

The California Prenatal Screening Program

Quad Marker Screening

Serum Integrated Screening

Full Integrated Screening



Provider Book

Genetic Disease Screening Program

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WELCOME to the California Prenatal Screening Program

The purpose of the Prenatal Screening Program is to provide all pregnant women in California with the opportunity to have prenatal screening for certain birth defects:

- **Down syndrome (DS; Trisomy 21; T21)**
- **Trisomy 18 (T18)**
- **Open Neural Tube Defects (NTD) and Abdominal Wall Defects (AWD)**
- **Smith-Lemli-Opitz syndrome (SLOS, SCD)**

The Program goal is to identify pregnant women at increased risk for these birth defects, so they can make informed decisions about their pregnancies. The California Prenatal Screening Program is administered by the Genetic Disease Screening Program of the California Department of Public Health.¹ Please see the Program website at www.cdph.ca.gov/programs/pns.

What is California's Prenatal Screening Program?

Prenatal screening offers blood tests to pregnant women in order to identify individuals who are at increased risk for carrying a fetus with a specific disorder. These blood tests can be drawn in the first and/or second trimester. Because **screening does not diagnose fetal defects, the Program provides diagnostic testing to women with Screen Positive results (increased risk)**. These women are referred for prenatal diagnosis at a State-approved Prenatal Diagnosis Center.

Types of Screening:

The Program offers several screening options:

Quad Marker Screening	One blood specimen drawn at 15 weeks – 20 weeks of pregnancy (second trimester).
Serum Integrated Screening	Combines first trimester blood test results (drawn at 10 weeks – 13 weeks 6 days) with second trimester blood test results. Improved detection of T21 and T18 in the second trimester.
Full Integrated Screening	Combines Nuchal Translucency (NT) ultrasound results with first and second trimester blood test results. Allows preliminary risk for T21 and T18 in the first trimester and improves the detection of T21 and T18 in the second trimester.

Screening results are reported as “Screen Negative” or “Screen Positive”.

- A **“Screen Negative”** result indicates that the patient's risk for the screened birth defects is low enough that the Program does not offer follow-up tests.
- A **“Screen Positive”** result indicates that the patient is at **increased risk** for one or more of the screened birth defects and the Program will offer follow-up tests.

¹ California Code of Regulations Title 17, sections 6521-6532. Copies of these regulations are available from the Genetic Disease Screening Program.



The details of these screening options are presented in **Table 1** below.

Table 1. Types of Screening offered by the California Prenatal Screening Program.

For Patients without Nuchal Translucency (NT)	Time Frame
Quad Marker Screening (Or Quad + NT) Second trimester blood specimen Risk Assessments for T21, T18, SCD, NTD Analytes: AFP, hCG, uE3, Inhibin	Second trimester blood specimen: 15 wks 0 days to 20 wks 0 days
OR	
Serum Integrated Screening First trimester blood specimen <i>Plus</i> Second trimester blood specimen Risk Assessments for T21, T18, SCD, NTD First trimester analytes: PAPP-A, hCG Second trimester analytes: AFP, hCG, uE3, Inhibin	First trimester blood specimen: 10 wks 0 days to 13 wks 6 days PLUS Second trimester blood specimen: 15 wks 0 days to 20 wks 0 days
For Patients with Nuchal Translucency (NT)	Time Frame
Full Integrated Screening Step 1 First Trimester Screening First trimester blood specimen combined with Nuchal Translucency (NT) Risk Assessment for T21 and T18 Analytes: PAPP-A, hCG	First trimester blood specimen: 10 wks 0 days to 13 wks 6 days PLUS NT Ultrasound: 11 wks 2 days to 14 wks 2 days by a State-registered NT Practitioner
Step 2 Second Trimester Screening Second trimester blood specimen Refined Risk Assessments for T21, T18 Additional Risk Assessments for SCD, NTD First trimester analytes: PAPP-A, hCG, NT Second trimester analytes: AFP, hCG, uE3, Inhibin	 PLUS Second trimester blood specimen: 15 wks 0 days to 20 wks 0 days

The Prenatal Screening Program offers at no cost to the provider:

- Regional Coordinators to facilitate Program participation for patients and providers/clinicians
- Patient education booklets with consent/refusal forms
- First and Second Trimester Screening Forms (formerly called “AFP Form”)
- Supplies to draw and mail serum samples
- Authorized follow-up services at State-approved Prenatal Diagnosis Centers
- Screen Positive patient education booklets

Note: The California Prenatal Screening Program DOES NOT PAY for Nuchal Translucency ultrasound.

ROLE OF CLINICIAN - a summary

Supplies: Order free patient education booklets, blood collection kits and First and Second Trimester Screening Forms by faxing an order form to (510) 412-1553 or by calling (866) 718-7915 toll free. See *Appendix I*.

Offer Screening: Regulations require that the clinician offer the Prenatal Screening Program to all pregnant women who are seen before the 20th gestational week. Discuss with the patient which types of screening are available and appropriate for her considering her medical, pregnancy, and family histories.

Consider Nuchal Translucency (NT) ultrasound for patients (optional): The California Prenatal Screening Program does not pay for NT. NT ultrasound measurements are accepted by the Program when provided by a credentialed NT Practitioner who is registered with the California Prenatal Screening Program. A full list of registered NT Practitioners can be found at www.cdph.ca.gov/programs/pns.

Consent/refusal to participate: Have the patient read the booklet, “The California Prenatal Screening Program” provided by the Genetic Disease Screening Program. After a discussion and answering her questions, ask her to sign the consent/refusal form in the patient education booklet. In addition, if she consents to participate, she may accept or decline to have her specimen used for research. Place the patient’s consent/refusal form in the patient’s medical record. If she declines to have her specimen used for research, this should be indicated on the “Patient Declined Research” field on the First and Second Trimester Screening Forms.

For Patients who consent to Prenatal Screening:

- Fully and accurately complete the First and/or Second Trimester Screening Form provided by the Genetic Disease Screening Program. See *page 11 and Appendix J*.
- Use only ONE method of gestational dating. Dating by NT CRL is the most accurate. If an NT ultrasound was not performed, ultrasound dating by CRL or BPD is the next best method of gestational dating for screening purposes. See *page 10*.
- **TIMING OF THE TEST: First trimester specimens** are drawn between 10 weeks 0 days and 13 weeks 6 days. **Second trimester specimens** are drawn between 15 weeks 0 days and 20 weeks 0 day of pregnancy. See *page 9 and Appendix F*.
- **BLOOD COLLECTION:** Blood specimens may be collected by the clinician, or the patient may be sent to a laboratory. Read the instructions on the cover page of the First and Second Trimester Screening Form on how to collect and handle the blood. **Note:** All specimens should be centrifuged per the instructions on the cover page of the First and Second Trimester Screening Forms. ***First Trimester specimens that have not been centrifuged will not be analyzed.***
- **RESULTS:** You will receive the results by mail within 7-10 days of specimen collection.
- A Prenatal Screening Coordinator calls the clinician if patient information needs clarification or if the test result is *Screen Positive*.
- Only a licensed health professional should explain a patient’s result and assist the patient in deciding what action to take after a *Screen Positive* result.

- The Prenatal Screening Coordinator assists the clinician in referring a patient with a *Screen Positive* result to a State-approved Prenatal Diagnosis Center (PDC) if that is the patient's decision. See the current list of PDCs on the California Prenatal Screening Program website: www.cdph.ca.gov/programs/pns.

Program Fee: The current fee (March 2009) for the Prenatal Screening Program is \$162. This fee covers the blood test(s) as well as follow-up services when the result is *Screen Positive*. The Prenatal Screening Program fee is subject to change.

The fee DOES NOT cover the cost of an NT ultrasound.

Program Billing: Enter the patient's Medi-Cal information on the First and/or Second Trimester Screening Form, or send a copy of the patient's insurance card or Medi-Cal card with the specimen. The insurance company or Medi-Cal will be billed for the Prenatal Screening Program participation. If no insurance information is provided, the patient will receive a bill about 2 weeks after the first test. Because the Program cannot guarantee that insurance will cover the full cost of the screening, be sure to inform the patient of the charge for the Prenatal Screening Program. See page 23.

Provide the Program with patient insurance information to avoid unnecessary patient billing.

Clinician obligations for patients who have Prenatal Screening:

- Report to the Genetic Disease Screening Program all cases of NTDs and/or chromosomal abnormalities diagnosed before one year of age, including stillborns.
- Complete the "Request for Pregnancy Outcome" form which is sent to clinicians regarding selected patients participating in the Program.

Clinician obligations for patients who have *Screen Positive* Results:

- Verify all the patient data with the Prenatal Screening Coordinator within 1-3 days of her/his call.
- After a first trimester *Screen Positive*, offer the patient a referral to a State-approved PDC or a second trimester blood test.
- After a second trimester *Screen Positive*, offer a referral for follow-up at a State-approved PDC.
- Inform patients that follow-up diagnostic services are available at no additional cost **only** at State-approved Prenatal Diagnosis Centers.

Patients' rights: Since the Prenatal Screening Program is voluntary, patients have the right to decline screening or diagnostic services at any time.

Documentation: Your patient's decisions regarding screening and follow-up services should always be thoroughly documented in the patient's chart.

SERUM MARKERS used for prenatal screening

Pregnancy-Associated Plasma Protein A (PAPP-A)

PAPP-A is produced by both the embryo and placenta during pregnancy. PAPP-A normally increases with gestation. This analyte is used for prenatal screening in the first trimester. Low levels during the first trimester may be associated with fetal chromosomal anomalies, including trisomies 13, 18, and 21.

Human chorionic gonadotropin (hCG)

Human chorionic gonadotropin is a hormone synthesized and secreted by the placenta. Levels of Intact hCG are used in both the first and second trimester prenatal screening tests. The levels rise rapidly in early pregnancy and then decline between the 10th and the 20th week. Maternal serum levels may be higher in a pregnancy in which the fetus has Down syndrome. The level of hCG is often lower than usual in a pregnancy with a fetus affected with trisomy 18 or SLOS.

Alpha-fetoprotein (AFP)

AFP is a protein produced mainly in the fetal liver and released into the fetal serum and amniotic fluid. A small amount crosses the placenta and becomes measurable in the maternal serum towards the end of the first trimester. Levels rise steadily through the second trimester. This analyte is used for prenatal screening in the second trimester. In most fetuses affected with open spina bifida, anencephaly, or an abdominal wall defect, an increased amount of AFP enters the amniotic fluid and subsequently causes a higher than usual level of AFP in the maternal serum. In contrast, maternal serum AFP may be reduced in a pregnancy in which the fetus has Down syndrome, trisomy 18, or Smith-Lemli-Opitz syndrome (SLOS).

Inhibin (Dimeric Inhibin-A; DIA; INH)

Dimeric Inhibin-A is a protein produced by the ovaries and fetal placenta. Levels rise during the first trimester, then decline after the 10th week of pregnancy and remain stable between the 15th and 20th week. This analyte is used for prenatal screening in the second trimester. Maternal levels of DIA, on average, are twice as high in pregnancies affected by Down syndrome as in unaffected pregnancies.

Unconjugated estriol (uE3)

Unconjugated estriol is a hormone produced by the fetal adrenal glands, the fetal liver and the placenta. Levels rise throughout normal pregnancy. This analyte is used for prenatal screening in the second trimester. Maternal serum levels of uE3 may be lower in a pregnancy in which the fetus has Down syndrome or trisomy 18. It is often very low in a pregnancy with a fetus affected with SLOS. Since it is only stable for 10 days, specimens in transit over 10 days will have no uE3 analytic values reported.

NON-SERUM MARKERS used for prenatal screening

Nuchal Translucency (NT) Ultrasound

Nuchal translucency (NT) measurements have proven to be very valuable in improving the detection of Down syndrome and Trisomy 18. When NT measurements are added to serum analytes for screening, detection rates are higher for Down syndrome and Trisomy 18.

The NT measurement generally increases with gestational age during the NT screening window. The expected range for NT thickness during this time period (11 weeks 2 days to 14 weeks 2 days) is 1.2 – 2.7 mm. NT measurements of 3.5 mm or greater are associated with an increased risk of chromosomal or other abnormalities, even without serum markers.

NT Practitioners, credentialed by either the Nuchal Translucency Quality Review Program (NTQR) or the Fetal Medicine Foundation (FMF) must register to participate in the California Prenatal Screening Program. A current list of registered NT Practitioners can be found on the Prenatal Screening Program website at <http://www.cdph.ca.gov/programs/pns>.

The Prenatal Screening Program will only accept NT ultrasound information from practitioners registered with the Genetic Disease Screening Program of the California Department of Public Health.

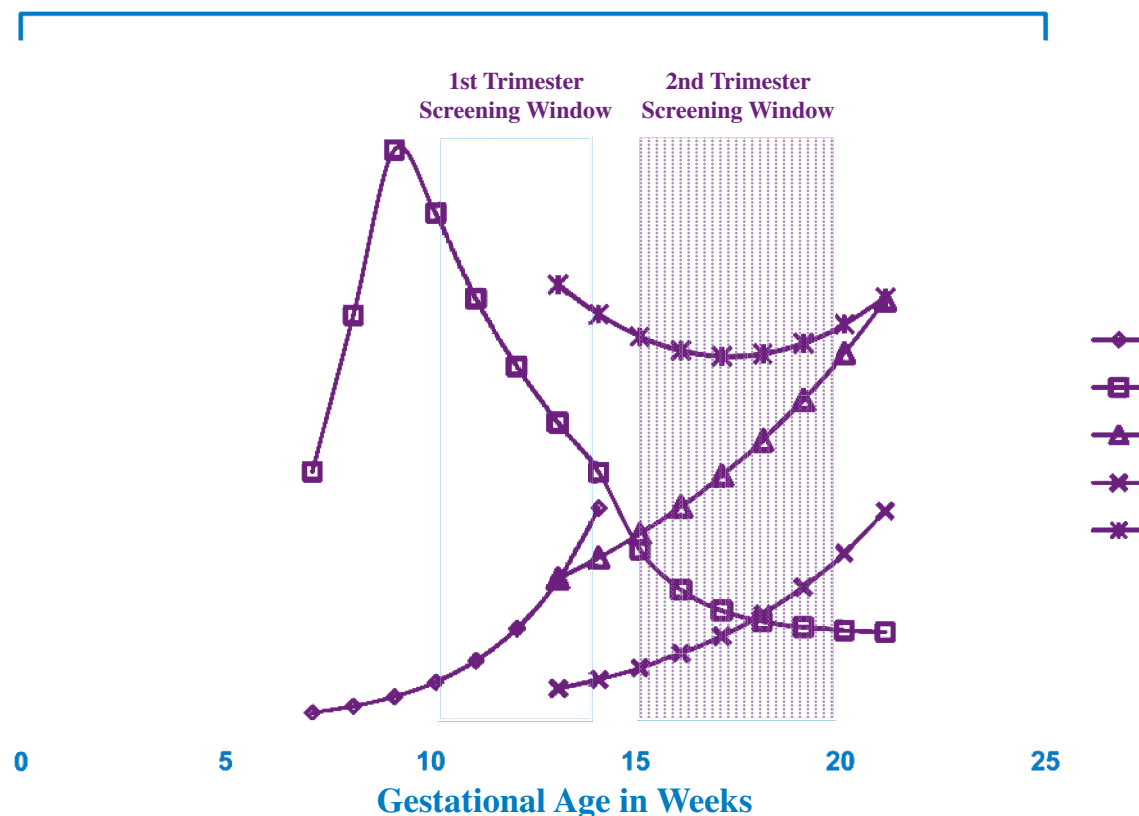
MULTIPLE OF THE MEDIAN (MoM)

The concentrations of each serum marker change during the time window for screening, as shown in **Figure 1** on page 7. The Prenatal Screening Program has established the median concentrations of PAPP-A and First Trimester hCG for California's pregnant population, for each day between 10 weeks 0 days and 13 weeks 6 days. The Program has also established medians for Second Trimester hCG, AFP, uE3 and INH for each day between 15 weeks 0 days and 20 weeks 0 days gestation.

