CHAPTER 3

ELIGIBILITY CRITERIA

3.1 Inclusion Criteria

3.1.1 Age

1. Males: 8 years 7 months up to and including 10 years 10 months on the date of Screening Visit 1 (SV1).
2. Females: 7 years 10 months up to and including 10 years 1 month on the date of SV1.
3. Examples:

Range of Dates for SV1

Birthdate	Males	Females
1/1/80	8/ 1/88 - 11/ 1/90	11/ 1/87 - 2/ 1/90
2/28/80	9/28/88 - 12/28/90	12/28/87 - 3/28/90
4/28/80	11/28/88 - 2/28/91	2/28/88 - 5/28/90
4/29/80	11/29/88 - 2/28/91	2/29/88 - 5/29/90
4/30/80	11/30/88 - 2/28/91	2/29/88 - 5/30/90
8/30/80	3/30/89 - 6/30/91	6/30/88 - 9/30/90
8/31/80	3/31/89 - 6/30/91	6/30/88 - 9/30/90

For a more detailed table of acceptable dates for SV1 given a child's birthdate, see Chapter 6, Exhibit 6-1. If there are problems with scheduling SV1, such as postponement of an appointment because of illness or having to move SV1 earlier because of vacation plans, it is permissible, occasionally, to extend the time window for SV1 by as much as ± 2 weeks. For the example of a birthdate of 4/30/78, the extended SV1 window is 11/16/88 - 3/14/91 for males and 2/15/88 - 6/13/90 for females. The use of this extended time window should be restricted to special cases where the originally scheduled appointment for SV1 has to be changed.

3.1.2 Serum Cholesterol

1. (Optional) Serum total cholesterol at Prescreening Assessment $\geq$ 176 mg/dl.
2. Serum LDL-cholesterol at SV1 in males $\geq$ 105 mg/dl and $\leq$ 170 mg/dl and in females $\geq$ 110 mg/dl and $\leq$ 170 mg/dl.
3. Mean of serum LDL-cholesterol at SV1 and Screening Visit 2 (SV2) in males $\geq$ 111.5 mg/dl and $\leq$ 164.5 mg/dl and in females $\geq$ 117.5 mg/dl and $\leq$ 164.5 mg/dl.

3.1.3 Informed Consent

1. Informed consent by parent/guardian and assent by child for participation in Prescreening Assessment obtained before or during Prescreening Assessment.
2. Informed consent by parent/guardian and assent by child for participation in SV1 and SV2 obtained before or during SV1.
3. Informed consent by parent/guardian and assent by child for participation in the trial obtained before or during Baseline Visit (BV).

3.2 Exclusion Criteria for the Child

3.2.1 Medical Conditions

The medical conditions listed below that affect growth, serum cholesterol level, or life expectancy for the period of the trial will exclude the child from the trial (determined primarily by questionnaire at SV1 and supplemented by physical examination at SV2). The conditions are generally chronic diseases, and even if they are in remission during screening, the chance for a flare-up during the study remains. Therefore, the presence of a disease by reliable history only, without laboratory support, is generally sufficient to exclude a child from consideration for the study.

1. Hypothyroidism, defined by the presence of a low thyroid hormone level, the requirement of oral thyroid supplements, or being under the care of an endocrinologist who is regulating thyroid hormone supplementation.
2. Liver disease, particularly, active obstructive liver disease or the presence of active hepatitis within one year of SV1.
3. Insulin-dependent diabetes mellitus. (A further eligibility check with respect to diabetes will be made at SV2 using the fasting serum glucose determination provided by the DISC Central Laboratory).
4. Severe long-term intestinal disease, in particular, inflammatory bowel disease such as Crohn's disease or ulcerative colitis. Patients who are taking steroids or other medications consistent with the therapy for inflammatory bowel disease should be excluded. Other bowel diseases such as irritable bowel syndrome and ulcerative proctitis are not exclusion criteria.
5. Kidney disease, particularly any chronic renal disease such as end-stage renal disease requiring dialysis or dietary modification, any etiology for nephrotic syndrome, or any chronic nephritis. Acute urinary tract infection is not an exclusion unless it is associated with some other chronic kidney ailment. The child should pass through the various screening visits off antibiotic therapy and with no evidence of acute infection.
6. Hemophilia.
7. Anorexia, or extreme undereating leading to weight loss.
8. Bulimia, or binge eating often accompanied by self-induced vomiting.

9. Other diseases or medical conditions that are life-threatening, such as leukemia.

3.2.2 Medications

1. Currently used medications that affect growth, serum cholesterol, or iron nutriture (determined at SV1).
   a. Ritalin.
   b. Phenobarbital.
   c. Dilantin.
   d. Diuretics (e.g., Lasix, Diuril, Hydrodiuril).
   e. Retinoids (e.g., Acutane).
   f. Steroids (e.g., cortisone, cortisol, prednisone, steroids for asthma); intermittent topical steroid therapy for skin rashes is not an exclusion criterion.
   g. Lipid-lowering medications (e.g., Questran, Colestid, nicotinic acid).
   h. Thyroid (e.g., Syhthroid).
   i. Therapeutic iron (e.g., Fer-in-sol). Previous, but not current, use of therapeutic iron is not an exclusion criterion. Also, the use of iron in a multivitamin is not an exclusion.
2. Occasionally, but not currently, used medications: Steroids and retinoids are exclusion criteria if used occasionally. The use of these medications may increase as children age through the study or, in the case of asthma, could become more chronic.

