting Adverse Outcome data on consecutive second trimester amniocentesis procedures under the conditions outlined in Section N.
3. Each of the physicians performing or supervising first trimester TC CVS procedures must perform at least 25 first trimester CVS procedures annually (either TC CVS, TA CVS or a combination of both), with at least 5 being first trimester TC CVS procedures performed on women planning to continue their pregnancies, or they may be placed on provisional approval status or have approval withdrawn. Performing less than five first trimester TC CVS procedures annually will result in approval being withdrawn.
 4. Any State-approved TC CVS Practitioner that provides direct supervision over a Fellow in an ABOG/ACGME recognized Fellowship Program or another TC CVS practitioner may include supervised first trimester TC CVS procedure(s) referred to in Section K.2.c. toward their annual volume requirement.
- L. All first trimester Transabdominal Chorionic Villus Sampling (TA CVS) procedures must be performed by physicians who:
1. Have approval as TA CVS Practitioners, are certified by the American Board of Obstetrics and Gynecology or have Active Candidate status for the next certification examination, and have had specific training and special expertise in prenatal diagnosis. This training must include detailed obstetrical ultrasonography, as well as basic genetic information and appropriate counseling procedures for chromosomal, biochemical, and neural tube defects. Such physicians shall have:
 - a. Been approved for and experienced in the performance of amniocentesis with ultrasound guidance, and have performed at least 25 first trimester TA CVS procedures. These may be performed on women who are not planning to continue their pregnancies or on women referred for prenatal genetic indications and planning to continue their pregnancies. However, a minimum of 5 first trimester TA CVS procedures must be performed on women referred for prenatal genetic indications and planning to continue their pregnancies. All first trimester TA CVS procedures performed on continuing pregnancies must have on-site supervision in the procedure room by an OB/GYN who is experienced in TA CVS. (Experienced is defined as having performed a minimum of 25 TA CVS procedures on women planning to continue their pregnancies); or

- b. Been approved as a TC CVS Practitioner and an Amniocentesis Practitioner; or
 - c. Met the Standards for approval as a TC CVS Practitioner and Amniocentesis Practitioner; or
2. Have interim approval to perform first trimester Transabdominal Chorionic Villus Sampling procedures under supervision as Interim Approval TA CVS Practitioners. Each Interim Approval TA CVS Practitioner must:
- a. Currently be in a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME or have completed a Maternal-Fetal Medicine or equivalent specialized training program recognized by the ABOG and/or ACGME; and
 - b. Apply to and be approved by GDSP as an Interim Approval TA CVS Practitioner. Part of the application process is to identify each on-site supervisor who must be in the procedure room immediately adjacent to the practitioner during the procedure. The supervisor must be a State-approved TA CVS Practitioner who is an OB/GYN experienced in first trimester TA CVS procedures. Each supervisor must provide a written acknowledgment that they shall be in the room and immediately adjacent to the performing Interim Approval TA CVS Practitioner during the supervised procedure(s). After approval, Interim Approval TA CVS Practitioners may then perform TA CVS procedures on California Prenatal Screening Program patients; and,
 - c. Perform at least 25 first trimester TA CVS procedures on women planning to continue their pregnancies with on-site supervision by the supervising State-approved TA CVS Practitioner who shall be in the room and immediately adjacent to the practitioner performing the procedure. The Interim Approval TA CVS Practitioner must perform a minimum of 5 TA CVS procedures annually or they will have approval withdrawn; and
 - d. Submit a log for review every six months with the following parameters of the 25 supervised procedures to GDSP. The practitioner is required to identify:
 - i. A patient identifier;
 - ii. The indication for performing the procedure;
 - iii. The date the procedure was performed;
 - iv. The gestational age at the time of the procedure;
 - v. The name of the in-room Supervisor;
 - vi. The type of CVS (TC or TA), if applicable;
 - vii. The number of fetuses;
 - viii. The number of insertion attempts;