For each blood specimen received, the analytic value for every serum marker tested is converted to a multiple of the median (MoM), based on the gestational age at blood collection. The median level for each day equals a MoM of 1.00. For example, an AFP result of 1.5 MoM means the patient has one and a half times the median level of AFP; an hCG result of 0.30 MoM means the patient has 30% of the median level of hCG. NT measurement values are also converted to MoMs.

The risk assessment for prenatal screening, resulting in *Screen Positive* and *Screen Negative* results, is determined by the MoMs, not the initial analytic value of the serum markers. **This is why the correct gestational age at blood collection is so important for prenatal screening.**

Figure 1. The Concentration of a Serum Marker varies by Gestational Age



MARKERS used for different birth defects

Down Syndrome and Trisomy 18: The MoMs for PAPP-A, hCG, AFP, uE3, INH and NT ultrasound measurements can be used in conjunction with the woman's age and other factors to calculate an individualized risk for Down syndrome and trisomy 18. A woman's age is an essential component of the risk analysis because it is an important predictor of risk for these chromosomal abnormalities. See page 18 and Appendices C, G and H for more information.

Open Neural Tube Defects/Abdominal Wall Defects: The level of maternal serum AFP is used to calculate the AFP MoM. Risk assessment for NTD/AWD is based on the AFP MoM, and whether the pregnancy has one fetus or twins. Some other conditions associated with an elevated maternal serum AFP are mentioned on page 19. See Appendices C and D for more information.

Smith-Lemli-Opitz Syndrome: Measurements of the levels of AFP, hCG and uE3 are used to calculate the risk of having a fetus with SLOS. The most important analyte for SLOS detection is uE3; the patient's age is not a factor in the risk calculation. See page 19 and Appendix C for more information.

PRIOR TO OFFERING prenatal screening

Important Questions: Clinicians should review a patient's medical and family history to determine if any of the following situations apply:

Does the patient have a history of:

- Birth Defects
- Genetic Disorders
- Multiple Miscarriages
- Teratogen Exposure
- Suspected Fetal Anomaly
- Insulin Dependent Diabetes?

Does the patient or her partner have a family history of birth defects or genetic disorders? Are they known carriers of genetic traits such as Tay-Sachs, sickle cell or cystic fibrosis?

Is there a history of an NTD in the patient, her partner, a sibling or half sibling of the fetus, or two second degree relatives of the fetus?

Has the patient taken certain teratogens (one month prior to conception or during the first trimester) for seizures or any other indication?

For example:

- Carbamazepine (Tegretol, Carbatrol, Atretol),
- Valproic Acid/Valproate/Divalproex (Depakene, Depakote)
- Oxcarbazepine (Trileptal)

Note: This is not a complete list.

If any one of the answers is “yes”: She should be referred directly to a State-approved Prenatal Diagnosis Center for genetic counseling to assess risk, and to discuss screening versus diagnosis. This pre-test genetic counseling is not covered by the Prenatal Screening Program. Many health plans and Medi-Cal cover genetic counseling for these indications. The Prenatal Screening Program will pay for diagnostic tests only if the Prenatal Screening result is *Screen Positive*.

Did the patient have amniocentesis? Do not order either a First or Second Trimester Prenatal Screening test if the patient is scheduled for, or has already had, an amniocentesis.

Did the patient have chorionic villus sampling (CVS)? When the patient has already had or is scheduled for CVS, she can be offered screening for NTDs and SLOS in the second trimester. On the Second Trimester Screening Form, the question “Has the patient had CVS?” is asked. If the “Yes” box is checked, the Prenatal Screening Program will report risk for NTDs and SLOS in the second trimester, but not for chromosomal abnormalities.

Is the pregnancy the result of a donated ovum? If so, indicate this on the First and Second Trimester Screening Form, including the age of the donor at time of donation. Two Risk Assessments for Down syndrome and for trisomy 18 will be calculated: one using the patient's date of birth and the other using the donor's age.

SOME PREGNANCIES ARE NOT ELIGIBLE for screening

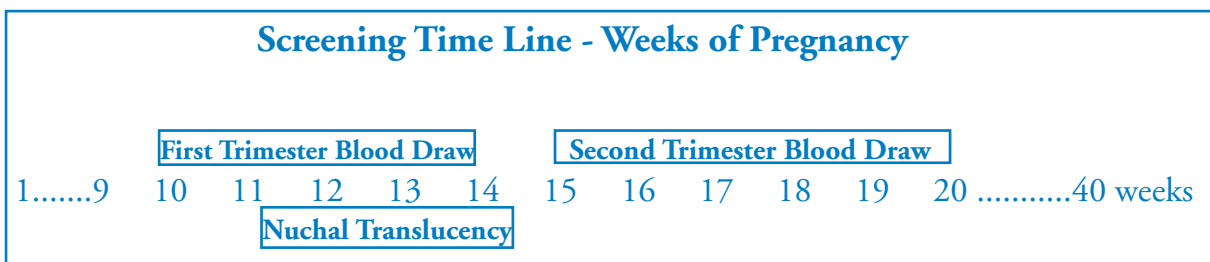
Fetal Reduction: Do not order Prenatal Screening. Women who have undergone procedures to reduce the number of fetuses usually have very high serum AFP levels and this prevents an accurate risk assessment. The effect of fetal reduction on PAPP-A, hCG, INH and uE3 is unknown. If a blood specimen is submitted, the results are considered invalid and no follow-up services are authorized.

Multiple gestation of 3 or more fetuses: Do not order Prenatal Screening. Women who are carrying 3 or more fetuses (or the pregnancy started with 3 fetuses) usually have very high serum AFP levels preventing an accurate risk assessment. The effect of multiple fetuses on PAPP-A, hCG, INH and uE3 is unknown. If a blood specimen is submitted, the results are considered invalid and no follow-up services are authorized.

Fetal demise:

- A fetal loss \geq 8 weeks gestation (from 2 fetuses to one) makes this pregnancy ineligible for screening at any gestation.
- A fetal loss prior to 8 weeks gestation (from 2 fetuses to one) makes the pregnancy ineligible for first trimester screening. The patient remains eligible for second trimester screening.

TIMING for screening tests



- **First Trimester specimens** are drawn between 10 weeks 0 days and 13 weeks 6 days.
- **Second Trimester specimens** are drawn between 15 weeks 0 days and 20 weeks 0 days.
- **NT ultrasounds** are done between 11 weeks 2 days and 14 weeks 2 days.

No risk assessment is provided for specimens collected before 10 weeks, after 20 weeks or during the 14th week of gestation.

Important: Screening late in each time window may compromise a woman's ability to make choices about follow-up services and pregnancy options.

PREGNANCY DATING

Dating when NT CRL is available: Gestational age by NT CRL is the best dating method for screening, if the NT ultrasound is done by a credentialed NT Practitioner registered on the California Prenatal Screening Program website: www.cdph.ca.gov/programs/pns.

NT ultrasound results may be given to the Program in one of three ways:

- Many of the approved NT practitioners have the ability to enter the NT and CRL measurements directly into the Program's computer, if the blood specimen has already been processed at the Screening Lab.
- When there is no blood specimen yet, the NT Practitioner can put the NT ultrasound information directly on the First Trimester Screening Form, if provided by the referring clinician.
- The NT Practitioner can send NT ultrasound results to the prenatal provider, who must put the NT information on the First or Second Trimester Screening Form.

First Trimester Screening results require CRL and NT measurements.

Dating when ultrasound is available: If an NT ultrasound is not done, gestational age by ultrasound dating is the next best dating method, preferably with dating by crown-rump length (CRL) or biparietal diameter (BPD). Why use BPD for Prenatal Screening? In other obstetrical contexts, multiple dating parameters may be more useful, but for screening, BPD is useful because:

- Studies show that fetuses with spina bifida often have smaller BPDs which result in a higher AFP MoM. The use of BPD increases the detection of open spina bifida by increasing the possibility that the AFP MoM will be over the cutoff of 2.5 MoM.
- Fetuses affected with Down syndrome often have shorter femurs and other long bones. Using femur length measurements instead of BPD could date the pregnancy earlier, thereby reducing the detection of Down syndrome.

See Appendix E for a more detailed description of ultrasound dating advantages.

Dating with LMP: If no ultrasound dating is available, a reliable last menstrual period (LMP) date can be used as a method of gestational dating for Prenatal Screening.

Exam dating: Exam dating is the least reliable dating for screening. It cannot be used with First Trimester analytes for Serum Integrated Screening. If no other method is available, Exam dating will be used for Second Trimester screening.

Corrections and updates to pregnancy dating: A woman will have different risk estimates for Down syndrome and Trisomy 18 depending on whether NT CRL, ultrasound, or LMP dating is used, even if the gestational ages are the same by all methods. Re-dating an LMP-dated or physical exam-dated pregnancy by ultrasound or NT CRL may significantly change a woman's Down syndrome risk estimate, and the new estimate provides a better risk assessment. If ultrasound dating information becomes available after the Prenatal Screening sample has been submitted, clinicians are encouraged to call the Prenatal Screening Coordinator (printed on all results mailers) and request that the screening result be recalculated using the new dating.

**Changes and corrections to pregnancy dating
(or other patient information) affecting prenatal screening results
will not be accepted by the Program after 24 weeks gestation.**

INFORMATION NECESSARY for an accurate result

Prenatal Screening Test Request Form: The Test Request Form is the primary source of patient information used to interpret a patient's screening test results. Clinicians are responsible for the accuracy of all information on Prenatal Screening Test Request Forms.

**Incomplete or inaccurate information can delay results
or cause an erroneous interpretation of results.**

A First or Second Prenatal Screening Test Request Form must accompany each blood specimen. The cover page of the Form contains specific instructions for providing the required information. Please read and follow the directions exactly. (A sample of each Form is in *Appendix J*.)

- **Date of birth:** A patient's age is used to determine an individualized risk for carrying a fetus with Down syndrome or trisomy 18.
- **Gestational age:** The median level of each analyte changes each day during pregnancy. It is important to choose the most accurate gestational dating method. NT CRL is the most accurate dating, followed by ultrasound dating based on CRL or BPD.
- **Weight:** Heavier pregnant women have lower median values while lighter pregnant women have higher median values.
- **Race:** Some races have different median values. For example: Black pregnant women have higher medians for AFP. Asian and Hispanic pregnant women have higher medians for uE3.
- **Number of fetuses:** The level of each analyte is usually increased with a multiple gestation. Levels are approximately double for twins. However, since there are no established median values for more than two fetuses, pregnancies with more than 2 fetuses are not eligible for screening.
- **Diabetic status:** The amount of maternal serum AFP is usually lower in diabetics who are insulin dependent prior to and throughout pregnancy. This does not apply to gestational diabetes with or without insulin.
- **Smoking status:** If a patient smokes cigarettes, it will affect one or more of the analytes.

Matching specimens for Integrated Screening: First and second trimester results must be combined to benefit from the improved detection rates of integrated screening. Data from both First and Second Trimester forms are used for matching. It is important to enter the First Trimester Screening Form number on the Second Trimester Screening Form. The easiest method is to use the peel-off label provided on your (pink) copy of the First Trimester Screening form. **Affix the label or hand copy the First Trimester Screening Form number onto "Part A" of the Second Trimester Screening Form.**

Always include the following prenatal care provider information:

**Name, Professional License Number or NPI,
Address & Zip Code, Phone and Fax Numbers.**

Stamps are encouraged for this information if they are legible and efficiently correspond to the fields on the forms. Since the Program uses some optical character recognition (OCR) technology for data entry, it is essential that you order a stamp that fits the clinician information area of the form. When you order your stamp, make sure that it "fits" the Test Request Form.

BLOOD COLLECTION & SHIPPING

Blood collection kits, mailing supplies and First and Second Trimester Prenatal Screening Test Forms are supplied by the Genetic Disease Screening Program at no cost. *See Appendix I for a description of Program supplies and materials.*

Instructions are on the cover sheet of every First and Second Trimester Screening Form.

- Specimens should be mailed as soon as possible after collection. Specimens held too long or delayed in transit over 10 days cannot be analyzed for uE3.
- If unable to mail the specimen immediately, centrifuge and refrigerate until mailed. Do not freeze specimens.
- Unlabeled or mislabeled specimens will not be analyzed. Hemolyzed specimens cannot be analyzed.
- It is highly recommended that all specimens be centrifuged.
- **First trimester specimens MUST be centrifuged or they cannot be analyzed.**

PRENATAL SCREENING COORDINATORS

There are Prenatal Screening Coordinator offices throughout California. Each clinician is assigned a Coordinator on the basis of zip code. The prenatal care provider's primary source of information regarding the Program is the Prenatal Screening Coordinator. It is helpful to have a designated contact person in each clinician's office or clinic for the Coordinator to call.

A Prenatal Screening Coordinator will call your office when there is missing or incomplete information or to verify information for certain results such as positives, specimens drawn too early or too late, or any other non-negative test result.

See Appendix B for a list of Prenatal Screening Coordinator offices.

Clinicians should call their Prenatal Screening Coordinator when:

- NT ultrasound information is received from a credentialed NT practitioner and is not on a First and/or Second Trimester Screening Form
- New or corrected information (such as a new gestational age by ultrasound) becomes available prior to 24 weeks gestation.
- A result mailer has not been received by 10 days after blood collection
- There are any questions or concerns regarding the Program or a specific patient's Prenatal Screening result
- The office or clinic has a new clinician, address, phone or fax number

Your Coordinator's phone number is included on every result mailer.

INFORMING CLINICIAN of test results

Results for First and Second Trimester blood tests are communicated to the clinician in two ways:

- 1 RESULT MAILER:** Results are mailed after laboratory analysis is completed. Clinicians typically receive printed results within 7-10 days of blood collection.
- 2 TELEPHONE CALL:** A Prenatal Screening Coordinator calls the clinician's office with all results, except *Screen Negative*, generally on the same day the results are available, in order to verify information and facilitate redraws or referrals.

If no results are received by 10 days after blood draw, call the Prenatal Screening Coordinator!

Other types of correspondence from the Program:

Acknowledgement Letter	Mailed to the clinician and to the patient for first trimester serum only (No NT ultrasound information provided).
Reminder Letter	Mailed to the clinician if an expected second trimester specimen is not received by 17 weeks 3 days gestation, when a first trimester specimen has been received.
New Result Mailer (Modified Mailer)	Mailed to the clinician whenever the patient information changes, since this often modifies the MoM (multiple of the median) and may change the interpretation. For example, if the clinician calls in an NT ultrasound measurement when one was not previously reported, this will trigger a new result mailer. A corrected blood collection date or date of birth can change a result from <i>Screen Positive</i> to <i>Screen Negative</i> or vice versa.
Confirmation of Contact	Mailed to the clinician to officially document verbal or fax communication between the Prenatal Screening Coordinator and the clinician or his/her staff. For example, the clinician agreed to a referral for prenatal diagnosis.
Patient Letter	Mailed to the patient three days after most result mailers are sent to the clinician, except for <i>Screen Negative</i> results. This letter serves as a "safety net" in case the clinician's office is unsuccessful in contacting a patient about her result. The patient letter (in English and Spanish) instructs the patient to call her prenatal provider concerning her Prenatal Screening result.

Erroneous or missing information may lead to an incorrect screening result!