3.2.3 Anthropometric, Maturation, and Blood Pressure Measures

1. Height < 5th percentile for age, sex and race (determined at Prescreening or SV1; see Chapter 6, Exhibit 6-2).

2. Weight < 5th percentile for height for sex and race (determined at Prescreening or SV1; see Chapter 6, Exhibits 6-3 and 6-4).
3. Weight > 90th percentile for height for sex and race (determined at Prescreening or SV1; see Chapter 6, Exhibits 6-3 and 6-4).
4. Weight loss or gain from SV1 to SV2 > 5% of SV1 body weight. In practical terms, the child is excluded if the ratio of the SV2 body weight (i.e., mean of two closest weight measurements reported on Form 04 plus 0.5 kg for clothing allowance) to the SV1 body weight, calculated to four decimal places, is $\leq$ .9499 or $\geq$ 1.0501.
5. History of intentional weight loss or gain $\geq$ 7 pounds in $\leq$ 2 weeks (determined at SV1).
6. Tanner Stage > 1 for any of the Tanner criteria at SV2. If Tanner staging is not done, the child is excluded.
7. Systolic blood pressure (mean of the two readings at each visit) $\geq$ 125 mmHg or 4th phase diastolic blood pressure (mean of two readings) $\geq$ 80 mmHg at <u>both</u> SV2 and BV. To clarify, this does not mean that the SV2 and BV values should be averaged together, but that the average of the two readings at SV2 <u>and</u> the average of the two readings at BV both equal or exceed the cutpoints for exclusion. If 4th phase diastolic blood pressure cannot be measured at SV2 or BV, 5th phase diastolic blood pressure is to be used in its place as an exclusion criterion. If neither 4th nor 5th phase diastolic blood pressure can be measured at either or both SV2 and BV, this will <u>not</u> be a reason for excluding the child. However, the child will be excluded if both SV2 and BV

systolic blood pressures are missing or if one is missing and the other is $\geq$ 125 mmHg.

3.2.4 Laboratory Measures

1. Mean SV1 and SV2 serum triglycerides > 200 mg/dl.
2. Mean SV1 and SV2 serum HDL-cholesterol < 30 mg/dl.
3. Albumin < 3 gm/dl at SV2.
4. Fasting plasma glucose > 140 mg/dl at SV2.
5. SGPT > 60 units (twice the upper limit of normal at Central Laboratory) at SV2.
6. T4 < 6.4 and TSH $\geq$ 10 units, or T4 > 13.2 units at SV2.

3.2.5 Dietary Factors

1. Dietary fat intake not adequate to provide margin for intervention (determined at SV1).
2. Child eats fruits or vegetables or drinks juice less than one time/week and is unwilling to eat these foods more frequently (determined at SV1).
3. Child and/or parents/guardians unwilling to make any changes in diet (determined at SV1).
4. Aberrant eating pattern (determined at SV1).
5. Nutritionist does not believe child would be a good participant (determined at SV1).
6. Vitamin and mineral supplements (determined at SV1): intake of more than one multivitamin per day or more than one gram of Vitamin C per day or daily use of any other vitamin, mineral, or diet supplement except fluoride.

3.2.6 Mental, Physical, and Behavioral Problems

The following mental or physical handicaps or behavior problems that could impede the child's ability to participate fully in the intervention are exclusion criteria (determined at SV1 unless noted otherwise):

1. Deafness, blindness, or other significant physical handicap.
2. Child attends special education class for one of the following reasons:
   a. Mental retardation.
   b. Severe learning disability.
   c. Significant behavior problem.
   d. Any other reason that, in the interviewer's judgment, could impede the child's ability to participate in the intervention.
3. Child repeated two or more grades in school.
4. Child is usually absent from school $\geq$ two times/week.
5. Child does not read and speak English.
6. Achenbach Child Behavior Checklist: score of 1 or 2 on item 18 or item 91 or total behavior score > 98th percentile (T-score for all scales combined > 70) (determined at SV2). For the child to be eligible for the study, the Achenbach test must be taken by at least one parent/guardian. If this test is taken by both parents/guardians at SV2, the child will be excluded if the score is greater than the 98th percentile for either parent/guardian.
7. Any other problem that, in the interviewer's judgment, could impede the child's ability to participate in the intervention.

3.2.7 Other Exclusion Factors

1. Other child in household enrolled in DISC (determined at SV2).

2. Child plans to move > 50 miles from DISC Clinical Center area in the next three years (determined at SV1).

3.3 Exclusion Criteria for the Parents/Guardians

1. Child living with a parent or guardian who had a myocardial infarction or coronary bypass surgery before 45 years of age (determined at SV1).
2. Household member almost always follows a physician-prescribed cholesterol lowering diet (determined at SV1).
3. More than three adults decide what the child eats at ≥ 6 meals during a typical week and the family is unwilling to change this practice (determined at SV1).
4. Child living with a parent or guardian who usually drinks either (a) ≥ 3 alcoholic beverages 7 days/week or (b) ≥ 5 alcoholic beverages ≥ 2 days/week (determined at SV1).
5. Child's parents or guardians unwilling or unable to participate in intervention.
    a. Person who decides what child eats unwilling or unable to attend intervention sessions and adequate alternative arrangements cannot be worked out (determined at SV1).
    b. Adults in household would be unwilling or unable to pack a lunch for the child to take to school if this were necessary (determined at SV1).
    c. The main food preparer in the household and/or the adult who would attend DISC intervention sessions do not read or speak English (determined at SV1).
7. Family plans to move > 50 miles from the DISC Clinical Center area in the next three years (determined at SV1).