- ix. Whether an inadequate volume of chorionic villi (less than 5 milligrams) was obtained, with a reason for inadequate sample size;
 - x. Whether fetal anomalies were observed on ultrasound, with details of any fetal anomalies;
 - xi. Whether the cytogenetic or cytogenomic results were normal or abnormal, with details for any abnormal result;
 - xii. Whether the procedure was followed by failure to obtain a test result, with reason for any failure;
 - xiii. Whether the procedure was followed by normal fetal loss, with gestational age at fetal loss;
 - xiv. Name of person reporting the cytogenetic or cytogenomic results, and the date results were reported; and
 - xv. Whether an elective termination occurred prior to reporting of results.
- e. Upon completion of the required 25 supervised TA CVS procedures and submission of the log(s), the Interim Approval TA CVS Practitioner may be granted full approval as a TA CVS Practitioner and then they must begin collecting Adverse Outcome data on consecutive second trimester amniocentesis procedures under the conditions outlined in Section N.
3. Each of the physicians performing or supervising first trimester TA CVS procedures must perform at least 25 first trimester CVS procedures annually (either TC CVS, TA CVS or a combination of both) on women planning to continue their pregnancies, or they may be placed on provisional approval status or have approval withdrawn. Performing less than five first trimester TA CVS procedures annually will result in approval being withdrawn.
4. Any State-approved TA CVS Practitioner that provides direct supervision over a Fellow in an ABOG/ACGME recognized Fellowship Program or another TA CVS practitioner may include supervised first trimester TA CVS procedure(s) referred to in Section L.2.c. toward their annual volume requirement.
- M. In Centers offering first trimester CVS, if either TA or TC CVS is clinically contraindicated or unsuccessful, and the alternative CVS prenatal diagnosis procedure is not available at that Prenatal Diagnosis Center, a referral must be made to another State-approved Prenatal Diagnosis Center.
- N. Amniocentesis and CVS Practitioners must participate in Adverse Outcome Studies on prenatal diagnostic procedures performed on women who are planning to continue their pregnancies as follows:
- 1. Practitioners must collect Adverse Outcome data under the following conditions:

- a. Following initial approval as an Amniocentesis or CVS Practitioner, all practitioners must collect Adverse Outcome data on consecutive procedures performed on or after January 1 or July 1 (whichever is sooner).
 - b. Three years following the completion date of each study, all practitioners must collect Adverse Outcome data on consecutive procedures performed on or after January 1 or July 1 (whichever is sooner) for additional Adverse Outcome Studies.
 - c. Low Volume Provisional Practitioners are required to collect Adverse Outcome data as outlined in Section T.
 - d. Practitioners who supervise procedures performed by others may not count these supervised procedures on their own Adverse Outcome Studies.
2. Prenatal Diagnosis Centers must submit each prenatal diagnostic practitioner's individual Adverse Outcome data. For practitioners required to submit Adverse Outcome Studies, the Prenatal Diagnosis Center will be required to report every six months on outcomes obtained at the time of reporting cytogenetic results until their study is complete. If reports are not received within six months of the due date, practitioner approval may be withdrawn.
 3. Reports on Adverse Outcomes must include the PDC number, PDC name, and practitioner name, and for each patient:
 - a. A patient identifier;
 - b. The indication for performing the procedure;
 - c. The date procedure was performed;
 - d. The gestational age at the time of the procedure;
 - e. The type of CVS (TC or TA), if applicable;
 - f. The number of fetuses;
 - g. The number of insertion attempts;
 - h. Whether no, or an inadequate volume of, amniotic fluid (less than 10 cc's) or chorionic villi (less than 5 milligrams) was obtained, with reason for inadequate sample size;
 - i. Whether fetal anomalies were observed on ultrasound, with details of any fetal anomalies;
 - j. Whether the cytogenetic results were normal or abnormal, with details for any abnormal result;
 - k. Whether the procedure was followed by failure to obtain a result, with reason for any failure;
 - l. Whether the procedure was followed by normal fetal loss, with gestational age at fetal loss;