Please verify the Prenatal Screening Results mailer, upon receipt, for correctness of patient information. Please call the Prenatal Screening Coordinator with any questions or to make any necessary corrections or changes.

INFORMING YOUR PATIENT of her blood test results

A health care professional should inform the patient of her test results, whether *Screen Negative* or *Screen Positive*. Please be certain that office staff who discuss screening with patients understand the scope and purpose of the Prenatal Screening Program. Explaining the difference between screening and diagnosis before the blood test helps patients to better understand their results.

Patients with a Screen Positive Result

Information to help your patient understand her result:

- The Prenatal Screening test is a screening test, which gives the risk, or chance of carrying an affected fetus. It is NOT a diagnostic test. It cannot give a definite answer about whether the fetus has a birth defect.
- A *Screen Positive* result does not mean that there is a problem, only that there is an increased risk for a problem and additional diagnostic tests are offered.
- The most common outcome of a *Screen Positive* result is a normal baby.

Guidelines to help reduce anxiety:

- Do not leave anxiety-producing news of *Screen Positive* results on a patient's answering machine.
- Avoid calling *Screen Positive* results late on Friday or before holidays, unless you have someone available to respond to questions.
- Do not use the inappropriate term "abnormal" result. Instead, use "*Screen Positive* result".
- Refer the patient to a genetic counselor at a State-approved Prenatal Diagnosis Center to answer her questions and help her decide whether or not to have diagnostic tests. Assure the patient that CVS or amniocentesis is voluntary.
- Inform the patient that there is no charge for authorized follow-up services at a State-approved Prenatal Diagnosis Center. Insurance approval is not required. Services include genetic counseling, ultrasound, and CVS or amniocentesis if indicated.

Patients with Screen Negative Results

Information to help your patient understand her result:

- A Screen Negative result means that the risk for these birth defects is low enough that diagnostic tests are not offered or covered by the Program.
- A Screen Negative result does not guarantee an absence of birth defects.
- The First Trimester blood test + NT ultrasound screens for Down syndrome and trisomy 18 only. A second Trimester blood test must be submitted to receive a refined integrated risk for Down syndrome and T18 and screening for NTD and SLOS.
- The Second Trimester blood test (Quad, Quad + NT, Serum Integrated or Full Integrated) is a screening test for Down syndrome, trisomy 18, NTD and SLOS.
- The Prenatal Screening test only screens for certain birth defects. It is not a test for all birth defects.

RESULTS AND INTERPRETATIONS for screening tests

FIRST TRIMESTER RESULTS		
Prenatal Screening Results	Interpretation	Action Authorized
1st Trimester Serum-only specimen (no valid NT).	No interpretation or numerical risk assessment. An Acknowledgement letter is sent to verify receipt of the specimen.	In order to get a risk assessment: report valid NT and/or draw 2 nd trimester specimen for Integrated Screening.
<i>“Preliminary risk assessment”</i> (Screen Negative) 1 st T specimen + NT	This is called 1 st T Combined “preliminary risk assessment” and the risks for DS or T18 are below the cutoffs for first trimester Screen Positive.	Screening will not be considered complete until a 2 nd trimester specimen is received. Draw 2 nd trimester specimen for full Integrated Screening.
<i>Screen Positive</i> for Down syndrome 1 st T specimen + NT	1 st T Combined case, Increased risk for DS: Risk is ≥ 1 in 100.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC) or draw a 2 nd T specimen for an Integrated Screening result.
<i>Screen Positive</i> for trisomy 18 1 st T specimen + NT	1 st T Combined case, Increased risk for T18: Risk is ≥ 1 in 50.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC) or draw a 2 nd T specimen for an Integrated Screening result.

SECOND TRIMESTER RESULTS (Quad Marker, Quad + NT, Serum Integrated and Full Integrated Cases)		
Prenatal Screening Results	Interpretation	Action Authorized
<i>Screen Negative</i>	The risks for NTD, AWD, DS, T18 or SLOS are below the cutoffs for second trimester <i>Screen Positive</i> .	No follow-up authorized by the Program. Do not draw another specimen.
<i>Screen Positive</i> for SLOS	Increased risk for SLOS: Risk is ≥ 1 in 250. Also called SCD screening, to note risk of <u>S</u> LOS, <u>C</u> ongenital anomalies or fetal <u>D</u> emise.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).

SECOND TRIMESTER RESULTS, cont'd
(Quad Marker, Quad + NT, Serum Integrated and Full Integrated Cases)

Prenatal Screening Results	Interpretation	Action Authorized
<i>Screen Positive for trisomy 18</i>	Increased risk for T18: Risk is ≥ 1 in 100.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).
<i>Screen Positive for Down syndrome, for Quad Marker case</i>	Increased risk for DS: Risk is ≥ 1 in 150.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).
<i>Screen Positive for Down syndrome, for Quad + NT, Serum Integrated or Full Integrated case</i>	Increased risk for DS: Risk is ≥ 1 in 200.	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).
<i>Screen Positive for NTD</i>	Increased risk for NTD or AWD. Screening cutoffs: <ul style="list-style-type: none"> ≥ 2.5 AFP MoM (for single fetus) or ≥ 4.5 AFP MoM (for twins) 	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).
<i>Too early, High AFP</i> (Specimen drawn between 14 weeks 0 days and 14 weeks 6 days.)	Increased risk for NTD or AWD. Screening cutoffs: <ul style="list-style-type: none"> ≥ 2.5 AFP MoM (for single fetus) or ≥ 4.5 AFP MoM (for twins) 	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC), or draw another 2 nd trimester specimen.
<i>Too late, High AFP</i> (Specimen drawn between 20 weeks 1 day and 21 weeks 0 days.)	Increased risk for NTD or AWD. Screening cutoffs: <ul style="list-style-type: none"> ≥ 2.5 AFP MoM (for single fetus) or ≥ 4.5 AFP MoM (for twins) 	Refer patient to a State-Approved Prenatal Diagnosis Center (PDC).

The cutoffs for Down syndrome screening, trisomy 18 screening and SLOS/SCD screening are different because their receiver operator curves are different. (A receiver operator curve relates detection rates to screen positive rates.) Cutoffs are chosen for each screening test to maximize detection with reasonable screen positive rates. See Appendix H for a summary of screen positive and detection rates.



RESULTS FOR INVALID SPECIMENS		
Prenatal Screening Results	Interpretation	Action Authorized
<i>1st Trimester, Too Early</i>	This result indicates that the blood specimen was drawn prior to 10 weeks 0 days of gestation.	Draw a 1 st trimester specimen between 10 weeks 0 days and 13 weeks 6 days of gestation and/or draw 2 nd trimester specimen between 15 weeks 0 days and 20 weeks 0 days.
<i>2nd Trimester, Too Early</i>	2 nd trimester specimen was drawn before 15 weeks 0 days.	Draw a 2 nd trimester specimen between 15 weeks 0 days and 20 weeks 0 days gestation.
<i>2nd Trimester, Too Late</i>	2 nd trimester specimen was drawn after 20 weeks 0 days of gestation.	None. Do not draw another specimen.
<i>Unexpected specimen</i>	This indicates that a second specimen was received after a valid specimen for the same trimester.	None. The results of an unauthorized test in the same trimester are not statistically valid.
<i>Inadequate specimen</i>	This indicates that the blood specimen could not be analyzed due to hemolysis, incorrect labeling, broken tube, 1 st trimester specimen not centrifuged, insufficient quantity or no blood, EDTA contamination, or other reasons.	Draw another specimen in the 1 st and/or 2 nd trimester.
<i>Pregnancy not screenable</i>	Reasons include: <ul style="list-style-type: none">• Fetal reduction• Fetal demise \geq 8 weeks gestation• More than 2 fetuses	None. Only submit another specimen if instructed by your Coordinator.
<i>Pregnancy not screenable (in the first trimester)</i>	Fetal reduction < 8 weeks gestation. 1 st trimester specimen is not valid.	None. Only submit another specimen if instructed by your Coordinator.
<i>Values inconsistent with pregnancy</i>	This result indicates that the analyte levels appear to be inconsistent with pregnancy.	The clinician is asked to verify pregnancy status. Only submit another specimen if instructed by your Coordinator.

EXPLANATION OF RESULTS

Screen Negative: No follow-up services authorized

Approximately 9 out of 10 women have *Screen Negative* results. This means that the patient's individual risk is low enough that diagnostic tests are not offered or covered by the Prenatal Screening Program. No screening test can detect all birth defects and there is still a chance that the fetus has a birth defect. Clinicians always have the option of ordering diagnostic tests using other financial or insurance resources.

Screen Positive Down syndrome: Increased risk for T21

First Trimester + NT: The Prenatal Screening Program combines maternal age with PAPP-A, hCG and NT MoMs to determine an individualized midtrimester risk for Down syndrome. *Screen Positive* patients may have high hCG and low PAPP-A levels, and/or high NT measurements. The Down syndrome risk is calculated for a pregnancy with a single or twin gestation.

Second Trimester (Quad, Quad + NT, Serum Integrated or Full Integrated): The Prenatal Screening Program combines maternal age and second trimester MoMs (AFP, hCG, uE3, INH) with any available first trimester MoMs (PAPP-A, hCG, and/or NT), to determine an individualized midtrimester risk for Down syndrome. *Screen Positive* patients often have high hCG and Inhibin levels. The Down syndrome risk is calculated for a pregnancy with a single or twin gestation. *Please see Appendix H for a summary of screen positive rates and detection rates.*

A common reason for a *Screen Positive* result for Down syndrome screening is overestimation of gestational age. Screen Positive results may also be associated with other chromosomal syndromes or with normal variation of pregnancy markers.

Note: When a 2nd trimester specimen is delayed more than 10 days between blood collection and analysis, there is no uE3 value reported due to the instability of the analyte. In these cases, the Down syndrome risk is calculated without uE3, but with all other available 1st and 2nd trimester analytes. Although the detection rate is slightly less, the risk assessment is accurate and reliable.

Screen Positive Trisomy 18: Increased risk for T18

First Trimester + NT: The Prenatal Screening Program combines maternal age with PAPP-A, and hCG to determine an individualized midtrimester risk for trisomy 18. *Screen Positive* patients may have low hCG and PAPP-A levels, and/or high NT measurements.

Second Trimester (Quad, Quad + NT, Serum Integrated or Full Integrated): The Prenatal Screening Program combines maternal age and second trimester MoMs (AFP, hCG, uE3, INH) with any available first trimester MoMs (PAPP-A, hCG, and/or NT), to determine an individualized midtrimester risk for trisomy 18. Low levels of any or all of the analytes may be associated with increased risk for trisomy 18. Very early pregnancy, some other chromosomal syndromes, and normal variation may be associated with these *Screen Positive* results. *Please see Appendix H for a summary of screen positive rates and detection rates.*

Due to the potential for IUGR in a fetus with trisomy 18, redating the pregnancy is not usually allowed because new ultrasound dating may not be accurate.

The T18 risk is only calculated for a pregnancy with a twin gestation when NT information is available.

Screen Positive NTD: Increased risk for an open NTD or AWD

The Prenatal Screening Program utilizes only the second trimester AFP analyte for this risk assessment. A patient is classified as *Screen Positive* and at increased risk for a fetus with an open NTD or AWD when the AFP value is elevated over the selected cutoff, which is currently ≥ 2.5 MoM (multiple of the median) for a pregnancy with a single fetus, or ≥ 4.5 MoM for a pregnancy with two fetuses.

Screen Positive rate

Among program participants, 1.00% are initially *Screen Positive* for NTD.

Detection rates

Among women who have Prenatal Screening and diagnostic services, the Program identifies approximately:

- 97% of fetuses with anencephaly
- 80% with open spina bifida
- 85% of AWDs (gastroschisis and omphalocele)

Other reasons for this *Screen Positive* result are underestimation of gestational age, multiple gestation, fetal demise, placental abnormalities, and normal variation.

Some apparently normal pregnancies have maternal serum AFP levels over the selected cutoff of 2.50 MoMs. Elevation of AFP is frequently associated with a high risk pregnancy even if no birth defect is found. An increased risk for low birth weight, preterm delivery and fetal demise is associated with otherwise unexplained high midtrimester maternal serum AFP values. *See the Bibliography.* Early identification of these high risk pregnancies may facilitate better obstetrical management. The Prenatal Screening Program does not cover costs associated with obstetrical management, additional testing or treatment beyond prenatal diagnosis.

Screen Positive SLOS: Increased risk for SLOS (SCD)

The Prenatal Screening Program utilizes the second trimester analyte MoMs for AFP, hCG and uE3 to determine an individualized risk for Smith-Lemli-Opitz syndrome. The most relevant finding is a very low uE3 value; AFP and hCG may also be low. The patient's age is not a factor in determining risk. A patient is classified as *Screen Positive* when the risk is ≥ 1 in 250.

The most common findings with SLOS *Screen Positive* results are congenital anomalies and fetal demise. That is why this is sometimes referred to as SCD screening, although the numeric risk is for SLOS.

Among program participants, about 0.20% are Screen Positive for SLOS. The Program identifies approximately 60% of the fetuses with SLOS assuming all Screen Positive women receive amniocentesis.

No SLOS risk assessment can be calculated when there is more than one fetus.

FOLLOW-UP DIAGNOSTIC SERVICES

Follow-up services authorized by the California Prenatal Screening Program are only provided at State-approved Prenatal Diagnosis Centers (PDCs). See the program website www.cdph.ca.gov/programs/pns for a current list of State-approved PDCs.

When follow-up services are authorized by the Program, the clinician is notified by a Prenatal Screening Coordinator. The clinician should contact the patient and offer a referral to a State-approved PDC for authorized services at no additional cost.

- Authorized services for first trimester *Screen Positive* patients include genetic counseling, CVS (<15 weeks) or ultrasound and amniocentesis (>15 weeks) if indicated.
- Authorized services for second trimester *Screen Positive* patients include genetic counseling, ultrasound and amniocentesis if indicated. **The referral must be made as soon as possible in order to allow the patient access to all available follow-up services and options.**

No follow-up services are authorized after 24 weeks gestation.

Genetic Counseling

All patients receive counseling by a professional genetic counselor. The counseling includes taking a family history, explanations of possible reasons for a *Screen Positive* result, as well as the risks, limitations and benefits of diagnostic procedures.

Comprehensive Ultrasound

At State-approved PDCs, ultrasound examinations are performed by consultative sonologists. The ultrasound exam meets ACOG¹, AIUM² and ACR³ standards. With services after 15 weeks, a comprehensive survey of fetal anatomy is performed to detect abnormalities associated with birth defects.

For cases without NT data, ultrasound information may indicate under- or over-estimation of gestational age. However, prenatal screening cases with gestational age dating by NT CRL, including second trimester cases, will not be redated after an ultrasound.

For second trimester *Screen Positive* results, if the ultrasound indicates a gestational age which changes the second trimester result, the Prenatal Screening Coordinator is contacted by the PDC and then informs the clinician of the new result. A modified result mailer is issued by the Program. If, after ultrasound, the new result changes to *Screen Negative* or too late, no further services are authorized and the Coordinator notifies the clinician. If the ultrasound indicates that the blood was drawn too early for the second trimester, the clinician is asked to obtain another Prenatal Screening blood test at 15-20 weeks gestation, if possible.

¹ ACOG: American College of Obstetrics and Gynecology

² AIUM: American Institute of Ultrasound in Medicine

³ ACR: American College of Radiology

Amniocentesis and CVS

If the ultrasound findings do not explain the second trimester Screen Positive results, or the findings suggest a chromosomal disorder, open NTD, or AWD, amniocentesis is usually offered to the patient. The amniotic fluid is used to determine fetal karyotype, amniotic fluid AFP levels and the presence of acetylcholinesterase, if appropriate. If the Prenatal Screening result is Screen Positive for SLOS, the amniotic fluid is also tested for elevated levels of 7-DHC.