8. Nutritionist does not feel parents or guardians would make good participants (determined at SV1).
9. Difficulty scheduling screening visits (determined at SV1 and SV2).
10. No parents/guardians attend SV1, SV2 or BV.

3.4 Exclusion for Lack of Information

For all of the inclusion and exclusion criteria listed in the preceding sections (except for diastolic blood pressure as noted above), failure to obtain the requisite information will be reason for exclusion of the child from the study. If information on an eligibility criterion is not obtained on the first attempt, it is permissible to invite the child and/or parents back to the Clinic in an attempt to obtain the required information. This information will be acceptable as long as it is obtained within the designated time window for the visit.

If a child has not fasted for at least 12 hours at SV1 or SV2, blood should not be drawn and the child should be asked to come in at a later date, fasting for at least 12 hours, to have blood drawn. If the SV1 or SV2 lab results are based on non-fasting (i.e., < 12 hours) specimens, the child will not be eligible for DISC unless fasting specimens can subsequently be obtained.

3.5 Time Windows

1. The official date of SV1 is the date of the SV1 venipuncture. If prescreen height and weight are used in place of SV1 height and weight, the SV1 venipuncture must be completed within four weeks of prescreen. Otherwise, height and weight must be measured on the same day as the SV1 venipuncture.

2. SV2 -- both the venipuncture and the clinic visit, if done on different days -- must be completed a minimum of three weeks and a maximum of eight weeks following the date of SV1.
3. BV must be completed a minimum of three weeks and a maximum of 16 weeks following the date of SV1.

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CHAPTER 4

OVERVIEWS OF DATA COLLECTION VISITS

4.1 Prescreening Assessment

4.1.1 Before the Visit

1. Send the DISC brochure, a letter asking for consent of parent/guardian, and a consent form for prescreening to each child's home.

4.1.2 At the Visit

1. Collect signed parental consent forms including information on whether the parent/guardian wants the results of the prescreening to be sent to the child's physician and, if yes, the name and address of the child's physician.
2. Determine total cholesterol. Cutpoint for eligibility $\geq$ 176 mg/dl.
3. Complete the Prescreening Log (Form 20).
4. (Optional) Measure height and weight.

4.1.3 Form Used at Visit

1. Form 20, Prescreening Log.

4.1.4 After the Visit

1. Assign a DISC ID number to each child invited to Screening Visit 1 (SV1) and record on Form 20. Optionally, this step may be done at SV1 and ID numbers assigned only to those children who actually come to SV1. If ID numbers are assigned at SV1, it is still necessary to record ID numbers on Form 20.

2. Send letter to child's parent/guardian.

   a. If child is eligible for DISC, send:

      (1) Letter to parent/guardian including cholesterol results and an invitation to SV1.

      (2) Two brochures -- "Dietary Guidelines for Americans" and "How to Make Your Heart Last A Lifetime."

      (3) A consent form for participation in SV1 and SV2.

      (4) Form 01, Screening Visit 01 Form.

   b. If child is not eligible for DISC:

      (1) If child has normal total cholesterol, send a letter to parent/guardian including cholesterol results.

      (2) If child has elevated total cholesterol but does not meet DISC eligibility criteria for height or weight/height, send a different letter to parent/guardian including cholesterol results.

      (3) A copy of the letter to parent/guardian should be sent to the child's physician, if this was requested by parents/guardians.

3. Send a copy of Form 20 to the Coordinating Center.

4.2 Screening Visit 1 (SV1)

4.2.1 Before the Visit

1. Either administer Form 12, Preliminary Screening Form, by telephone, or send form to child's parent/guardian.

2. Send the following materials to the child's parent/guardian:

   a. Letter including cholesterol results from Prescreening Assessment and an invitation to SV1.

   b. Two brochures -- "Dietary Guidelines for Americans" and "How to Make Your Heart Last a Lifetime."

c. Consent form for participation in SV1 and SV2.

d. Form 01, Screening Visit 01 Form.

3. Make appointment for SV1.

4. Appointment reminder by telephone or letter; include instructions about fasting -- i.e., no food or liquid except prescribed medications and water for 12 hours before venipuncture. Also remind parent/guardian to bring the child's medications/prescriptions to SV1.

4.2.2 At the Visit

1. Assign child an ID number if not done previously.

2. Collect completed parental consent and child assent form for SV1 and Screening Visit 2 (SV2).

3. Collect Form 01 (and Form 12 if mailed out) and review with parent/guardian.

4. Ascertain whether the child's mother or female guardian or father or male guardian is willing and able to participate with the child in the intervention sessions if the child is assigned to the intervention group.

5. Measure child's height and weight and record on Form 02. Remove jackets, sweaters, shoes, belts, and heavy jewelry, and empty pockets before measuring.

6. Administer Dietary Eligibility Questionnaire (Form 21) to child and parent.

7. Perform venipuncture and complete appropriate section of Form 02.

8. Measure child's total cholesterol using DT-60 and give results to child and parents/guardians.

9. (Optional) Measure height and weight of child's parents/guardians and record on Baseline Visit Form (Form 09).

Remove jackets, sweaters, shoes, belts, and heavy jewelry, and empty pockets before measuring.

10. Complete Form 02, Screening Visit 01 Summary.

4.2.3 Forms Used at Visit

1. Form 01, Screening Visit 01 Form.
2. Form 02, Screening Visit 01 Summary.
3. Form 12, Preliminary Screening Form.
4. Form 21, Dietary Eligibility Questionnaire.
5. Form 50, Serum Shipment Log and Report Form (Lipids).
6. (Optional) Form 09, Baseline Visit Form.