- m. Name of person reporting the cytogenetic results, and the date results were reported; and
 - n. Whether an elective termination occurred prior to reporting of results.
4. For Amniocentesis Practitioners, each Adverse Outcome Study is considered complete when data has been submitted on 160 consecutive procedures, unless the practitioner is subject to provisions applying to Low Volume Provisional Amniocentesis Practitioners. The Amniocentesis Practitioner will be subject to review by the Perinatal Committee for continuation of approval (with GDSP having the final decision) if rates of Adverse Outcomes meet or exceed the following thresholds:
 - a. Excess insertions (greater than one) occurring in three percent of procedures;
 - b. No, or an inadequate volume of, amniotic fluid (less than 10 cc's) obtained in 1.5 percent of procedures;
 - c. Cell culture failure following one percent of procedures; and/or
 - d. Normal fetal loss following one percent of procedures.
 5. For TC or TA CVS Practitioners, each Adverse Outcome Study is considered complete when data has been submitted on 50 consecutive TC or TA CVS procedures, unless the practitioner is subject to provisions applying to Low Volume Provisional CVS Practitioners. Practitioners approved for both TC and TA CVS are required to submit data on both 50 TC CVS procedures and 50 TA CVS procedures. The CVS Practitioner will be subject to review by the Perinatal Committee for continuation of approval (with GDSP having the final decision) if rates of Adverse Outcomes meet or exceed the following thresholds:
 - a. Excess insertions (greater than one) occurring in ten percent of TC and/or TA CVS procedures;
 - b. No, or an inadequate volume of, chorionic villi (less than 5 milligrams and failure to obtain a karyotype) obtained in three percent of TC CVS procedures;
 - c. No, or an inadequate volume of, chorionic villi (less than 5 milligrams and failure to obtain a karyotype) obtained in one percent of TA CVS procedures;
 - d. Cell culture failure following one percent of TC CVS procedures; and/or
 - e. Cell culture failure following one percent of TA CVS procedures.
- O. Each Prenatal Diagnosis Center must maintain a minimum annual volume of 100 women seen for prenatal genetic services. Indications for prenatal genetic counseling and evaluation services include increased risks for adverse fetal outcomes including congenital anomalies, intellectual disability/autism, poor fetal growth, or fetal demise due to chromosomal, genetic, and teratogenic factors. These risks are being based on: abnormal maternal screening tests; abnormal fetal diagnostic tests; abnormal fetal

imaging (including ultrasound); family history (including, but not limited to, previous child with congenital anomalies, previous child with intellectual disability, a known genetic condition in a relative, parental consanguinity, multiple fetal losses, unexplained childhood deaths); advanced maternal age (defined as ≥ 35 years or ≥ 33 years for twin pregnancies); advanced paternal age (defined as ≥ 40 years); ART/Infertility; parental anxiety/concern; maternal conditions that may increase fetal risk such as diabetes, PKU, seizure disorders, infections, etc.; maternal exposure to teratogenic agents such as alcohol, valproic acid, isotretinoin, etc.

- P. Each Prenatal Diagnosis Center must have an Internal Continuous Quality Improvement Program. The PDC Director must provide oversight to the program and work with PDC staff to achieve improvement goals.
- Q. Abnormal or ambiguous results of cfDNA screening and/or amniocentesis or CVS procedures must be verbally communicated to referring physicians and/or patients by clinical genetics staff such as M.D. Clinical Geneticists, Clinical Cytogeneticists, or Genetic Counselors. The Center must have a written protocol in place and must take responsibility for reporting normal results of cfDNA screening and/or amniocentesis or CVS procedures.
- R. Each Prenatal Diagnosis Center must have the ability to perform or arrange for dysmorphism evaluation and/or pathologic examination of abortuses as well as cytogenetic and biochemical procedures.
- S. For cfDNA Screening, each Prenatal Diagnosis Center must utilize cfDNA screening Providers or Laboratories that have entered a formal agreement with the Prenatal Diagnosis Center to provide a mechanism for identifying specimens from authorized California Prenatal Screening Program patients and to accept payment from the PDC as payment in full for any cfDNA screening laboratory service authorized and successfully performed for a California Prenatal Screening Program patient.
- T. Providers will be placed on provisional approval status under the following terms:
 - 1. Approved Amniocentesis and CVS Practitioners that have one year of low volume, defined as less than 15 second trimester amniocentesis procedures performed per year, or less than 25 CVS procedures per year, will be placed on provisional approval status as a Low Volume Provisional Practitioner.
 - 2. Low Volume Provisional Practitioners must complete a new Adverse Outcome Study by collecting and reporting Adverse Outcome data. Prenatal Diagnosis Centers must report to GDSP the Adverse Outcomes of procedures performed by Low Volume Provisional Practitioners via a progress report or log every six months until their studies are completed. If there is no submission of data or explanation of failure to submit the data every six months, practitioner approval will be withdrawn. The provisional status will remain in place until the Adverse Outcome Study is completed as outlined in Section N, unless the practitioner continues to