In the first trimester, NT CRL is the only dating method used for screening results. CVS may be offered to the patient after first trimester Screen Positive results, depending on the patient's gestational age and the availability of CVS practitioners.

CVS or amniocentesis results are usually available within two weeks. The risk of miscarriage associated with CVS or amniocentesis is less than 1% when performed at State-approved PDCs.

If a birth defect is found...

The professional staff at the PDC discusses with the patient the type of defect found and how it may affect the fetus. Any available treatments are described. Options for continuing or terminating the pregnancy are discussed. Information is provided on support services for whatever decision the woman or couple makes.

The costs of any services recommended or provided for pregnancy management or termination are not covered by the Prenatal Screening Program.

See Appendix C for information about specific birth defects.

REPORTING BIRTH DEFECTS

Mandatory reporting to the Genetic Disease Screening Program of a neural tube defect (NTD) or a chromosomal abnormality is necessary to evaluate the effectiveness of prenatal screening as well as to monitor the geographical and racial/ethnic distributions of these birth defects. All cases of NTDs and chromosomal abnormalities must be reported, even if the patient did not have Prenatal Screening or if the screening result was negative.

Reporting NTDs

State regulations (CCR, Title 17, Section 6531) require the reporting of all cases of the initial diagnosis of a NTD in a fetus or an infant less than one year of age. The report should be made within 30 calendar days of the initial diagnosis on the form, *A Confidential Case Report of a NTD in a Fetus or an Infant Less than One Year of Age*, provided by the Genetic Disease Screening Program. Call a Prenatal Screening Coordinator to ask questions or to get copies of the form. The form is also available on the Program's web site at www.cdph.ca.gov/programs/pns.

One use of these reports is to inform women who had a previous pregnancy affected by a NTD of the benefits of folic acid supplementation in reducing the chance of a recurrence.

Reporting Chromosomal Disorders

State regulations (CCR, Title 17, Section 6532) require the reporting of all cases of Down syndrome or other chromosomal defects in a fetus or an infant less than one year of age. California cytogenetic laboratories are responsible for this reporting. **However, clinicians become responsible for this reporting if they send the specimen to a laboratory outside of California.**

The report should be made within 30 calendar days of the initial diagnosis on the form, *A Confidential Case Report of a Chromosomal Defect in a Fetus or an Infant Less Than One Year of Age*, provided by the Genetic Disease Screening Program. Call a Prenatal Screening Coordinator to ask questions or to get copies of the form. The form is also available on the Program's web site at www.cdph.ca.gov/programs/pns.

Outcomes of Pregnancy

State regulations (CCR, Title 17 Section 6527) require prenatal care providers to complete an Outcome of Pregnancy form for screened women who had a *Screen Positive* result or who have a pregnancy with a multiple gestation. The form is automatically mailed just after the patient's due date to the clinician who ordered the Prenatal Screening test. Clinicians should complete the form and return it to the address listed on the form as soon as possible. Some outcomes are requested on women who had *Screen Negative* test results in order to provide a comparison group for adverse outcomes.

COST/BILLING

Prenatal Screening Program Fee

- The fee (March 2009) for the Prenatal Screening Program is \$162. This fee covers all blood tests (first and/or second trimester) plus authorized follow-up services at a State-approved Prenatal Diagnosis Center.
- The fee is the same regardless of the number of specimens submitted or the number of analytes.
- Blood drawing and handling fees are not covered by the Prenatal Screening Program and will be charged to the patient or her insurance by the blood collection facility.
- NT ultrasounds are not covered by the Prenatal Screening Program.

Insurance or Medi-Cal information

To avoid billing the patient unnecessarily, please enter the patient's Medi-Cal information on the First and/or Second Trimester Screening Form or submit a copy of the patient's Medi-Cal card or insurance card with the First and/or Second Trimester Screening Form.

This will allow the Prenatal Screening Program to directly bill Medi-Cal or the patient's insurer.

If No Insurance or Medi-Cal Information is included with the specimen

If no Medi-Cal or insurance coverage information is provided with the specimen, the Prenatal Screening Program will mail a bill and an insurance form to the patient. If the patient has insurance and wants us to bill her insurance company directly, she will need to fill out the insurance form and return it. Health insurance companies are required to cover Prenatal Screening according to California law.

The Prenatal Screening Program will bill Medi-Cal directly if the Program receives a Medi-Cal ID number or a Presumptive Eligibility number. If a Medi-Cal patient receives a billing form from the Prenatal Screening Program, she should return the bill with her current Medi-Cal number written on it.

Special Billing Codes

Special billing codes are available for prepaid health plans, correctional facilities, military facilities, county health departments, and other facilities who do not want patients to receive a bill directly. The organization obtaining the billing code is responsible for 100% payment. A billing code can be obtained by calling the Prenatal Screening Program accounting office at (866) 718-7915. The billing code must be entered on the Prenatal Screening Test Form.

APPENDICES

Appendix A:

Prenatal Screening Program Website

Appendix B:

Prenatal Screening Coordinator Offices

Appendix C:

Birth Defects Detected by the California Prenatal Screening Program

Appendix D:

Prevention of Neural Tube Defects

Appendix E:

Ultrasound Dating and Down Syndrome Screening
(for women who don't have an NT ultrasound)

Appendix F:

Time Window for Blood Collection
for First and Second Trimester Specimens

Appendix G:

Midtrimester Risk for Chromosome Abnormalities
by Maternal Age at Term

Appendix H:

Estimated Screen Positive Rates and Detection Rates
for Down syndrome and Trisomy 18

Appendix I:

Program Supplies and Patient Education Materials

Appendix J:

First and Second Trimester Screening Forms

Appendix K:

Bibliography

Appendix A

Information available through the Prenatal Screening Program

Website: www.cdph.ca.gov/programs/pns

Program Information for Patients

Patient Education Booklet and Consent

English
Spanish
Chinese
Korean
Vietnamese

Information for Providers

Prenatal Care Provider Handbook

Supply Order Form 2009

Two-sided Program Summary for Clinical Staff

Two-sided Program Summary for Support Staff

Time Window for the Prenatal Screening Program, First Trimester

Time Window for the Prenatal Screening Program, Second Trimester

Resources

Prenatal Diagnosis Centers by County

List of Registered NT Practitioners

Form for Reporting a Neural Tube Defect

Form for Reporting a Chromosomal Defect

News, Hot Topics & Information

Announcement: California Expanded AFP Screening Program Update – January, 2009

Announcement: Regional Forums For Licensed Clinicians on Prenatal Screening

Health Information

First Trimester

Screen Positive Increased Risk for T21

English
Spanish
Chinese
Korean
Vietnamese

Screen Positive Increased Risk for T18

English
Spanish
Chinese
Korean
Vietnamese

Second Trimester

Screen Positive Increased Risk for T21

English
Spanish
Chinese
Korean
Vietnamese

Screen Positive Increased Risk for T18

English
Spanish
Chinese
Korean
Vietnamese

Screen Positive Increased Risk for NTD

English
Spanish
Chinese
Korean
Vietnamese

Screen Positive Increased Risk for SLOS

English
Spanish
Chinese
Korean
Vietnamese

Appendix B

Prenatal Screening Coordinator Offices

Southern California

Los Angeles County

(888) 330-9237 *toll free*

Fax: (323) 866-6755

(888) 844-9237 *toll free*

Fax: (323) 866-6789

(877) 567-9237 *toll free*

Fax: (323) 866-6796

Ventura and Santa Barbara Counties

(877) 568-9237 *toll free*

Fax: (323) 866-6791

Inyo, Mono, Orange, and San Bernardino Counties

(877) 224-4373 *toll free*

Fax: (877) 757-5437 *toll free*

San Diego, Imperial and Riverside Counties

(866) 366-4408 *toll free*

Fax: (858) 822-1284

Kaiser Permanente (for So. Calif.)

(626) 564-3322

Fax: (626) 564-3311

Northern and Central California

Northern California/Central Coast

(800) 559-5616 *toll free*

(800) 428-4279 *toll free*

Fax: (916) 734-0637

(800) 391-8669 *toll free*

(877) 871-6467 *toll free*

Fax: (916) 734-0625

Central Valley

(800) 237-7466 *toll free*

Fax: (559) 353-7215

Kaiser Permanente (for No. Calif.)

(510) 752-6190

Fax: (510) 752-6800

**A Prenatal Screening Coordinator office phone number is listed on all result mailers.
Call (866) 718-7915 *toll-free* for questions.**

Appendix C

Birth Defects Detected by the California Prenatal Screening Program

This brief description of birth defects is included for the use of providers and other personnel in the prenatal care office or clinic.

Neural tube defects (NTD)

Neural tube defects (anencephaly, spina bifida and encephalocele) occur in about one in 1,000 pregnancies in California.* Some studies have shown that Hispanic women are at a slightly higher risk than other ethnic or racial groups. Anencephaly and spina bifida account for approximately 95% of neural tube defects, and encephaloceles make up the remaining 5%. Most neural tube defects are isolated anomalies, but they may also occur in association with a genetic syndrome such as Meckel-Gruber syndrome, or with chromosomal abnormalities such as trisomy 18.

Approximately 95% of infants born with neural tube defects are born into families with no previous history of NTDs. This is why the Prenatal Screening test is the best method for detecting most open neural tube defects. Any couple with a family history of a neural tube defect should be referred for genetic counseling.

Anencephaly is a defect in which the top of the neural tube fails to close and the brain does not develop. Anencephaly is always fatal. Seventy-five percent of anencephalic fetuses are stillborn. Twenty-five percent are live born but die within hours or days of birth.

Spina bifida (also called meningocele) is a defect in which the neural tube fails to close and a portion of the spinal cord and nerves fails to develop properly. Spina bifida varies in severity depending upon the size and the position of the defect on the spine, whether it is covered by skin, and the amount of nerve damage.

About 80-85% of infants with spina bifida have the more serious form of the condition, an uncovered or open defect. Of these, about 8% are stillborn or die shortly after birth. At least 80% of those who survive to five years of age have a severe handicap (paralysis below the level of the defect, and bowel and bladder incontinence). Many have learning disabilities. Ten to fifteen percent have mental retardation due to associated anomalies of the brain. About 90% develop hydrocephalus, which increases the likelihood of mental retardation if not treated. Prenatal detection of spina bifida, with delivery at a tertiary care medical center, often improves the outcome of these infants.

Note: "Spina bifida occulta" (a defect in a bone of the spine) is not usually considered a neural tube defect. Call your Prenatal Screening Coordinator for more information.

An encephalocele is a sac, usually at the back of the skull, filled with spinal fluid and variable amounts of brain tissue. It carries a high risk for severe neurological deficit and mental retardation. Occasionally other anomalies such as kidney malformations, extra fingers or cleft palate are associated with this neural tube defect. Such findings suggest an inherited genetic disorder (such as Meckel-Gruber syndrome) or trisomy 13 and the couple should be referred for genetic counseling.

Important: Folic acid dietary supplementation reduces the incidence of neural tube defects.

Appendix C

Abdominal wall defects (AWD)

There are two types of abdominal wall defects: omphalocele and gastroschisis. These are often referred to as ventral wall defects. Omphalocele is a protrusion of part of the intestine into the umbilical cord through a defect in the abdominal wall. If the defect is large enough, other internal organs such as the liver and bladder may also develop outside the body. Gastroschisis involves protrusion of the abdominal organs through an opening to the right of the umbilical cord. Frequencies have been reported in the literature as 1 in 4,000 live births for omphalocele and 1 in 10,000 live births for gastroschisis. In California, the rate for all abdominal wall defects is 1 in 2,500 live births.*

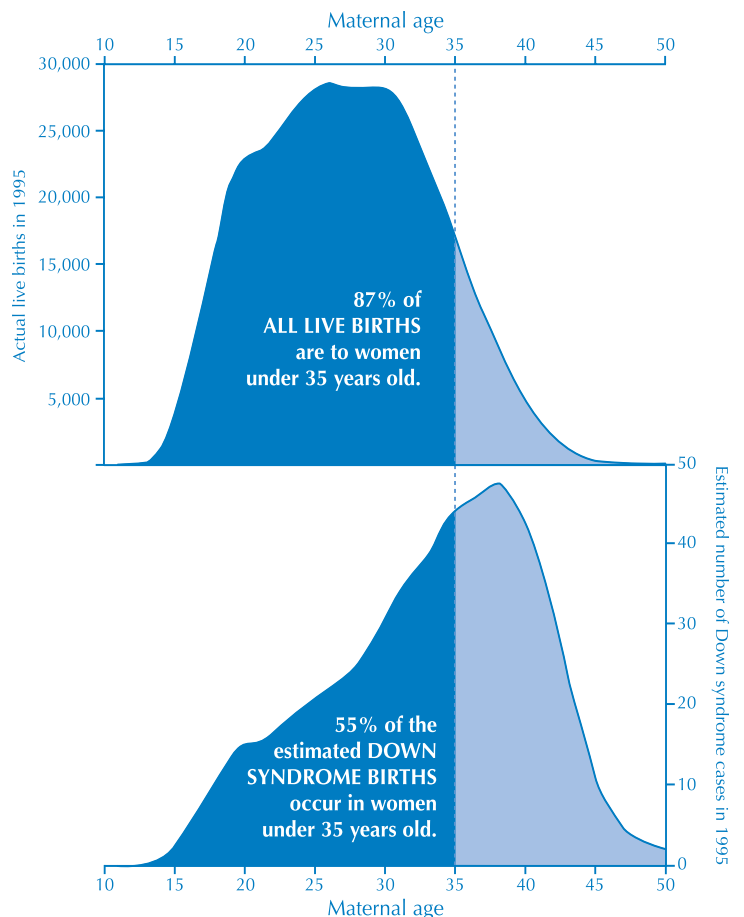
Omphalocele is associated with increased risk for trisomies 13 and 18. Therefore, amniocentesis with chromosome studies is usually performed when ultrasound findings reveal an omphalocele. Gastroschisis, on the other hand, is rarely associated with a chromosomal disorder although there may be other gastrointestinal problems. The severity of abdominal wall defects is variable and many infants, especially those with no other anomaly, have a good prognosis after neonatal surgery. Delivery at a tertiary care medical center often improves the outcome of these infants.

Chromosomal abnormalities

Both trisomy 21 and trisomy 18 can often be detected by prenatal screening. The risk of giving birth to a baby with a chromosomal abnormality, such as trisomy 21 or 18, increases with a woman's age. However, most babies with these conditions are born to younger mothers because younger women, as a group, have more babies. For younger women, a prenatal screening test is the best method for detecting trisomy 21 and 18.

Down syndrome (trisomy 21), the result of an extra chromosome #21, occurs in approximately 1 in 700 births in California*. The syndrome includes physical characteristics such as short stature, epicanthal folds, flat nasal bridge, and a single crease across the palm. Everyone with this disorder is mentally retarded, but the degree of retardation varies. Most individuals are moderately retarded. Approximately 40% also have congenital heart defects. The life span of individuals with Down syndrome varies and is influenced by the presence or absence of congenital heart defects. Any couple with a family history of Down syndrome (or any other chromosomal abnormality) should be referred for genetic counseling.

Total Births and Down Syndrome Births by Maternal Age



Appendix C

Trisomy 18

Trisomy 18 involves an extra chromosome #18. It occurs in approximately 1 in 6,500 live births. Approximately 70% of fetuses with trisomy 18 are miscarried before birth. For those who survive to term, 90-95% will not reach their first birthday. Those surviving have severe mental deficiencies and multiple anomalies including heart and kidney defects. Some have neural tube defects and/or abdominal wall defects. Any couple with a family history of trisomy 18 (or any other chromosomal abnormality) should be referred for genetic counseling.