4.2.4 Preparation of Blood Specimen

1. Collection: One 15 ml red-top tube.
2. Aliquots for shipping vials:
   a. 5 ml serum in 5 ml glass serum bottle (GSB) for lipids-lipoproteins.
   b. 0.5 ml serum in 2 ml GSB for apoproteins.
   c. Two 0.5 ml aliquots of serum in 2 ml GSB for long-term storage.
3. Labels: One for collection tube, four for shipping vials, one for shipment log.

4.2.5 Time Window for Completing SV1

If the height and weight taken at the Prescreening Assessment are to be used for SV1, then the date of the SV1 venipuncture must be no more than 4 weeks later than the date of the Prescreening Assessment.

4.2.6 After the Visit

1. If child is eligible for DISC based on Form 02:
   a. Send frozen serum samples to Central Laboratory along with Form 50.
   b. Send Forms 01, 02, 12, and 21 to the Coordinating Center.
2. If child is not eligible for DISC based on Form 02, as a minimum send Form 02 to the Coordinating Center. Any other forms listed in item 1b above that may have been completed should be sent to the Coordinating Center as well.
3. If child is eligible for DISC based on Form 02 and SV1 LDL-cholesterol:
   a. Send letter informing parents/guardians that based on SV1 results child is eligible and make appointment for SV2.
   b. Phone or send a letter to parents/guardians to remind them of SV2 appointment; include instructions about fasting.
4. If child is not eligible for DISC based on Form 02 or SV1 LDL-cholesterol:
   a. Send letter informing parent/guardian that child is not eligible for DISC and provide reason(s) why not eligible.
   b. Send letter to child's physician that child was screened for DISC but found ineligible and give following results:
      (1) Medical conditions identified.
      (2) Medications child taking.
      (3) Height.
      (4) Weight.
      (5) Blood pressure.
      (6) Plasma total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides.

4.3 Screening Visit 2 (SV2)

4.3.1 Before the Visit

1. Make appointment for SV2.
2. Send Form 07 to the child's parents/guardians.
3. Appointment reminder by telephone or letter; include instructions about fasting -- i.e., no food or liquid except prescribed medications and water for 12 hours before venipuncture.

4.3.2 At the Visit

1. Collect Form 07 and review with parent/guardian.
2. Perform anthropometric measurements (i.e., height, weight, girths, and skinfolds) with child in hospital gown, and record on Form 04.
3. Assess child's Tanner stages, measure testicular volume or areolar diameter, and record on Form 06.
4. Measure child's blood pressure and record on Form 05.
5. Perform physical examination on child and record on Form 06.
6. Administer Form 08, Child History Form, to child when child is not accompanied by parents.
7. Administer Achenbach Child Behavior Checklist to child's parent/guardian (or to both parents/guardians if present) and record on Form 31. If only one parent present at SV2, an attempt should be made to schedule the other parent to take the Achenbach at a convenient time, although this is not essential for determining eligibility.
8. Perform venipuncture and complete appropriate section of Form 03.
9. Measure child's total cholesterol using DT-60 and give results to child and parents/guardians.

10. (Optional) If not done at SV1, measure height and weight of child's parents/guardians and record on Form 09 (Baseline Visit Form).
11. Complete Form 03, Screening Visit 02 Form.

4.3.3 Forms Used at Visit

1. Form 03, Screening Visit 02 Form.
2. Form 04, Anthropometry and Maturity Form.
3. Form 05, Blood Pressure Form.
4. Form 06, Physical Examination Form.
5. Form 07, Parent/Guardian Information Form.
6. Form 08, Child History Form.
7. Form 31, Achenbach Child Behavior Checklist.
8. Form 50, Serum Shipment Log and Report Form (Lipids).
9. Form 51, Serum Shipment Log and Report Form - CDC.
10. Form 55, Serum Shipment Log - Hormones (for clinics participating in hormone ancillary study only)
11. (Optional) Form 09, Baseline Visit Form.

4.3.4 Preparation of Blood Specimen

1. Collection (in the order given below; vial designation on label given in brackets):
   a. [15] 15 ml red-top tube.
   b. [BL] 7 ml royal blue-top tube (especially for zinc and copper).
   c. [PR] 2 ml purple-top tube with EDTA for hemoglobin, hematocrit, and red cell folate only.
   d. [15] 15 ml red-top tube or 10 ml red top tube for clinics not in hormone ancillary study.

2. Aliquots for shipping vials (in priority given below):

   a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

   b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

   c. [CP] 1 ml serum in 2 ml GSB for chemistry panel (JHU).

   d. [FT] 1 ml serum in 2 ml GSB for ferritin and T4 (JHU).

   e. [FE] 1 ml serum in plastic vial (PV) for ferritin (CDC).

   f. [FO] 0.1 ml whole blood plus 1 ml of a 1 gm/dl solution ascorbic acid in PV for red cell folate--from purple-top tube (CDC).

   g. [ZN] 2 ml serum in PV for zinc and copper--from royal blue-top collection tube (CDC).

   h. [VA] 1 ml serum in PV for vitamin A, tocopherol, and carotenoids (CDC).

   i. [LO] 1 ml serum in PV for L/O ratio (CDC).

   j. [CB] 0.5 ml whole blood for hemoglobin and hematocrit from purple-top tube (local laboratory).

   k. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long-term storage (JHU).

   l. [H1] 1 ml serum in 2 ml GSB for steroids (NCI). Ancillary study only.

   m. [H2] 1 ml serum in 2 ml GSB for bioavailable fractions (NCI). Ancillary study only.

   n. [H3] 0.5 ml serum in 2 ml GSB for SHBG (NCI). Ancillary study only.