perform a low volume of procedures. Rates of Adverse Outcomes will be monitored as provided for in Section N.

3. A practitioner requesting a leave of absence for personal reasons or sabbatical leave should submit a letter to GDSP outlining specific reasons for the request and listing any outstanding approval conditions or reporting compliance issues. Leave of absence requests will be reviewed by the Perinatal Committee with final approval by GDSP.
 4. In order for an Amniocentesis Practitioner to be re-approved after having their practitioner approval status withdrawn, the practitioner must fulfill the requirements applying to Interim Approval Amniocentesis Practitioners outlined in Section C.2.
 5. In order for a TC CVS Practitioner to be re-approved after having practitioner approval status withdrawn, the practitioner must fulfill the requirements applying to Interim Approval TC CVS Practitioners outlined in Section K.2.
 6. In order for a TA CVS Practitioner to be re-approved after having practitioner approval status withdrawn, the practitioner must fulfill the requirements applying to Interim Approval TA CVS Practitioners outlined in Section L.2.
- U. An applicant for a new Comprehensive Prenatal Diagnosis Center or a new satellite site must:
1. Complete the application process, including the submission of all support documentation, within 30 calendar days from the date of notification by GDSP of any deficiencies in the application; and,
 2. Participate in a State site visit and successfully meet or resolve any documented findings from the State site visit within 30 calendar days from the date of notification by GDSP of any deficiencies. Upon satisfactory resolution of any documented findings, an approval date will be designated; and,
 3. Within 30 calendar days after the designated approval date, be operational to schedule patients;

Otherwise GDSP will consider the application withdrawn.

- V. Any PDC site that fails to meet the PDC Standards will have approval temporarily suspended for 30 calendar days, during which time the PDC must provide GDSP with documentation of steps taken to address any deficiencies. The PDC will be prohibited from providing services to California Prenatal Screening Program patients until deficiencies are satisfactorily resolved. The suspension will be extended for an additional two months for PDCs that can document a good faith effort of addressing the deficiencies. Failure to satisfactorily resolve deficiencies will result in approval being withdrawn for the PDC site.

II. SATELLITE PRENATAL DIAGNOSIS CENTER

A Satellite Prenatal Diagnosis Center is a State-approved center that:

- A. Provides on site genetic counseling, ultrasonography, cfDNA screening, and the collection of CVS and/or amniotic fluid specimens at a site which is not in the same suite as an existing Satellite or Comprehensive Prenatal Diagnosis Center.
- B. Provides on-site counseling prior to cfDNA screening, CVS and/or amniocentesis by an approved Clinical Geneticist, or Genetic Counselor. The Clinical Geneticist must be available whenever possible at the satellite site within three working days to provide consultation in person to all families with abnormal or questionable results. The Clinical Geneticist must be available within reasonable travel time (less than eight hours) to all assigned sites of service.
- C. Has monthly meetings conducted by the Clinical Geneticist with clinical staff who are assigned to the site to include, but not be limited to, case review.
- D. Has a written agreement with a State-approved Comprehensive Prenatal Diagnosis Center and an approved cytogenetic laboratory and an approved cytogenomic laboratory which also performs necessary laboratory studies. The Director of the Comprehensive Prenatal Diagnosis Center is responsible for the adequacy of the amniotic fluid/CVS samples and follow-up services.
- E. Has an established mechanism for safely and rapidly delivering satisfactory amniotic fluid/CVS samples to the affiliated Comprehensive Prenatal Diagnosis Center or to the approved cytogenetics laboratory.
- F. Complies with criteria B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U, and V as described for a Comprehensive Prenatal Diagnosis Center.
- G. Whenever a Satellite Prenatal Diagnosis Center decides to switch affiliation to another Comprehensive Prenatal Diagnosis Center or apply to become a Comprehensive Prenatal Diagnosis Center, the Satellite Center must submit a letter to the original Comprehensive Prenatal Diagnosis Center Director and to GDSP informing them of their intent to switch affiliations. The original Comprehensive Prenatal Diagnosis Center Director must then submit a letter to GDSP acknowledging the intent of the Satellite Center switch. The letter must include whether or not there are any outstanding issues with the site regarding compliance to the PDC Standards and California Prenatal Screening Program Guidelines. The letter must be sent to GDSP within thirty days from the original request of the Satellite Center requesting the switch.