Smith-Lemli-Opitz syndrome (SLOS)

SLOS is an autosomal recessive genetic syndrome, caused by an inborn error of metabolism in the cholesterol synthetic pathway. Affected individuals are deficient in the enzyme which is responsible for the conversion of 7-dehydrocholesterol (7-DHC) to cholesterol in the last step of cholesterol biosynthesis. Deficiency of this enzyme leads to elevation of the cholesterol precursors, 7-DHC and 8-DHC, in addition to decreased levels of cholesterol.

Patients with SLOS have distinctive facial characteristics, physical anomalies, mental retardation and growth retardation. Common malformations include cleft palate, polydactyly of hands and/or feet, 2-3 syndactyly of the toes, and cataracts.

Many severely affected patients die either before birth or early in the neonatal period. Many of the severely affected patients who survive the newborn period will require a gastrostomy tube for feeding and may never walk or talk. Recurrent infections may also be a problem. Other medical problems depend on whether there are other organ system anomalies present.

Patients with a mild to moderate biochemical defect have milder degrees of mental retardation and may not have such significant problems with growth. Most of these patients do walk and learn to communicate by speech, sign, or some combination of the two. Most patients do have some distinctive facial characteristics. Mildly affected patients may have more subtle distinctive facial characteristics, low muscle tone and mild cognitive delay. Most of these children generally grow well and do not have significant medical problems.

The diagnosis of SLOS is made by demonstration of elevated levels of 7-DHC in the blood after birth, or in amniotic fluid or chorionic villi prenatally. The estimated prevalence is approximately 1 in 100,000 births.

There is no treatment available at this time that will eliminate all of the problems that an individual with SLOS has. Supplementation of the diet with cholesterol, either as a natural food source (eggs) or as a medication using a crystalline form of cholesterol, has been shown to improve growth and development in many patients treated and is a promising form of therapy. Supplementation with cholesterol will most likely not eliminate the mental retardation.

* Source: California Birth Defects Monitoring Program

Appendix D

Prevention of Neural Tube Defects

All women of childbearing age:

Numerous published studies indicate that the incidence of neural tube defects is reduced in women taking 0.4 mg of folic acid per day. The federal government's Centers for Disease Control (CDC) and other organizations have, therefore, recommended that all women capable of becoming pregnant consume 0.4 mg of folic acid each day, either through diet or vitamin supplementation. A diet rich in folic acid includes leafy green vegetables, citrus fruits and juices, beans, and fortified bread. Since it may be difficult to eat enough of these foods to supply 0.4 mg of folic acid, one recommendation is that all women of child bearing age take a multiple vitamin with 0.4 mg (400 micrograms) of folic acid every day while fertile. Women should not wait until pregnancy has been diagnosed to begin taking folic acid, since the neural tube develops in the fetus during the first five weeks after conception.

From the available evidence, the CDC has estimated that as many as 50% of the cases of neural tube defects could be prevented by following this recommendation.

Women who have had a previous pregnancy in which an abnormality such as spina bifida, anencephaly or encephalocele was diagnosed:

The CDC has recommended that these women be counseled about the increased risk in future pregnancies and informed that folic acid supplementation substantially reduces the risk for neural tube defects in subsequent pregnancies. Without folate supplementation, there is an approximate risk of 3% for a recurrence.

Unless contraindicated, these women should be advised to increase the dose to 4.0 mg per day of folic acid beginning at least 4 weeks before conception and continuing through the first 3 months of pregnancy.

The 4.0 mg daily dose should be taken only under a physician's supervision. This folic acid dose should be obtained from pills containing only folic acid. Multivitamin preparations containing folic acid should not be used to obtain the 4.0 mg dose because this would cause a harmful overdose of vitamins A and D. Clinicians should be aware that high doses of folic acid (over 1 mg) could complicate the diagnosis of B₁₂ deficiency. The high doses of folic acid may prevent the anemia resulting from the B₁₂ deficiency, but the associated neurological damage could continue.

Appendix E

Ultrasound Dating and Down Syndrome Screening (for women who don't have an NT ultrasound)

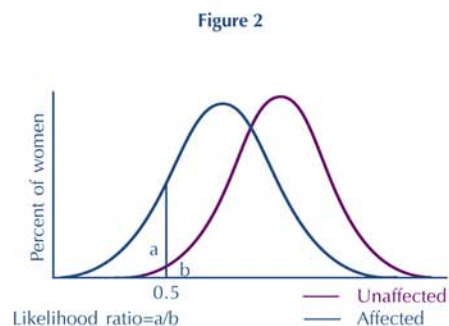
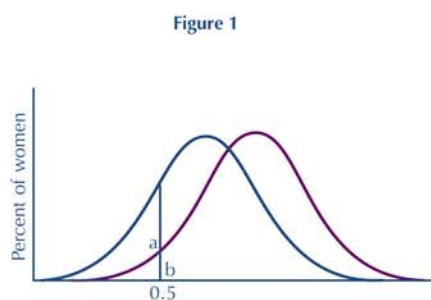
The California Prenatal Screening Program provides a screened woman with her individual risk for Down syndrome based on her age at term and the MoMs of the analytes PAPP-A, AFP, hCG, uE3 and Inhibin in her serum. Because the analyte levels in normal pregnancies vary significantly by gestational day, a woman's screening test result can only be interpreted if the prenatal care clinician provides gestational dating information, whether by ultrasound, LMP or physical exam. The Prenatal Screening Program calculates the gestational age at blood collection.

For the purposes of screening, ultrasound dating is the best way to determine gestational age. (In other obstetrical contexts, this may not be the case.)

Ultrasound dating allows the Program to use the parameters specific for ultrasound-dated pregnancies in order to calculate an individual Down syndrome risk estimate. These parameters give a better estimate of the woman's individual risk than do the LMP-based parameters. When the Prenatal Screening Program is given gestational ages established by more than one method, the interpretation will be based on the ultrasound information.

- ◆ Ultrasound dating gives a more precise estimate of a woman's individual risk of Down syndrome.
- ◆ Include ultrasound dating information on the test form when available, even when ultrasound confirms LMP dates. For screening purposes, dating using biparietal diameter [BPD] is preferred.
- ◆ If a woman has an ultrasound after her Prenatal Screening blood test, the prenatal care clinician may call the Coordinator for a recalculation of the test result based on the new dating information.

The calculation of a woman's risk estimate for Down syndrome compares her MoMs to the distributions of MoMs in the affected and unaffected populations. These distributions are pictured



in Figure 1 for LMP-dated pregnancies and in Figure 2 for ultrasound-dated pregnancies. The distributions of the test results (PAPP-A, AFP, hCG, uE3 and Inhibin) for both Down syndrome and non-Down syndrome pregnancies are narrower when ultrasound dating is used. Consequently, the separation between affected and unaffected pregnancies is more distinct. For example, if a woman's result is 0.5 MoM, Figure 1 (LMP-dated) shows that this MoM is more typical of an affected pregnancy. The ratio of the heights of the curves, called the likelihood ratio, measures how much more likely the pregnancy is to be affected. Alternatively, Figure 2 shows the same MoM with ultrasound dating. The ratio of the heights of the two curves indicates a much higher risk that the pregnancy is affected.

All of the analytes contribute to the risk estimate. The likelihood ratios for the analytes are combined with the woman's age-only risk to give her an individual risk estimate. Redating an LMP-dated or physical exam-dated pregnancy by ultrasound can result in a large change in the woman's individual risk estimate. A woman will have different individual risk estimates depending on whether LMP or ultrasound-dating is used, even if the gestational

ages are the same by both methods. A more detailed mathematical explanation of these concepts is available on request from the Genetic Disease Screening Program.

Prenatal Screening Program

Based on the 1st day of the Last Menstrual Period (LMP)

TIME WINDOW is from 70th through 97th days (between 10 weeks, 0 days and 13 weeks, 6 days)

For use during 365 day year

First Trimester Time Window

Ultrasound is preferred for prenatal screening purposes. If there is no ultrasound dating, use this "time window" chart based on LMP

LMP DATE	DRAW BLOOD FROM	THROUGH
01 Jan	12 Mar	08 Apr
02 Jan	13 Mar	09 Apr
03 Jan	14 Mar	10 Apr
04 Jan	15 Mar	11 Apr
05 Jan	16 Mar	12 Apr
06 Jan	17 Mar	13 Apr
07 Jan	18 Mar	14 Apr
08 Jan	19 Mar	15 Apr
09 Jan	20 Mar	16 Apr
10 Jan	21 Mar	17 Apr
11 Jan	22 Mar	18 Apr
12 Jan	23 Mar	19 Apr
13 Jan	24 Mar	20 Apr
14 Jan	25 Mar	21 Apr
15 Jan	26 Mar	22 Apr
16 Jan	27 Mar	23 Apr
17 Jan	28 Mar	24 Apr
18 Jan	29 Mar	25 Apr
19 Jan	30 Mar	26 Apr
20 Jan	31 Mar	27 Apr
21 Jan	01 Apr	28 Apr
22 Jan	02 Apr	29 Apr
23 Jan	03 Apr	30 Apr
24 Jan	04 Apr	01 May
25 Jan	05 Apr	02 May
26 Jan	06 Apr	03 May
27 Jan	07 Apr	04 May
28 Jan	08 Apr	05 May
29 Jan	09 Apr	06 May
30 Jan	10 Apr	07 May
31 Jan	11 Apr	08 May
01 Feb	12 Apr	09 May
02 Feb	13 Apr	10 May
03 Feb	14 Apr	11 May
04 Feb	15 Apr	12 May
05 Feb	16 Apr	13 May
06 Feb	17 Apr	14 May
07 Feb	18 Apr	15 May
08 Feb	19 Apr	16 May
09 Feb	20 Apr	17 May
10 Feb	21 Apr	18 May
11 Feb	22 Apr	19 May
12 Feb	23 Apr	20 May
13 Feb	24 Apr	21 May
14 Feb	25 Apr	22 May

LMP DATE	DRAW BLOOD FROM	THROUGH
15 Feb	26 Apr	23 May
16 Feb	27 Apr	24 May
17 Feb	28 Apr	25 May
18 Feb	29 Apr	26 May
19 Feb	30 Apr	27 May
20 Feb	01 May	28 May
21 Feb	02 May	29 May
22 Feb	03 May	30 May
23 Feb	04 May	31 May
24 Feb	05 May	01 Jun
25 Feb	06 May	02 Jun
26 Feb	07 May	03 Jun
27 Feb	08 May	04 Jun
28 Feb	09 May	05 Jun
01 Mar	10 May	06 Jun
02 Mar	11 May	07 Jun
03 Mar	12 May	08 Jun
04 Mar	13 May	09 Jun
05 Mar	14 May	10 Jun
06 Mar	15 May	11 Jun
07 Mar	16 May	12 Jun
08 Mar	17 May	13 Jun
09 Mar	18 May	14 Jun
10 Mar	19 May	15 Jun
11 Mar	20 May	16 Jun
12 Mar	21 May	17 Jun
13 Mar	22 May	18 Jun
14 Mar	23 May	19 Jun
15 Mar	24 May	20 Jun
16 Mar	25 May	21 Jun
17 Mar	26 May	22 Jun
18 Mar	27 May	23 Jun
19 Mar	28 May	24 Jun
20 Mar	29 May	25 Jun
21 Mar	30 May	26 Jun
22 Mar	31 May	27 Jun
23 Mar	01 Jun	28 Jun
24 Mar	02 Jun	29 Jun
25 Mar	03 Jun	30 Jun
26 Mar	04 Jun	01 Jul
27 Mar	05 Jun	02 Jul
28 Mar	06 Jun	03 Jul
29 Mar	07 Jun	04 Jul
30 Mar	08 Jun	05 Jul
31 Mar	09 Jun	06 Jul

LMP DATE	DRAW BLOOD FROM	THROUGH
01 Apr	10 Jun	07 Jul
02 Apr	11 Jun	08 Jul
03 Apr	12 Jun	09 Jul
04 Apr	13 Jun	10 Jul
05 Apr	14 Jun	11 Jul
06 Apr	15 Jun	12 Jul
07 Apr	16 Jun	13 Jul
08 Apr	17 Jun	14 Jul
09 Apr	18 Jun	15 Jul
10 Apr	19 Jun	16 Jul
11 Apr	20 Jun	17 Jul
12 Apr	21 Jun	18 Jul
13 Apr	22 Jun	19 Jul
14 Apr	23 Jun	20 Jul
15 Apr	24 Jun	21 Jul
16 Apr	25 Jun	22 Jul
17 Apr	26 Jun	23 Jul
18 Apr	27 Jun	24 Jul
19 Apr	28 Jun	25 Jul
20 Apr	29 Jun	26 Jul
21 Apr	30 Jun	27 Jul
22 Apr	01 Jul	28 Jul
23 Apr	02 Jul	29 Jul
24 Apr	03 Jul	30 Jul
25 Apr	04 Jul	31 Jul
26 Apr	05 Jul	01 Aug
27 Apr	06 Jul	02 Aug
28 Apr	07 Jul	03 Aug
29 Apr	08 Jul	04 Aug
30 Apr	09 Jul	05 Aug
01 May	10 Jul	06 Aug
02 May	11 Jul	07 Aug
03 May	12 Jul	08 Aug
04 May	13 Jul	09 Aug
05 May	14 Jul	10 Aug
06 May	15 Jul	11 Aug
07 May	16 Jul	12 Aug
08 May	17 Jul	13 Aug
09 May	18 Jul	14 Aug
10 May	19 Jul	15 Aug
11 May	20 Jul	16 Aug
12 May	21 Jul	17 Aug
13 May	22 Jul	18 Aug
14 May	23 Jul	19 Aug
15 May	24 Jul	20 Aug

LMP DATE	DRAW BLOOD FROM	THROUGH
16 May	25 Jul	21 Aug
17 May	26 Jul	22 Aug
18 May	27 Jul	23 Aug
19 May	28 Jul	24 Aug
20 May	29 Jul	25 Aug
21 May	30 Jul	26 Aug
22 May	31 Jul	27 Aug
23 May	01 Aug	28 Aug
24 May	02 Aug	29 Aug
25 May	03 Aug	30 Aug
26 May	04 Aug	31 Aug
27 May	05 Aug	01 Sep
28 May	06 Aug	02 Sep
29 May	07 Aug	03 Sep
30 May	08 Aug	04 Sep
31 May	09 Aug	05 Sep
01 Jun	10 Aug	06 Sep
02 Jun	11 Aug	07 Sep
03 Jun	12 Aug	08 Sep
04 Jun	13 Aug	09 Sep
05 Jun	14 Aug	10 Sep
06 Jun	15 Aug	11 Sep
07 Jun	16 Aug	12 Sep
08 Jun	17 Aug	13 Sep
09 Jun	18 Aug	14 Sep
10 Jun	19 Aug	15 Sep
11 Jun	20 Aug	16 Sep
12 Jun	21 Aug	17 Sep
13 Jun	22 Aug	18 Sep
14 Jun	23 Aug	19 Sep
15 Jun	24 Aug	20 Sep
16 Jun	25 Aug	21 Sep
17 Jun	26 Aug	22 Sep
18 Jun	27 Aug	23 Sep
19 Jun	28 Aug	24 Sep
20 Jun	29 Aug	25 Sep
21 Jun	30 Aug	26 Sep
22 Jun	31 Aug	27 Sep
23 Jun	01 Sep	28 Sep
24 Jun	02 Sep	29 Sep
25 Jun	03 Sep	30 Sep
26 Jun	04 Sep	01 Oct
27 Jun	05 Sep	02 Oct
28 Jun	06 Sep	03 Oct
29 Jun	07 Sep	04 Oct
30 Jun	08 Sep	05 Oct