3. Labels: Four for blood collection tubes, 14 for shipping bottles/vials, (11, if not in ancillary study) one for sample for hemoglobin and hematocrit locally, and three for shipment logs (two, if not in ancillary study).

4. Shipment Logs:

   a. Original of Form 50 to go with vials designated as LI, AP, ST, and ST.

   b. Photocopy of Form 50 to go with vials designated as FT and CP.

   c. Original of Form 51 to go with vials designated as FE, ZN, FO, VA, and LO.

   d. Original of Form 55 to go with vials designated as HI, H2, and H3. Ancillary study only.

   e. Photocopies of Forms 50, 51, and 55 (if in ancillary study) retained at the Clinic.

4.3.5 Time Window for Completing SV2

This visit is to be completed a minimum of three weeks and a maximum of eight weeks following the date of the SV1 venipuncture.

4.3.6 After the Visit

1. If child is eligible for DISC based on Form 03:

   a. Send frozen serum and plasma samples to Central Laboratory along with two copies of Form 50, a copy of Form 51, and a copy of Form 55 if your clinic is participating in the ancillary study.

   b. Send or take blood sample to local hematology laboratory for hemoglobin and hematocrit determinations.

   c. Send Forms 03, 04, 05, 06, 07, 08, and 31 to Coordinating Center.

2. If child is not eligible for DISC based on Form 03, as a minimum send Form 03 to Coordinating Center. Any other forms included in item 1c above that may have been completed should be sent to the Coordinating Center as well.

3. If child is eligible for DISC based on Form 03 and SV2 LDL-cholesterol:
   a. Send letter informing parent/guardian that based on SV2 results child is eligible and make appointment for the Baseline Visit (BV).
   b. Phone or send a letter to parents/guardians to remind them of BV appointment.
4. If child is not eligible for DISC based on Form 03 or SV2 LDL-cholesterol:
   a. Send letter informing parents/guardians that child is not eligible for DISC and provide reason(s) why not eligible.
   b. Send letter to child's physician that child was screened for DISC but found ineligible and give following results:
      (1) Medical conditions identified.
      (2) Weight.
      (3) Blood pressure.
      (4) Serum total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides.
      (5) Other biochemical and hematological findings.

4.4 Baseline Visit

4.4.1 Before the Visit

1. Make appointment for the child and both parents/guardians for the BV.
2. Appointment reminder by telephone or letter; include instructions for parents/guardians about fasting -- i.e., no food or liquid except prescribed medications and water for 12 hours before venipuncture.

4.4.2 At the Visit

1. Obtain signed consent from parent and assent from child for participation in the randomized trial.
2. If not done at SV1 or SV2, measure the height and weight of child's parents/guardians and record on Form 09.
3. Administer the Family Environment Form (Form 35) to both parents.
4. Measure child's blood pressure and record on Form 05.
5. Administer Physical Activity Form (Form 10) to the parents/guardians and child.
6. Administer the Woodcock-Johnson, CD, and How I Feel Forms (Forms 32, 33, 34) to the child; it is preferable to do the Woodcock-Johnson before the other two.
7. Administer a 24-hour dietary recall to the child covering the previous day's food intake, and record on Form 22.
8. Instruct the child on doing dietary recalls by telephone.
9. Complete the Baseline Visit Form (Form 09).

4.4.3 Forms Used at Visit

1. Form 05, Blood Pressure Form.
2. Form 09, Baseline Visit Form.
3. Form 10, Physical Activity Form.
4. Form 22, Dietary Recall Form.
5. Form 32, Woodcock-Johnson Form.
6. Form 33, CD Form.
7. Form 34, How I Feel Form.
8. Form 35, Family Environment Form.

4.4.4 Time Window for Completing the BV

This visit is to be completed a minimum of three weeks and a maximum of sixteen weeks following the date of the SV1 venipuncture.

4.4.5 After the Visit

1. If child is eligible for DISC based on Form 09:
    a. Send Forms 05, 09, 10, 32, 33, 34, and 35 to Coordinating Center.
    b. Administer two 24-hour dietary recalls by telephone within two weeks following the BV. (One of the three days should be a weekend day.)
    c. Notify the Coordinating Center by electronic mail when the third dietary recall has been obtained and request a treatment assignment for the child.
    d. If child is assigned to intervention group, send letter to parents/guardians giving information concerning schedule and content of intervention sessions.
2. If child is not eligible for DISC based on Form 09:
    a. As a minimum send Form 09 to the Coordinating Center. Any other forms listed in item 1b above that may have been completed should be sent to the Coordinating Center as well.
    b. Send letter to child's parent/guardian ... (to be prepared).

4.5 6-Month Follow-up Visit

4.6 12-Month Follow-up Visit

4.6.1 Before the Visit

1. Make appointment for the 12 month visit.
2. Appointment reminder by telephone or letter to parent/guardian. Include fasting instructions for child, i.e., no food or liquid except prescribed medications or water for 12 hours before the venipuncture.
3. Send Form 15 (Child Medical Information Follow-Up Form) to parent/guardian.