If there are outstanding data that are required to be submitted (e.g. quarterly Prenatal Diagnosis Center reports, Adverse Outcome Studies), GDSP will not approve the switch until the application and data have been successfully completed and submitted to GDSP. It is the responsibility of the Satellite Center requesting the switch to ensure that the data are complete before requesting the switch in affiliation. If the Comprehensive Prenatal Diagnosis Center that is taking on the new site(s) wants to assume the responsibility for

completing the data, they must submit assurance in writing to GDSP that the data will be submitted within a specified time period. The approval will be time limited until the data are submitted.

III. REQUIREMENTS FOR CONTINUED APPROVAL AS A STATE-APPROVED COMPREHENSIVE OR SATELLITE PRENATAL DIAGNOSIS CENTER

- A. Continued approval as a State-Approved Comprehensive Prenatal Diagnosis Center or State-Approved Satellite Prenatal Diagnosis Center is dependent on compliance with the provisions of the Prenatal Diagnosis Center Standards and Definitions, and contract provisions.
- B. Any changes in the location(s) where services are provided, or in personnel, may render the approval void. If there are any changes in the location(s) where services are provided, in the staffing of locations, or in providers of follow-up services, at any time during the year, the Director of the State-approved Comprehensive Prenatal Diagnosis Center must notify the Department within ten working days and submit documentation for approval of any new clinical staff or providers of follow-up services, verifying they meet the requirements of the Prenatal Diagnosis Center Standards and Definitions. If there are no findings of deficiencies, or if any findings of deficiencies are successfully complied with or resolved, the Department shall notify the applicant of continued approval of the State-approved Comprehensive Prenatal Diagnosis Center and any Satellite Prenatal Diagnosis Centers. The approval shall be valid only in the location(s) stated and with the personnel listed, and shall be subject to any conditions stated.
- C. Before the end of each calendar-year, the Department will provide to the State-approved Comprehensive Prenatal Diagnosis Center a list of the names of the sites, addresses, phone and facsimile numbers, any approval conditions, and the clinical staff approved to provide services at the State-Approved Comprehensive Prenatal Diagnosis Center and any State-Approved Satellite Prenatal Diagnosis Centers. The State-approved Comprehensive Prenatal Diagnosis Center must review the conditions of approval and submit requested information, and review the personnel listings for accuracy. Within thirty calendar days after receiving this information from the Department, the State-approved Comprehensive Prenatal Diagnosis Center must submit the following documentation:
 - 1. An Annual Reporting Cover Sheet that includes:
 - a. The name of the person submitting the documentation.
 - b. The date the submission was completed.
 - c. For the State-approved Comprehensive Prenatal Diagnosis Center site, the following clinical services information:
 - i. The name of the State-approved Comprehensive Prenatal Diagnosis Center.