Prenatal Screening Program

Based on the 1st day of the Last Menstrual Period (LMP)

TIME WINDOW is from 70th through 97th days (between 10 weeks, 0 days and 13 weeks, 6 days)

For use during 365 day year

First Trimester Time Window

Ultrasound is preferred for prenatal screening purposes. If there is no ultrasound dating, use this "time window" chart based on LMP

LMP DATE	FROM	THROUGH
01 Jul	09 Sep	06 Oct
02 Jul	10 Sep	07 Oct
03 Jul	11 Sep	08 Oct
04 Jul	12 Sep	09 Oct
05 Jul	13 Sep	10 Oct
06 Jul	14 Sep	11 Oct
07 Jul	15 Sep	12 Oct
08 Jul	16 Sep	13 Oct
09 Jul	17 Sep	14 Oct
10 Jul	18 Sep	15 Oct
11 Jul	19 Sep	16 Oct
12 Jul	20 Sep	17 Oct
13 Jul	21 Sep	18 Oct
14 Jul	22 Sep	19 Oct
15 Jul	23 Sep	20 Oct
16 Jul	24 Sep	21 Oct
17 Jul	25 Sep	22 Oct
18 Jul	26 Sep	23 Oct
19 Jul	27 Sep	24 Oct
20 Jul	28 Sep	25 Oct
21 Jul	29 Sep	26 Oct
22 Jul	30 Sep	27 Oct
23 Jul	01 Oct	28 Oct
24 Jul	02 Oct	29 Oct
25 Jul	03 Oct	30 Oct
26 Jul	04 Oct	31 Oct
27 Jul	05 Oct	01 Nov
28 Jul	06 Oct	02 Nov
29 Jul	07 Oct	03 Nov
30 Jul	08 Oct	04 Nov
31 Jul	09 Oct	05 Nov
01 Aug	10 Oct	06 Nov
02 Aug	11 Oct	07 Nov
03 Aug	12 Oct	08 Nov
04 Aug	13 Oct	09 Nov
05 Aug	14 Oct	10 Nov
06 Aug	15 Oct	11 Nov
07 Aug	16 Oct	12 Nov
08 Aug	17 Oct	13 Nov
09 Aug	18 Oct	14 Nov
10 Aug	19 Oct	15 Nov
11 Aug	20 Oct	16 Nov
12 Aug	21 Oct	17 Nov
13 Aug	22 Oct	18 Nov
14 Aug	23 Oct	19 Nov
15 Aug	24 Oct	20 Nov

LMP DATE	FROM	THROUGH
16 Aug	25 Oct	21 Nov
17 Aug	26 Oct	22 Nov
18 Aug	27 Oct	23 Nov
19 Aug	28 Oct	24 Nov
20 Aug	29 Oct	25 Nov
21 Aug	30 Oct	26 Nov
22 Aug	31 Oct	27 Nov
23 Aug	01 Nov	28 Nov
24 Aug	02 Nov	29 Nov
25 Aug	03 Nov	30 Nov
26 Aug	04 Nov	01 Dec
27 Aug	05 Nov	02 Dec
28 Aug	06 Nov	03 Dec
29 Aug	07 Nov	04 Dec
30 Aug	08 Nov	05 Dec
31 Aug	09 Nov	06 Dec
01 Sep	10 Nov	07 Dec
02 Sep	11 Nov	08 Dec
03 Sep	12 Nov	09 Dec
04 Sep	13 Nov	10 Dec
05 Sep	14 Nov	11 Dec
06 Sep	15 Nov	12 Dec
07 Sep	16 Nov	13 Dec
08 Sep	17 Nov	14 Dec
09 Sep	18 Nov	15 Dec
10 Sep	19 Nov	16 Dec
11 Sep	20 Nov	17 Dec
12 Sep	21 Nov	18 Dec
13 Sep	22 Nov	19 Dec
14 Sep	23 Nov	20 Dec
15 Sep	24 Nov	21 Dec
16 Sep	25 Nov	22 Dec
17 Sep	26 Nov	23 Dec
18 Sep	27 Nov	24 Dec
19 Sep	28 Nov	25 Dec
20 Sep	29 Nov	26 Dec
21 Sep	30 Nov	27 Dec
22 Sep	01 Dec	28 Dec
23 Sep	02 Dec	29 Dec
24 Sep	03 Dec	30 Dec
25 Sep	04 Dec	31 Dec
26 Sep	05 Dec	01 Jan
27 Sep	06 Dec	02 Jan
28 Sep	07 Dec	03 Jan
29 Sep	08 Dec	04 Jan
30 Sep	09 Dec	05 Jan

LMP DATE	FROM	THROUGH
01 Oct	10 Dec	06 Jan
02 Oct	11 Dec	07 Jan
03 Oct	12 Dec	08 Jan
04 Oct	13 Dec	09 Jan
05 Oct	14 Dec	10 Jan
06 Oct	15 Dec	11 Jan
07 Oct	16 Dec	12 Jan
08 Oct	17 Dec	13 Jan
09 Oct	18 Dec	14 Jan
10 Oct	19 Dec	15 Jan
11 Oct	20 Dec	16 Jan
12 Oct	21 Dec	17 Jan
13 Oct	22 Dec	18 Jan
14 Oct	23 Dec	19 Jan
15 Oct	24 Dec	20 Jan
16 Oct	25 Dec	21 Jan
17 Oct	26 Dec	22 Jan
18 Oct	27 Dec	23 Jan
19 Oct	28 Dec	24 Jan
20 Oct	29 Dec	25 Jan
21 Oct	30 Dec	26 Jan
22 Oct	31 Dec	27 Jan
23 Oct	01 Jan	28 Jan
24 Oct	02 Jan	29 Jan
25 Oct	03 Jan	30 Jan
26 Oct	04 Jan	31 Jan
27 Oct	05 Jan	01 Feb
28 Oct	06 Jan	02 Feb
29 Oct	07 Jan	03 Feb
30 Oct	08 Jan	04 Feb
31 Oct	09 Jan	05 Feb
01 Nov	10 Jan	06 Feb
02 Nov	11 Jan	07 Feb
03 Nov	12 Jan	08 Feb
04 Nov	13 Jan	09 Feb
05 Nov	14 Jan	10 Feb
06 Nov	15 Jan	11 Feb
07 Nov	16 Jan	12 Feb
08 Nov	17 Jan	13 Feb
09 Nov	18 Jan	14 Feb
10 Nov	19 Jan	15 Feb
11 Nov	20 Jan	16 Feb
12 Nov	21 Jan	17 Feb
13 Nov	22 Jan	18 Feb
14 Nov	23 Jan	19 Feb
15 Nov	24 Jan	20 Feb

LMP DATE	FROM	THROUGH
16 Nov	25 Jan	21 Feb
17 Nov	26 Jan	22 Feb
18 Nov	27 Jan	23 Feb
19 Nov	28 Jan	24 Feb
20 Nov	29 Jan	25 Feb
21 Nov	30 Jan	26 Feb
22 Nov	31 Jan	27 Feb
23 Nov	01 Feb	28 Feb
24 Nov	02 Feb	01 Mar
25 Nov	03 Feb	02 Mar
26 Nov	04 Feb	03 Mar
27 Nov	05 Feb	04 Mar
28 Nov	06 Feb	05 Mar
29 Nov	07 Feb	06 Mar
30 Nov	08 Feb	07 Mar
01 Dec	09 Feb	08 Mar
02 Dec	10 Feb	09 Mar
03 Dec	11 Feb	10 Mar
04 Dec	12 Feb	11 Mar
05 Dec	13 Feb	12 Mar
06 Dec	14 Feb	13 Mar
07 Dec	15 Feb	14 Mar
08 Dec	16 Feb	15 Mar
09 Dec	17 Feb	16 Mar
10 Dec	18 Feb	17 Mar
11 Dec	19 Feb	18 Mar
12 Dec	20 Feb	19 Mar
13 Dec	21 Feb	20 Mar
14 Dec	22 Feb	21 Mar
15 Dec	23 Feb	22 Mar
16 Dec	24 Feb	23 Mar
17 Dec	25 Feb	24 Mar
18 Dec	26 Feb	25 Mar
19 Dec	27 Feb	26 Mar
20 Dec	28 Feb	27 Mar
21 Dec	01 Mar	28 Mar
22 Dec	02 Mar	29 Mar
23 Dec	03 Mar	30 Mar
24 Dec	04 Mar	31 Mar
25 Dec	05 Mar	01 Apr
26 Dec	06 Mar	02 Apr
27 Dec	07 Mar	03 Apr
28 Dec	08 Mar	04 Apr
29 Dec	09 Mar	05 Apr
30 Dec	10 Mar	06 Apr
31 Dec	11 Mar	07 Apr

Prenatal Screening Program

Based on the 1st day of the Last Menstrual Period (LMP)

TIME WINDOW is from 105th through 140th days (between 15 weeks, 0 days and 20 weeks, 0 days)

For use during 365 day year

Second Trimester Time Window

Ultrasound is preferred for prenatal screening purposes. If there is no ultrasound dating, use this "time window" chart based on LMP

LMP DATE	DRAW BLOOD	
	FROM	THROUGH
01 Jan	16 Apr	21 May
02 Jan	17 Apr	22 May
03 Jan	18 Apr	23 May
04 Jan	19 Apr	24 May
05 Jan	20 Apr	25 May
06 Jan	21 Apr	26 May
07 Jan	22 Apr	27 May
08 Jan	23 Apr	28 May
09 Jan	24 Apr	29 May
10 Jan	25 Apr	30 May
11 Jan	26 Apr	31 May
12 Jan	27 Apr	01 Jun
13 Jan	28 Apr	02 Jun
14 Jan	29 Apr	03 Jun
15 Jan	30 Apr	04 Jun
16 Jan	01 May	05 Jun
17 Jan	02 May	06 Jun
18 Jan	03 May	07 Jun
19 Jan	04 May	08 Jun
20 Jan	05 May	09 Jun
21 Jan	06 May	10 Jun
22 Jan	07 May	11 Jun
23 Jan	08 May	12 Jun
24 Jan	09 May	13 Jun
25 Jan	10 May	14 Jun
26 Jan	11 May	15 Jun
27 Jan	12 May	16 Jun
28 Jan	13 May	17 Jun
29 Jan	14 May	18 Jun
30 Jan	15 May	19 Jun
31 Jan	16 May	20 Jun
01 Feb	17 May	21 Jun
02 Feb	18 May	22 Jun
03 Feb	19 May	23 Jun
04 Feb	20 May	24 Jun
05 Feb	21 May	25 Jun
06 Feb	22 May	26 Jun
07 Feb	23 May	27 Jun
08 Feb	24 May	28 Jun
09 Feb	25 May	29 Jun
10 Feb	26 May	30 Jun
11 Feb	27 May	01 Jul
12 Feb	28 May	02 Jul
13 Feb	29 May	03 Jul
14 Feb	30 May	04 Jul

LMP DATE	DRAW BLOOD	
	FROM	THROUGH
15 Feb	31 May	05 Jul
16 Feb	01 Jun	06 Jul
17 Feb	02 Jun	07 Jul
18 Feb	03 Jun	08 Jul
19 Feb	04 Jun	09 Jul
20 Feb	05 Jun	10 Jul
21 Feb	06 Jun	11 Jul
22 Feb	07 Jun	12 Jul
23 Feb	08 Jun	13 Jul
24 Feb	09 Jun	14 Jul
25 Feb	10 Jun	15 Jul
26 Feb	11 Jun	16 Jul
27 Feb	12 Jun	17 Jul
28 Feb	13 Jun	18 Jul
01 Mar	14 Jun	19 Jul
02 Mar	15 Jun	20 Jul
03 Mar	16 Jun	21 Jul
04 Mar	17 Jun	22 Jul
05 Mar	18 Jun	23 Jul
06 Mar	19 Jun	24 Jul
07 Mar	20 Jun	25 Jul
08 Mar	21 Jun	26 Jul
09 Mar	22 Jun	27 Jul
10 Mar	23 Jun	28 Jul
11 Mar	24 Jun	29 Jul
12 Mar	25 Jun	30 Jul
13 Mar	26 Jun	31 Jul
14 Mar	27 Jun	01 Aug
15 Mar	28 Jun	02 Aug
16 Mar	29 Jun	03 Aug
17 Mar	30 Jun	04 Aug
18 Mar	01 Jul	05 Aug
19 Mar	02 Jul	06 Aug
20 Mar	03 Jul	07 Aug
21 Mar	04 Jul	08 Aug
22 Mar	05 Jul	09 Aug
23 Mar	06 Jul	10 Aug
24 Mar	07 Jul	11 Aug
25 Mar	08 Jul	12 Aug
26 Mar	09 Jul	13 Aug
27 Mar	10 Jul	14 Aug
28 Mar	11 Jul	15 Aug
29 Mar	12 Jul	16 Aug
30 Mar	13 Jul	17 Aug
31 Mar	14 Jul	18 Aug

LMP DATE	DRAW BLOOD	
	FROM	THROUGH
01 Apr	15 Jul	19 Aug
02 Apr	16 Jul	20 Aug
03 Apr	17 Jul	21 Aug
04 Apr	18 Jul	22 Aug
05 Apr	19 Jul	23 Aug
06 Apr	20 Jul	24 Aug
07 Apr	21 Jul	25 Aug
08 Apr	22 Jul	26 Aug
09 Apr	23 Jul	27 Aug
10 Apr	24 Jul	28 Aug
11 Apr	25 Jul	29 Aug
12 Apr	26 Jul	30 Aug
13 Apr	27 Jul	31 Aug
14 Apr	28 Jul	01 Sep
15 Apr	29 Jul	02 Sep
16 Apr	30 Jul	03 Sep
17 Apr	31 Jul	04 Sep
18 Apr	01 Aug	05 Sep
19 Apr	02 Aug	06 Sep
20 Apr	03 Aug	07 Sep
21 Apr	04 Aug	08 Sep
22 Apr	05 Aug	09 Sep
23 Apr	06 Aug	10 Sep
24 Apr	07 Aug	11 Sep
25 Apr	08 Aug	12 Sep
26 Apr	09 Aug	13 Sep
27 Apr	10 Aug	14 Sep
28 Apr	11 Aug	15 Sep
29 Apr	12 Aug	16 Sep
30 Apr	13 Aug	17 Sep
01 May	14 Aug	18 Sep
02 May	15 Aug	19 Sep
03 May	16 Aug	20 Sep
04 May	17 Aug	21 Sep
05 May	18 Aug	22 Sep
06 May	19 Aug	23 Sep
07 May	20 Aug	24 Sep
08 May	21 Aug	25 Sep
09 May	22 Aug	26 Sep
10 May	23 Aug	27 Sep
11 May	24 Aug	28 Sep
12 May	25 Aug	29 Sep
13 May	26 Aug	30 Sep
14 May	27 Aug	01 Oct
15 May	28 Aug	02 Oct