4.6.2 At the Visit

1. Collect Form 15 and review with the parent/guardian.
2. Perform venipuncture on child and record information on Form 16. See Section 4.6.4 for details on volume, preparation, and labeling.
3. Perform DT-60 for total cholesterol for the child, on blood collected during the venipuncture. Return the results to parent/guardian and child.
4. Perform physical exam on child. (Form 06)
5. Perform anthropometric measurements (i.e., height, weight, girths, and skinfolds) with child in hospital gown, and record on Form 04. Skinfolds should be done using the new method which requires the anthropometric observer to hold the skinfold during the measurement. For Cohort 1 children only, skinfolds should be repeated using the old previous method which required the anthropometric observer to release the skinfold after the calipers were applied, but before the measurement was taken. This information should be recorded on the Form 04A.

6. Assess child's Tanner stage, measure testicular volume or areolar diameter; ask for menstrual history in girls. Record these data on Form 06.
7. Measure child's blood pressure and record on Form 05.
8. Administer Form 08 (Child History Form) to the child when the parents are not present.
9. Administer Achenbach Child Behavior Checklist to child's parent/guardian (or to both parents/guardians if present) and record on Form 31. If only one parent is present, an attempt should be made to schedule the other parent/guardian to take the Achenbach at a convenient time.
10. Administer Form 35 (Family Environment Form) to the child's parent/guardian (or to both parents/guardians if present).
11. Administer a 24 hour dietary recall to the child covering the previous day's food intake and record on Form 22.
12. Schedule times for two more 24 hour dietary recalls to be done by phone within two weeks of the 12 month visit.
13. Administer the Physical Activity Assessment (Form 10) to the parent(s)/guardian(s) and child together.
14. Administer the psychosocial battery (Forms 31, 32, 33, and 34) to the child. Remember to try to administer the Woodcock-Johnson Math and Reading Tests early in the visit before the child becomes fatigued.

4.6.3 Forms Used at the Visit (See Intervention Manual of Operations for Forms Used at Intervention Sessions.)

1. Form 04 - Anthropometry Form
2. Form 4A - Duplicate Anthropometry Form (Cohort 1 only)
3. Form 05 - Blood Pressure Form
4. Form 06 - Physical Examination Form

5. Form 08 - Child History Form
6. Form 10 - Physical Activity Assessment Form
7. Form 15 - Child Medical History Follow-Up Form
8. Form 16 - Twelve Month Visit Summary
9. Form 31 - Achenbach CBCL (standardized form)
10. Form 32 - Woodcock-Johnson (standardized form)
11. Form 33 - CD Form
12. Form 34 - How I Feel Form
13. Form 35 - Family Environment Form
14. Form 50 - DISC Serum Shipment and Report Form (Lipids)
15. Form 51 - Serum Shipment Log and Report Form (CDC)
16. Form 55 - Serum Shipment Log - Hormones (NCI). Ancillary study only.
17. Form 61 - Central Lipoprotein Laboratory External Surveillance Form
18. Form 62 - Nutrition Coding Center External Surveillance

4.6.4 Preparation of Blood Specimens

1. Collection (in the order given below; vial designation on label given in brackets):
   a. [15] 15 ml red-top tube.
   b. [BL] 7 ml royal blue-top tube (especially for zinc and copper).
   c. [PR] 2 ml purple-top tube with EDTA for CBC and red cell folate only.
   d. [15] 15 ml red-top tube or [10] 10 ml red top tube if not participating in ancillary study.
2. Aliquots for shipping vials (in priority given below):
   a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).
   b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

c. [CP] 1 ml serum in 2 ml GSB for albumin (JHU).

d. [FE] 1 ml serum in plastic vial (PV) for ferritin (CDC).

e. [FO] 0.1 ml whole blood plus 1 ml of a 1 gm/dl solution ascorbic acid in PV for red cell folate -- from purple top tube (CDC).

f. [ZN] 2 ml serum in PV for zinc and copper -- from royal blue-top collection tube (CDC).

g. [VA] 1 ml serum in PV for vitamin A, tocopherol, and carotenoids (CDC).

h. [CB] 0.5 ml whole blood for CBC from purple-top tube (local laboratory).

i. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).

j. [H1] 1 ml serum in 2 ml GSB for steroids (NCI). Ancillary study only.

k. [H2] 1 ml serum in 2 ml GSB for bioavailable fractions (NCI). Ancillary study only.

l. [H3] 0.5 ml serum in 2 ml GSB for SHBG (NCI). Ancillary study only.

3. Labels: Four for blood collection tubes, 14 for shipping bottles/vials, (11, if not in ancillary study) one for sample for CDC locally, and three for shipment logs (two, if not in ancillary study).

4. Shipment Logs:

a. Original of Form 50 to go with vials designated as LI, AP, and ST.

b. Photocopy of Form 50 to go with vial designated as CP.

c. Original of Form 51 to go with vials designated as FE, ZN, FO, and VA.

d. Original of Form 55 to go with vials designated as H1, H2, and H3. (Ancillary study only).

e. Photocopies of Forms 50, 51, and 55 (if in ancillary study) retained at the clinic.

5. Duplicate Quality Control Samples for the Central Laboratory: Collect an extra 15 ml of blood in a red-top tube from children with ID numbers designated for quality control procedures. Aliquot as in 2a. to 2c. above and label with an assigned pseudo-identification number. Freeze samples with pseudo-ID numbers. Use the same labeling procedures as used with primary samples.

4.6.5 Time Windows for Completing the 12 Month Visit

Windows for follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the 12 month visit is plus or minus two months from the first anniversary of randomization. If the 12 month visit cannot be completed within 14 months of the date of randomization, an attempt should be made to reschedule it within 18 months of the date of randomization. Visits not made within this broader window will be labeled "missed".