- ii. The physical location where genetic counseling services are provided, and the telephone number and facsimile number of that location.
- iii. The name of the ultrasound practice, the ultrasound practice's American Institute of Ultrasound in Medicine/American College of Radiology accreditation number and expiration date, and the physical location, telephone number, and facsimile number of the location where ultrasound services are performed.
- iv. The number of amniocentesis procedures performed from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals.
- v. The number of chorionic villus sampling procedures performed from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals.
- vi. The total number of women seen for prenatal genetic services from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals. If a State-approved Comprehensive Prenatal Diagnosis Center has not seen the minimum annual volume of one hundred patients for genetic counseling, a letter of justification for maintaining approval must be submitted to the Department.
- vii. The full name, mailing address (street number, street name, city and zip code), telephone number, facsimile number, and email address of the Director of the State-approved Comprehensive Prenatal Diagnosis Center.
- viii. The full name, mailing address (street number, street name, city and zip code), telephone number, facsimile number, and email address of the Prenatal Diagnosis Center Contact Person.
- ix. The full name, telephone number, and email address of the Back-up Prenatal Diagnosis Center Contact Person.
- x. The full name, mailing address (street number, street name, city and zip code), telephone number, and email address of the Quarterly Report Contact Person.
- xi. The name of each Laboratory authorized by the Department and utilized by the State-approved Comprehensive Prenatal Diagnosis Center for cytogenomic and/or cytogenetic tests; the name of the Director of each Laboratory; the California Laboratory License number for each Laboratory Director; the

physical location of each Laboratory; and the full names and California Laboratory License numbers for each of the Clinical Cytogeneticists employed by each facility.

- d. For each State-approved Satellite Prenatal Diagnosis Center, the following clinical services information:
- i. The name and Department-assigned code of the State-approved Satellite Prenatal Diagnosis Center.
 - ii. The physical location where genetic counseling services are provided, and the telephone number and facsimile number of that location.
 - iii. The name of the ultrasound practice and the ultrasound practice's American Institute of Ultrasound in Medicine/American College of Radiology accreditation number and expiration date, and the physical location where ultrasound services are performed.
 - iv. The number of amniocentesis procedures performed from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals.
 - v. The number of chorionic villus sampling procedures performed from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals.
 - vi. The total number of women seen for prenatal genetic services from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals. If a State-approved Satellite Prenatal Diagnosis Center site has not seen the minimum annual volume of one hundred patients for genetic counseling, a letter of justification for maintaining approval must be submitted to the Department.
2. Annual statistics for each approved Amniocentesis Practitioner, Interim Approval Amniocentesis Practitioner, Transabdominal Chorionic Villus Sampling Practitioner, Interim Approval Transabdominal Chorionic Villus Sampling Practitioner, Transcervical Chorionic Villus Sampling Practitioner, Interim Approval Transcervical Chorionic Villus Sampling Practitioner, and Consultative Sonologist for procedures performed from November 1 of the prior year to October 31 of the current year, including California Prenatal Screening Program referrals. For Amniocentesis Practitioners and Interim Approval Amniocentesis Practitioners, only procedures performed prior to 24 weeks gestational age should be reported. For Consultative Sonologists, only examinations performed after 15 weeks gestational age should be reported. Procedures included should be restricted to those performed at the State-approved

Comprehensive Prenatal Diagnosis Center and any State-approved Satellite Prenatal Diagnosis Centers, unless a Practitioner has not performed enough procedures to meet the minimum requirements of the Prenatal Diagnosis Centers Standards and Definitions, incorporated by reference, but performs procedures at other non-State-approved sites. Those procedures may be reported but should be listed separately from the procedures performed at the State-approved Comprehensive and any Satellite Prenatal Diagnosis Centers, and a note of this exception should be made when reporting.

3. A Director's Agreement.
 4. A Clinical Staff Schedule.
- D. If documentation submitted to meet the requirements of subsection (C.) above is incomplete, the State-approved Comprehensive Prenatal Diagnosis Center shall have ten working days to complete the reporting process, including the submission of support documentation, from the date of notification by the Department that additional information is required.
 - E. If there are findings of deficiencies from documentation submitted to meet the requirements of subsection (C.), above the State-approved Comprehensive Prenatal Diagnosis Center will be notified of the findings and shall have thirty calendar days from the date of notification by the Department to successfully comply with or resolve any findings of deficiencies.
 - F. Failure to meet any requirements of this Section will cause the Department to consider suspension or revocation of approval.

IV. WAIVERS TO THE STANDARDS

Any requests for exceptions to the Standards must be documented in a letter to GDSP requesting a waiver and outlining temporary coverage as well as future plans to comply with the Standards. Waivers will be considered only in extreme circumstances and must be justified as necessary to provide access to services in underserved areas. Final decisions are made by GDSP.