LMP DATE	DRAW BLOOD	
	FROM	THROUGH
16 May	29 Aug	03 Oct
17 May	30 Aug	04 Oct
18 May	31 Aug	05 Oct
19 May	01 Sep	06 Oct
20 May	02 Sep	07 Oct
21 May	03 Sep	08 Oct
22 May	04 Sep	09 Oct
23 May	05 Sep	10 Oct
24 May	06 Sep	11 Oct
25 May	07 Sep	12 Oct
26 May	08 Sep	13 Oct
27 May	09 Sep	14 Oct
28 May	10 Sep	15 Oct
29 May	11 Sep	16 Oct
30 May	12 Sep	17 Oct
31 May	13 Sep	18 Oct
01 Jun	14 Sep	19 Oct
02 Jun	15 Sep	20 Oct
03 Jun	16 Sep	21 Oct
04 Jun	17 Sep	22 Oct
05 Jun	18 Sep	23 Oct
06 Jun	19 Sep	24 Oct
07 Jun	20 Sep	25 Oct
08 Jun	21 Sep	26 Oct
09 Jun	22 Sep	27 Oct
10 Jun	23 Sep	28 Oct
11 Jun	24 Sep	29 Oct
12 Jun	25 Sep	30 Oct
13 Jun	26 Sep	31 Oct
14 Jun	27 Sep	01 Nov
15 Jun	28 Sep	02 Nov
16 Jun	29 Sep	03 Nov
17 Jun	30 Sep	04 Nov
18 Jun	01 Oct	05 Nov
19 Jun	02 Oct	06 Nov
20 Jun	03 Oct	07 Nov
21 Jun	04 Oct	08 Nov
22 Jun	05 Oct	09 Nov
23 Jun	06 Oct	10 Nov
24 Jun	07 Oct	11 Nov
25 Jun	08 Oct	12 Nov
26 Jun	09 Oct	13 Nov
27 Jun	10 Oct	14 Nov
28 Jun	11 Oct	15 Nov
29 Jun	12 Oct	16 Nov
30 Jun	13 Oct	17 Nov

Prenatal Screening Program

Based on the 1st day of the Last Menstrual Period (LMP)

TIME WINDOW is from 105th through 140th days (between 15 weeks, 0 days and 20 weeks, 0 days)

For use during 365 day year

Second Trimester Time Window

Ultrasound is preferred for prenatal screening purposes. If there is no ultrasound dating, use this "time window" chart based on LMP

LMP DATE	DRAW BLOOD		LMP DATE	DRAW BLOOD	
	FROM	THROUGH		FROM	THROUGH
01 Jul	14 Oct	18 Nov	16 Aug	29 Nov	03 Jan
02 Jul	15 Oct	19 Nov	17 Aug	30 Nov	04 Jan
03 Jul	16 Oct	20 Nov	18 Aug	01 Dec	05 Jan
04 Jul	17 Oct	21 Nov	19 Aug	02 Dec	06 Jan
05 Jul	18 Oct	22 Nov	20 Aug	03 Dec	07 Jan
06 Jul	19 Oct	23 Nov	21 Aug	04 Dec	08 Jan
07 Jul	20 Oct	24 Nov	22 Aug	05 Dec	09 Jan
08 Jul	21 Oct	25 Nov	23 Aug	06 Dec	10 Jan
09 Jul	22 Oct	26 Nov	24 Aug	07 Dec	11 Jan
10 Jul	23 Oct	27 Nov	25 Aug	08 Dec	12 Jan
11 Jul	24 Oct	28 Nov	26 Aug	09 Dec	13 Jan
12 Jul	25 Oct	29 Nov	27 Aug	10 Dec	14 Jan
13 Jul	26 Oct	30 Nov	28 Aug	11 Dec	15 Jan
14 Jul	27 Oct	01 Dec	29 Aug	12 Dec	16 Jan
15 Jul	28 Oct	02 Dec	30 Aug	13 Dec	17 Jan
16 Jul	29 Oct	03 Dec	31 Aug	14 Dec	18 Jan
17 Jul	30 Oct	04 Dec	01 Sep	15 Dec	19 Jan
18 Jul	31 Oct	05 Dec	02 Sep	16 Dec	20 Jan
19 Jul	01 Nov	06 Dec	03 Sep	17 Dec	21 Jan
20 Jul	02 Nov	07 Dec	04 Sep	18 Dec	22 Jan
21 Jul	03 Nov	08 Dec	05 Sep	19 Dec	23 Jan
22 Jul	04 Nov	09 Dec	06 Sep	20 Dec	24 Jan
23 Jul	05 Nov	10 Dec	07 Sep	21 Dec	25 Jan
24 Jul	06 Nov	11 Dec	08 Sep	22 Dec	26 Jan
25 Jul	07 Nov	12 Dec	09 Sep	23 Dec	27 Jan
26 Jul	08 Nov	13 Dec	10 Sep	24 Dec	28 Jan
27 Jul	09 Nov	14 Dec	11 Sep	25 Dec	29 Jan
28 Jul	10 Nov	15 Dec	12 Sep	26 Dec	30 Jan
29 Jul	11 Nov	16 Dec	13 Sep	27 Dec	31 Jan
30 Jul	12 Nov	17 Dec	14 Sep	28 Dec	01 Feb
31 Jul	13 Nov	18 Dec	15 Sep	29 Dec	02 Feb
01 Aug	14 Nov	19 Dec	16 Sep	30 Dec	03 Feb
02 Aug	15 Nov	20 Dec	17 Sep	31 Dec	04 Feb
03 Aug	16 Nov	21 Dec	18 Sep	01 Jan	05 Feb
04 Aug	17 Nov	22 Dec	19 Sep	02 Jan	06 Feb
05 Aug	18 Nov	23 Dec	20 Sep	03 Jan	07 Feb
06 Aug	19 Nov	24 Dec	21 Sep	04 Jan	08 Feb
07 Aug	20 Nov	25 Dec	22 Sep	05 Jan	09 Feb
08 Aug	21 Nov	26 Dec	23 Sep	06 Jan	10 Feb
09 Aug	22 Nov	27 Dec	24 Sep	07 Jan	11 Feb
10 Aug	23 Nov	28 Dec	25 Sep	08 Jan	12 Feb
11 Aug	24 Nov	29 Dec	26 Sep	09 Jan	13 Feb
12 Aug	25 Nov	30 Dec	27 Sep	10 Jan	14 Feb
13 Aug	26 Nov	31 Dec	28 Sep	11 Jan	15 Feb
14 Aug	27 Nov	01 Jan	29 Sep	12 Jan	16 Feb
15 Aug	28 Nov	02 Jan	30 Sep	13 Jan	17 Feb

LMP DATE	DRAW BLOOD		LMP DATE	DRAW BLOOD	
	FROM	THROUGH		FROM	THROUGH
16 Nov	01 Mar	05 Apr	01 Dec	16 Mar	20 Apr
17 Nov	02 Mar	06 Apr	02 Dec	17 Mar	21 Apr
18 Nov	03 Mar	07 Apr	03 Dec	18 Mar	22 Apr
19 Nov	04 Mar	08 Apr	04 Dec	19 Mar	23 Apr
20 Nov	05 Mar	09 Apr	05 Dec	20 Mar	24 Apr
21 Nov	06 Mar	10 Apr	06 Dec	21 Mar	25 Apr
22 Nov	07 Mar	11 Apr	07 Dec	22 Mar	26 Apr
23 Nov	08 Mar	12 Apr	08 Dec	23 Mar	27 Apr
24 Nov	09 Mar	13 Apr	09 Dec	24 Mar	28 Apr
25 Nov	10 Mar	14 Apr	10 Dec	25 Mar	29 Apr
26 Nov	11 Mar	15 Apr	11 Dec	26 Mar	30 Apr
27 Nov	12 Mar	16 Apr	12 Dec	27 Mar	01 May
28 Nov	13 Mar	17 Apr	13 Dec	28 Mar	02 May
29 Nov	14 Mar	18 Apr	14 Dec	29 Mar	03 May
30 Nov	15 Mar	19 Apr	15 Dec	30 Mar	04 May
01 Dec	16 Mar	20 Apr	16 Dec	31 Mar	05 May
02 Dec	17 Mar	21 Apr	17 Dec	01 Apr	06 May
03 Dec	18 Mar	22 Apr	18 Dec	02 Apr	07 May
04 Dec	19 Mar	23 Apr	19 Dec	03 Apr	08 May
05 Dec	20 Mar	24 Apr	20 Dec	04 Apr	09 May
06 Dec	21 Mar	25 Apr	21 Dec	05 Apr	10 May
07 Dec	22 Mar	26 Apr	22 Dec	06 Apr	11 May
08 Dec	23 Mar	27 Apr	23 Dec	07 Apr	12 May
09 Dec	24 Mar	28 Apr	24 Dec	08 Apr	13 May
10 Dec	25 Mar	29 Apr	25 Dec	09 Apr	14 May
11 Dec	26 Mar	30 Apr	26 Dec	10 Apr	15 May
12 Dec	27 Mar	01 May	27 Dec	11 Apr	16 May
13 Dec	28 Mar	02 May	28 Dec	12 Apr	17 May
14 Dec	29 Mar	03 May	29 Dec	13 Apr	18 May
15 Dec	30 Mar	04 May	30 Dec	14 Apr	19 May
16 Dec	31 Mar	05 May	31 Dec	15 Apr	20 May

Appendix G

Midtrimester Risk for Chromosome Abnormalities , By Maternal Age at Term

Maternal Age	Risk for Trisomy 21 ^{1,2}	Risk for Trisomy 18 ^{1,2}
20	1:1140	1:4430
21	1:1130	1:4380
22	1:1110	1:4320
23	1:1090	1:4250
24	1:1060	1:4150
25	1:1030	1:4020
26	1:990	1:3860
27	1:940	1:3660
28	1:880	1:3420
29	1:810	1:3140
30	1:720	1:2820
31	1:630	1:2460
32	1:540	1:2090
33	1:441	1:1720
34	1:351	1:1370
35	1:272	1:1060
36	1:205	1:800
37	1:153	1:600
38	1:114	1:444
39	1:85	1:333
40	1:65	1:255
41	1:51	1:200
42	1:42	1:162
43	1:35	1:136
44	1:30	1:117
45	1:27	1:104
46	1:24	1:94
47	1:22	1:87
48	1:21	1:82
49	1:20	1:79
50	1:19	1:76

The numbers in this table are approximate risks based on data currently available. These numbers are **population-based** risk estimates and should not be presented as a woman's individual risk.

These numbers represent the estimated risk for a fetus with Down Syndrome or Trisomy 18 at **midtrimester**. Approximately 23% of Down Syndrome fetuses² and 70% of Trisomy 18 fetuses³ will be lost between midtrimester and term.

¹ Morris JK et al.: Revised estimates of the maternal age specific live birth prevalence of Down's syndrome. J Med 2002; 9:2-6

² Hook, E.B.:Chromosome abnormalities and spontaneous fetal deaths following amniocentesis; further data and associations with maternal age Am J Hum Genet 1983 35:110-116.

³ Hook, E.B., Cross, PK., Schreinemachers, D.M.: Chromosomal abnormality rates at amniocentesis and live-born infants J Am Med Assoc 1983, 249: 2034-2038

Appendix H

Prenatal Screening for Trisomy 18 Estimated Positive Rates and Detection Rates (by maternal age at term)

Age	Quad		Serum Integrated		(Full) Integrated			
					First Trimester		Total after Second Trimester(*)	
	Positive Rate	Detection Rate	Positive Rate	Detection Rate	Positive Rate	Detection Rate	Positive Rate	Detection Rate
18	0.08%	50%	0.06%	74%	<0.1%	28%	0.08%	68%
19	0.12%	50%	0.07%	74%	<0.1%	29%	0.05%	68%
20	0.07%	51%	0.06%	74%	<0.1%	29%	0.10%	68%
21	0.08%	51%	0.08%	74%	<0.1%	29%	0.07%	68%
22	0.05%	51%	0.07%	74%	<0.1%	29%	0.08%	69%
23	0.10%	51%	0.08%	75%	<0.1%	29%	0.06%	69%
24	0.10%	51%	0.10%	75%	<0.1%	30%	0.10%	69%
25	0.10%	52%	0.10%	75%	<0.1%	30%	0.09%	70%
26	0.11%	52%	0.08%	75%	<0.1%	30%	0.07%	71%
27	0.06%	53%	0.09%	76%	<0.1%	30%	0.09%	71%
28	0.10%	53%	0.09%	75%	0.05%	32%	0.10%	71%
29	0.12%	55%	0.09%	77%	0.10%	33%	0.07%	73%
30	0.13%	55%	0.10%	78%	0.07%	36%	0.19%	74%
31	0.16%	56%	0.12%	78%	0.08%	38%	0.21%	76%
32	0.20%	58%	0.14%	80%	0.11%	40%	0.22%	77%
33	0.30%	62%	0.18%	81%	0.12%	43%	0.25%	79%
34	0.37%	63%	0.31%	83%	0.16%	48%	0.27%	82%
35	0.36%	67%	0.35%	85%	0.23%	57%	0.51%	84%
36	0.78%	69%	0.37%	86%	0.39%	61%	0.81%	86%
37	0.97%	73%	0.65%	88%	0.45%	66%	0.95%	89%
38	1.39%	75%	0.84%	90%	0.72%	70%	1.27%	91%
39	1.70%	78%	1.12%	91%	1.13%	74%	1.92%	92%
40	2.44%	79%	1.27%	92%	1.40%	77%	2.29%	93%
41	2.90%	81%	1.62%	93%	1.65%	79%	2.78%	94%
42	3.94%	83%	1.80%	94%	2.77%	81%	4.12%	95%
43	4.45%	83%	2.17%	95%	2.84%	83%	4.17%	95%
44	5.12%	85%	2.33%	95%	3.78%	84%	5.15%	96%
45	5.89%	85%	2.49%	95%	4.15%	85%	5.54%	96%
46	5.43%	86%	3.07%	95%	4.50%	86%	6.07%	96%
47	6.07%	86%	3.12%	95%	4.75%	86%	6.50%	97%
48	7.24%	87%	3.05%	96%	4.77%	87%	6.62%	97%
49	7.24%	86%	2.95%	96%	5.03%	87%	6.82%	97%
50	7.24%	87%	3.13%	95%	5.06%	87%	6.70%	97%
< 35	0.13%	55%	0.11%	75%	0.05%	36%	0.12%	76%
>=35	1.38%	77%	0.80%	91%	0.82%	72%	1.41%	91%
All Ages	0.31%	67%	0.21%	79%	0.16%	59%	0.31%	81%

(*) Second Trimester rates assume patients with positive results in first trimester accept referral and all patients with preliminary (negative) risk assessments return for second trimester screening

Appendix H

Prenatal Screening for Down Syndrome Estimated Positive Rates and Detection Rates (by maternal age at term)

Age					(Full) Integrated			
	Quad		Serum Integrated		First Trimester		Total after Second Trimester(*)	
	Positive Rate	Detection Rate	Positive Rate	Detection Rate	Positive Rate	Detection Rate	Positive Rate	Detection Rate
18	2%	61%	2%	71%	1%	55%	2%	81%
19	2%	61%	2%	72%	1%	55%	2%	81%
20	2%	61%	2%	73%	1%	55%	2%	81%
21	2%	61%	2%	72%	1%	55%	2%	81%
22	2%	62%	2%	72%	1%	55%	2%	81%
23	2%	62%	2%	72%	1%	55%	2%	81%
24	2%	62%	2%	73%	1%	56%	2%	81%
25	2%	63%	2%	73%	1%	57%	2%	82%
26	2%	63%	2%	73%	1%	58%	2%	83%
27	2%	64%	2%	74%	1%	58%	2%	83%
28	2%	65%	3%	74%	1%	59%	3%	83%
29	3%	67%	3%	76%	1%	61%	3%	84%
30	3%	68%	3%	77%	1%	61%	3%	84%
31	3%	69%	4%	78%	2%	64%	4%	86%
32	4%	72%	4%	80%	2%	66%	4%	87%
33	5%	74%	5%	82%	3%	69%	5%	88%
34	7%	78%	6%	84%	3%	72%	6%	89%
35	8%	81%	7%	86%	5%	75%	8%	91%
36	10%	84%	10%	88%	6%	79%	9%	92%
37	12%	86%	12%	90%	8%	81%	12%	93%
38	16%	89%	15%	92%	10%	84%	14%	94%
39	19%	91%	18%	94%	13%	86%	18%	94%
40	23%	93%	21%	94%	16%	89%	21%	96%
41	26%	94%	25%	95%	20%	90%	25%	96%
42	29%	95%	28%	96%	22%	92%	27%	97%
43	32%	95%	31%	96%	26%	93%	31%	97%
44	34%	96%	33%	97%	28%	94%	33%	97%
45	37%	96%	35%	97%	30%	94%	36%	97%
46	38%	97%	37%	97%	32%	94%	38%	98%
47	40%	97%	39%	98%	35%	95%	39%	98%
48	41%	97%	40%	98%	35%	95%	40%	98%
49	42%	97%	40%	98%	36%	95%	41%	98%
50	43%	97%	41%	98%	37%	95%	42%	98%
< 35	3%	68%	3%	77%	1%	62%	3%	85%
>=35	15%	90%	14%	93%	10%	86%	14%	94%
All Ages	4.5%	80%	4.5%	85%	2.5%	75%	4.5%	90%

(*) Second Trimester rates assume patients with positive results in first trimester accept referral and all patients with preliminary (negative) risk assessments return for second trimester screening

Appendix I

Program Supplies and Patient Education Materials

The following materials are available free of charge. Call (866) 718-7915 toll free to order.