4.6.6 After the Visit

1. Complete Follow-Up Visit Summary Form 16. Copy other forms completed for the visit and send the originals to the Coordinating Center.

2. Prepare duplicate aliquots of serum as required by the Central Lipoprotein Laboratory External Surveillance Procedures and as described in Section 4.6.4.5.

3. Send frozen serum and plasma samples to Central Laboratory along with two copies of Form 50, a copy of Form 51 and a copy of Form 55 (if your clinic is participating in the ancillary study).
4. Send or take blood sample to local hematology laboratory for CBC and indices.
5. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples.
6. Administer two 24 hour dietary recalls to the child over the phone within two weeks of the 12 month visit.
7. Handcopy duplicates of 24 hour recalls gathered at the 12 month visit for designated ID numbers as required by the NCC External Surveillance Procedures. Assign a pseudo-ID to the recall and send to the NCC at least one month after the original record has been sent. Record relevant information on Form 62 and send to the Coordinating Center.
8. Score Form 31, the Achenbach test booklet, using your PC scoring diskette. Send print-out, original test booklet, and COPY of your computer diskette containing data to the Coordinating Center. DO NOT send your original scoring program diskette. Store scoring results on your computer's hard disk, and transfer them to another diskette for sending.
9. Check physical exam and behavioral referral criteria, and notify staff medical personnel, psychologist, or parent/guardian when indicated.

4.7 Twenty-Four Month Follow-up Visit

4.7.1 Before the Visit

1. Make appointment for the 24-hour visit.
2. Appointment reminder by telephone or letter to parent/guardian.

4.7.2 At the Visit

1. Perform height and weight measurements with child in hospital gown and record on Form 26.
2. After a brief physical exam, assess child's Tanner stage, measure testicular volume or areolar diameter, and ask for menstrual history for girls, and record on Form 26.

4.7.3 Forms Used at the Visit (See Intervention Section for Additional Forms Used at Intervention Sessions)

1. Form 26 - Stature - Maturity Form
2. Form 28 - Twenty-Four Month Visit Summary

4.7.4 Time Windows for Completing the Twenty-Four Month Visit

Windows for follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the twenty-four month visit is plus or minus two months from the second anniversary of randomization. If the twenty-four month visit cannot be completed within 26 months of the date of randomization, an attempt should be made to reschedule it within 30 months of the date of randomization. Visits not made within this broader window will be labeled "missed."

4.7.5 After the Visit

1. Complete the Twenty-Four Month Visit Summary Form 28. Copy the other forms completed for the visit and send to the Coordinating Center.

4.8 Thirty-Six Month Follow-up Visit

4.8.1 Before the Visit

1. Call the female parent/guardian of all DISC girls six-weeks before the MN36 visit and administer Form 54. If parental consent is obtained for girls who have reached menarche, mail a Form 64 DISC calendar to the girl every week for the four consecutive full weeks before the MN36 visit. Collect all calendars mailed back for review at the MN36 visit. Photocopy the Form 54 Telephone Interview and mail the original to the Coordinating Center within one week of the last phone call.
2. Make an appointment for the 36 month visit.
3. Appointment reminder by telephone or letter to parent/guardian. Include fasting instructions for child AND PARENTS (no food or liquid, except prescribed medications or water, for 12 hours before the venipuncture).
4. Send Form 68 (Child Medical Information Follow-up Form) to the parent/guardian.

4.8.2 At the Visit

1. For the DISC Child:
   a. Perform venipuncture on child and record information on Form 65. See Section 4.8.4 for details on volume, preparation, and labeling.
   b. Perform DT-60 for total cholesterol on child from blood collected during the venipuncture. Return results to parent/guardian and child. Record information on Form 65.
   c. Measure child's blood pressure and record results on Form 05.

d. Perform physical exam on child. Assess child's Tanner stage, measure testicular volume or areolar diameter; ask for menstrual history in girls. Record results on Form 57.

e. For girls who have reached menarche, review Form 64 Calendars for the preceding four consecutive full weeks. Complete any Calendars that have not been returned.

f. Perform anthropometric measurements (i.e. height, weight, girths, and skinfolds) with child in hospital gown, and record on Form 04.

g. Administer Form 67 (Child History Form) to the child when the parents are not present.

h. Administer a 24-hour dietary recall to the child covering the previous day's food intake and record on Form 22.

i. Schedule times for two more 24-hour dietary recalls to be done by phone within two weeks of the MN36 visit.

j. Administer the Physical Activity Assessment (Form 10) to the parent/guardian(s) and the child together.

k. Administer the psychosocial battery (Forms 32, 33, 34) to the child. Remember to administer the Woodcock-Johnson Math and Reading Tests early in the visit before the child becomes fatigued.

l. Schedule a visit to draw a second blood specimen on the child at MN37.

2. <u>For the Parent/Guardian(s):</u>

a. Perform venipuncture and take blood pressure measurements. Record results on Form 65. See Section 4.8.4 for details on volume, preparation, and labeling of samples.

b. Perform DT-60 for total cholesterol on parents(s) with blood collected during the venipuncture. Return results to the parent and record on Form 65.

c. Perform parent(s) physical examination (height, weight, blood pressure, and current smoking habits). Ask for menstrual and reproductive history in women. Record information on Form 38.

d. Collect Form 68 and review with the parent/guardian(s).

e. Administer Achenbach Child Behavior Checklist (Form 31) to parent/guardian(s). If only one parent is present, an attempt should be made to schedule the other parent/guardian to complete the Achenbach at a convenient time.

f. Administer Form 35 (Family Environment Form) to both parents if present.

g. Administer the Form 30 (Participant Information Form) to at least one parent/guardian. Retain the form at the clinic.

h. Give the female parent/guardians of girls at menarche a set of DISC Calendars (Form 64) for ALL of the weeks (or parts of a week) until the girl's MN37 visit.