Program Supplies

First Trimester Test Forms – Test Request Forms for drawing blood from 10 weeks 0 days to 13 weeks 6 days.

Second Trimester Test Forms – Test Request Forms, for drawing blood from 15 weeks 0 days to 20 weeks 0 days.

Blood Shipping Kits – each kit contains one serum separator tube, one tray, one absorbent pouch, and one box to mail the blood specimen. The kits meet the shipping requirements of the U.S. Postal Service.

Tubes – 3.5ml Beckton-Dickinson serum separator tubes with a yellow hemoguard. These tubes must be used for the Prenatal Screening Program. **No other tubes are allowed.**

All Prenatal Screening Program supplies are the property of the State of California. Other use is strictly prohibited.

Patient Education Materials

Patient Booklet – *The California Prenatal Screening Program.*

This booklet describes the Prenatal Screening Program, its purpose and cost. It also contains the consent form. It is available in English, Spanish, Chinese, Vietnamese, and Korean.

Important Information for Parents About the Newborn Screening Test

Provides a description of the Newborn Screening Tests. (Required by State law for prospective parents.)

Folate Pamphlet – *Folic Acid: Every Woman, Every Day.*

This brochure informs women about the benefits of folic acid particularly in preventing birth defects. It is available in English and Spanish.

Prenatal Diagnosis of Birth Defects

This brochure describes genetic counseling, ultrasound, amniocentesis, and CVS. It provides a checklist for women to use to see whether prenatal diagnosis may be recommended for them in this pregnancy. It is available in English, Spanish, and Chinese.

Screen Positive Booklets

These booklets are only for women with **Screen Positive** Prenatal Screening blood test results. They are given to women receiving follow-up services at a State-Approved Prenatal Diagnosis Center (PDC).

For **first trimester** *Screen Positive* results, there are separate booklets for trisomy 21 and for trisomy 18, in English and Spanish. Electronic copies for Chinese, Korean, and Vietnamese are available on the Prenatal Screening Program website.

For **second trimester** *Screen Positive* results, there are separate booklets each for trisomy 21, trisomy 18, SLOS, and neural tube defects (NTD), in English and Spanish. Electronic copies for Chinese, Korean, and Vietnamese are available on the Prenatal Screening Program website.

These and other Program materials, including Supplies Order Forms, are available on the Program website: www.cdph.ca.gov/programs/pns.

FIRST TRIMESTER SCREENING

10 WEEKS 0 DAYS TO 13 WEEKS 6 DAYS

CALIFORNIA DEPARTMENT OF PUBLIC HEALTH
CALIFORNIA PRENATAL SCREENING PROGRAM

(866) 718-7915 Toll Free

ACCESSION LABEL
FOR STATE LAB USE ONLY
DO NOT COVER

PART A:

PLEASE WRITE CLEARLY. USE CAPITAL LETTERS.

1. PATIENT INFORMATION									
LAST NAME		FIRST NAME				MAIDEN NAME			
ADDRESS									
BIRTH DATE									
SSN		PHONE NUMBER				MEDICAL RECORD #			
2. RACE/ETHNICITY (mark all races that apply)									
<div><input type="checkbox"/> WHITE<input type="checkbox"/> NATIVE AMERICAN<input type="checkbox"/> JAPANESE<input type="checkbox"/> SAMOAN<input type="checkbox"/> CAMBODIAN<input type="checkbox"/> MIDDLE EASTERN<input type="checkbox"/> OTHER</div> <div><input type="checkbox"/> BLACK<input type="checkbox"/> HAWAIIAN<input type="checkbox"/> KOREAN<input type="checkbox"/> FILIPINO<input type="checkbox"/> LAOS<input type="checkbox"/> INDIAN SUBCONTINENT<input type="checkbox"/> UNKNOWN</div> <div><input type="checkbox"/> HISPANIC/LATINA<input type="checkbox"/> CHINESE<input type="checkbox"/> GUAMANIAN<input type="checkbox"/> VIETNAMESE<input type="checkbox"/> OTHER SOUTHEAST ASIAN</div>									
3. BILLING INFORMATION					4. PATIENT'S/AUTHORIZED PERSON'S SIGNATURE FOR INSURANCE OR MEDICAL BILLING				
PATIENT'S MEDI-CAL #, BIC, OR PE #					I authorize the release of any medical or other information necessary to process an insurance claim and assign payment of medical benefits to the California Department of Public Health, Genetic Disease Screening Program for services rendered. I understand and agree that I am ultimately responsible for payment.				
PNS BILLING CODE					X Signature of Patient/Insured/Authorized Person				
5. CLINICIAN TO BE NOTIFIED OF PATIENT'S RESULTS					Date				
LICENSE # OR NPI #					LAST NAME		FIRST NAME		
FACILITY					PHONE NUMBER		EXT		
ADDRESS					FAX				
6. PREGNANCY DATING: ULTRASOUND PREFERRED. IF NO ULTRASOUND, PROVIDE EITHER LMP OR EXAM (not both).									
ULTRASOUND DATE PERFORMED		GESTATIONAL AGE ON DATE OF ULTRASOUND		LMP - FIRST DAY OF LAST NORMAL MENSTRUAL PERIOD		DATE OF MOST RECENT PHYSICAL EXAM		UTERINE SIZE IN WEEKS	
MONTH DAY YEAR		WEEKS AND DAYS OR DECIMAL WEEKS		MONTH DAY YEAR		MONTH DAY YEAR		WEEKS	
7. NUMBER OF FETUSES IN THIS PREGNANCY					8. PATIENT'S MOST RECENT WEIGHT		9. IS PATIENT INSULIN-DEPENDENT DIABETIC (prior to pregnancy)?		
<input type="checkbox"/> 1 (ONE) <input type="checkbox"/> 2 (TWINS) <input type="checkbox"/> (UNKNOWN)					LBS OR KILOS		<input type="checkbox"/> YES <input type="checkbox"/> NO		
10. WAS THERE AN OVUM DONOR FOR THIS PREGNANCY?					11. HAS PATIENT SMOKED CIGARETTES IN THE LAST 7 DAYS?				
<input type="checkbox"/> YES <input type="checkbox"/> NO If yes, age of donor at time of donation. Years					<input type="checkbox"/> YES <input type="checkbox"/> NO				
12. NUCHAL TRANSLUCENCY INFORMATION (if NT done)									
NT PRACTITIONER CRED #		NT SUPERVISOR CRED #		CRL (FETUS A)		TWIN PREGNANCY?		CRL (FETUS B)	
						<input type="checkbox"/> YES <input type="checkbox"/> NO			
NT SITE CODE		NT EXAM DATE		NT (FETUS A)		IF TWINS, WHAT IS CHORIONICITY?		NT (FETUS B)	
						<input type="checkbox"/> MONOCHORIONIC <input type="checkbox"/> DICHORIONIC <input type="checkbox"/> UNABLE TO DETERMINE			
13. PATIENT CONSENT FROM BOOKLET:									
IF PATIENT MARKED "I DECLINE THE USE OF MY SPECIMEN FOR RESEARCH" ON THE CONSENT FORM, FILL IN THE BOX AT RIGHT. <input type="checkbox"/> PATIENT DECLINED RESEARCH									
PART B: MUST BE COMPLETED AT TIME OF SPECIMEN COLLECTION. SEE COVER FOR COLLECTION AND MAILING INSTRUCTIONS.						14. THIS FORM COMPLETED BY (please print name)			
COLLECTION DATE IS MANDATORY! BLOOD SPECIMEN COLLECTED ON: FACILITY WHERE BLOOD COLLECTED						ADDRESSOGRAPH			
COLLECTOR'S INITIALS TELEPHONE									

CDPH 4092 (5/08)

ADDRESSOGRAPH

DISTRIBUTION: WHITE ORIGINAL MUST ACCOMPANY SPECIMEN.

ENCLOSE A COPY OF **INSURANCE CARD** OR PROVIDE **MEDI-CAL NUMBER** IN #3 ABOVE TO ALLOW CORRECT BILLING.

FIRST TRIMESTER SCREENING (10 WEEKS 0 DAYS-13 WEEKS 6 DAYS)

Appendix J



SECOND TRIMESTER SCREENING

15 WEEKS 0 DAYS TO 20 WEEKS 0 DAYS

CALIFORNIA DEPARTMENT OF PUBLIC HEALTH
CALIFORNIA PRENATAL SCREENING PROGRAM

(866) 718-7915 Toll Free

ACCESSION LABEL
 FOR STATE LAB USE ONLY
 DO NOT COVER

PART A:

1. IF 1ST TRIMESTER SPECIMEN DRAWN,
 ENTER FORM # OR APPLY LABEL
 FROM PINK PAGE OF 1ST TRI FORM.

--	--	--	--	--	--	--	--	--	--	--	--	--

PLEASE WRITE CLEARLY. USE CAPITAL LETTERS.

2. PATIENT INFORMATION

LAST NAME	LAST NAME	FIRST NAME	FIRST NAME	MAIDEN NAME	MAIDEN NAME
ADDRESS					
STREET ADDRESS				APT	
CITY				ST	ZIP
BIRTH DATE	MM-DD-YY	SSN	SSN	MEDICAL REC. NO.	MEDICAL RECORD #
PHONE NUMBER	PHONE	NUMBER			

3. RACE/ETHNICITY (mark all races that apply)

<input type="checkbox"/> WHITE	<input type="checkbox"/> NATIVE AMERICAN	<input type="checkbox"/> JAPANESE	<input type="checkbox"/> SAMOAN	<input type="checkbox"/> CAMBODIAN	<input type="checkbox"/> MIDDLE EASTERN	<input type="checkbox"/> OTHER
<input type="checkbox"/> BLACK	<input type="checkbox"/> HAWAIIAN	<input type="checkbox"/> KOREAN	<input type="checkbox"/> FILIPINO	<input type="checkbox"/> LAOS	<input type="checkbox"/> INDIAN SUBCONTINENT	<input type="checkbox"/> UNKNOWN
<input type="checkbox"/> HISPANIC/LATINA	<input type="checkbox"/> CHINESE	<input type="checkbox"/> GUAMANIAN	<input type="checkbox"/> VIETNAMESE	<input type="checkbox"/> OTHER SOUTHEAST ASIAN		

4. BILLING INFORMATION

PATIENT'S MEDI-CAL #, BIC, OR PE #

--	--	--	--	--	--	--	--	--	--	--	--	--

PNS BILLING CODE

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5. PATIENT'S/AUTHORIZED PERSON'S SIGNATURE FOR INSURANCE OR MEDI-CAL BILLING

I authorize the release of any medical or other information necessary to process an insurance claim and assign payment of medical benefits to the California Department of Public Health, Genetic Disease Screening Program for services rendered. I understand and agree that I am ultimately responsible for payment.

X

Signature of Patient/Insured/Authorized Person

Date

6. CLINICIAN TO BE NOTIFIED OF PATIENT'S RESULTS

LICENSE # OR NPI #	LAST NAME	FIRST NAME
FACILITY NAME	PHONE NUMBER	EXT
ADDRESS	SUITE	FAX
CITY	ST	ZIP

7. PREGNANCY DATING: ULTRASOUND PREFERRED. IF NO ULTRASOUND, PROVIDE EITHER LMP OR EXAM (not both).

ULTRASOUND DATE PERFORMED	GESTATIONAL AGE ON DATE OF ULTRASOUND	LMP - FIRST DAY OF LAST NORMAL MENSTRUAL PERIOD	DATE OF MOST RECENT PHYSICAL EXAM	UTERINE SIZE IN WEEKS
MONTH DAY YEAR	WEEKS AND DAYS OR DECIMAL WEEKS	MONTH DAY YEAR	MONTH DAY YEAR	WEEKS

8. NUMBER OF FETUSES IN THIS PREGNANCY

☐ 1(ONE) ☐ 2 (TWINS) ☐ (UNKNOWN)

9. PATIENT'S MOST RECENT WEIGHT

LBS OR KILOS

--	--	--	--	--	--

10. IS PATIENT INSULIN-DEPENDENT DIABETIC (prior to pregnancy)?

☐ YES ☐ NO

11. WAS THERE AN OVUM DONOR FOR THIS PREGNANCY?

☐ YES ☐ NO If yes, age of donor at time of donation. Years

12. HAS PATIENT SMOKED CIGARETTES IN LAST 7 DAYS?

☐ YES ☐ NO

13. HAS PATIENT HAD CVS?

☐ YES ☐ NO

14. NUCHAL TRANSLUCENCY INFORMATION (if NT done)

NT PRACTITIONER CRED #	NT SUPERVISOR CRED #	CRL (FETUS A)	TWIN PREGNANCY?	CRL (FETUS B)	FILL IN BOX IF UNABLE TO MEASURE CRL
NT SITE CODE	NT EXAM DATE	NT (FETUS A)	<input type="checkbox"/> YES <input type="checkbox"/> NO	NT (FETUS B)	FILL IN BOX IF UNABLE TO MEASURE NT
			IF TWINS, WHAT IS CHORIONICITY?		
			<input type="checkbox"/> MONOCHORIONIC		
			<input type="checkbox"/> DICHORIONIC		
			<input type="checkbox"/> UNABLE TO DETERMINE		

15. PATIENT CONSENT FROM BOOKLET:

IF PATIENT MARKED "I DECLINE THE USE OF MY SPECIMEN FOR RESEARCH" ON THE CONSENT FORM, FILL IN THE BOX AT RIGHT. ☐ PATIENT DECLINED RESEARCH

PART B: MUST BE COMPLETED AT TIME OF SPECIMEN COLLECTION. SEE COVER FOR COLLECTION AND MAILING INSTRUCTIONS.

COLLECTION DATE IS MANDATORY!

BLOOD SPECIMEN COLLECTED ON:

MM-DD-YY

FACILITY WHERE BLOOD COLLECTED

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COLLECTOR'S INITIALS

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TELEPHONE

PHONE					
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16. THIS FORM COMPLETED BY (please print name)

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CDPH 4091 (5/09)

ADDRESSOGRAPH

DISTRIBUTION: WHITE ORIGINAL MUST ACCOMPANY SPECIMEN.

ENCLOSE A COPY OF **INSURANCE CARD** OR PROVIDE **MEDI-CAL NUMBER** IN #4 ABOVE TO ALLOW CORRECT BILLING.

SECOND TRIMESTER SCREENING (15 WEEKS 0 DAYS-20 WEEKS 0 DAYS)

Appendix K

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Appendix K

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