4.8.3 Forms Used at the MN36 Visit

1. Form 04, Anthropometry Form
2. Form 05, Blood Pressure Form (Child)
3. Form 10, Physical Activity Assessment Form
4. Form 30, Participant Information Form
5. Form 31, Achenbach CBCL
6. Form 32, Woodcock-Johnson Math and Reading Clusters
7. Form 33, CD Form

8. Form 34, How I Feel Form
9. Form 35, Family Environment Form
10. Form 38, Parent Physical Exam
11. Form 50, DISC Serum Shipment and Report Form (Lipids) (Use separate logs for child and adult lipid specimens).
12. Form 51, Serum Shipment Log and Report Form (CDC)
13. Form 54, Telephone Interview (Menses Data-Girls Only)
14. Form 55, Serum Shipment Log (Hormones)
15. Form 57, Thirty-Six Month Physical Exam Form
16. Form 61, Central Lipoprotein Laboratory External Surveillance Form
17. Form 62, Nutrition Coding Center External Surveillance Form
18. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only)
19. Form 65, Thirty-Six Month Visit Summary
20. Form 67, Child History Form
21. Form 68, Child Medical History Follow-up Form

4.8.4 Preparation of Blood Specimens (Revised 8/24/93)

1. For the DISC Child:
   a. Collection for children (in order given below; vial designation on label given in brackets):
      (1) [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage.
      (2) [15] 15 ml red-top tube (non-lipid tests and hormones
      (3) [BL] 7 ml royal blue-top (Zinc and copper)
      (4) [PR] 2 ml purple-top tube with EDTA (CBC and red cell folate only)

b. Aliquots for shipping vials for children (in priority given below):

(1) [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

(2) [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

(3) [CP] 1 ml serum in 2 ml GSB for chemistry panel (JHU).

(4) [FE] 1 ml serum in plastic vial (PV) for ferritin (CDC).

(5) [FO] 0.1 ml whole blood plus 1 ml of a 1 gm/dl solution ascorbic acid in PV for red cell folate -- from purple-top tube (CDC).

(6) [ZN] 2 ml serum in PV for zinc and copper -- from royal blue-top collection tube (CDC).

(7) [VA] 1 ml serum in PV for vitamin A, tocopherol, and carotenoids (CDC).

(8) [CB] 0.5 ml whole blood for CBC from purple-top tube (local laboratory).

(9) [ST] two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).

(10) [H1] 1 ml serum in GSB for steroids (Hormone Study) (JHU).

(11) [H2] 1 ml serum in GSB for bioavailable fractions (Hormone Study) (JHU).

(12) [H3] 0.5 ml serum in GSB for SHBG (Hormone Study) (JHU).

c. Labels: Four for blood collection tubes, 12 for shipping bottles/vials, one for sample CBC locally and three for shipment logs.

2. For the DISC Adults

a. Collection for adults:

[15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)

b. Aliquots for shipping vials for adults (in priority given below):

(1) [HD] 3 ml serum in GSB for HDL (JHU) (Extra aliquot. See Manual of Operations Chapter 13, p 13-18)

(2) [LI] 4 ml serum in GSB for TC/TG (JHU).

(3) [AP] 0.5 ml serum in GSB for apoAI/apoB (JHU).

c. Labels for adults: One for blood collection tube, three for shipping bottles/vials, and one for shipment log.

3. Shipment Logs for Children and Adults:

a. Original of Form 50 to go with vials labeled LI, AP, ST and HD. (Use separate shipment logs for child and adult specimens.)

b. Photocopy of Form 50 to go with vial labeled CP.

c. Original of Form 51 to go with vials labeled FE, ZN, FO, and VA.

d. Original of Form 55 to go with vials labeled H1, H2 and H3.

e. Photocopies of Forms 50, 51, and 55 retained at the clinic.

4. Duplicate Quality Control Samples for the Central Laboratory: Collect an extra 15 ml of blood in a red-top tube from children (or two 15 ml samples from a fasting volunteer with total cholesterol in the 170-220 mg/dl range). Aliquot as in 4.8.4.1.b1. above and label with an assigned pseudo-ID number(s). Freeze samples with pseudo-ID numbers. Labels with the central part of the participant ID number left blank have been provided by the Coordinating Center for quality control purposes. The middle part of the pseudo-ID should be filled in.

4.8.5 Time Windows for Completing the 36-Month Visit (Revised 8/24/93)

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the 36-month visit is plus or minus two months from the third anniversary of randomization. If the 36-month visit cannot be completed within two months of the third anniversary date of randomization, an attempt should be made to reschedule it within six months of the third anniversary date. Visits not made within this broader window will be labeled "missed".

For the 36-month visit, if the participant cannot be seen within the visit window, the 36-month information should be obtained at any time the participant is seen subsequent to the missed visit, even if this occurs closer to the 48-month or 60-month visit window. Under these circumstances, the Coordinating Center should be contacted as to the appropriate forms to use.

4.8.6 After the Visit

1. Complete a Form 64 Calendar Cover Sheet for each girl who has reached menarche and attache ALL completed calendars. Use a separate cover sheet for Calendars to be used in the validation study.
2. For girls who have reached menarche, mail a Form 64 Calendar to the girl for each of the consecutive weeks (or parts of a week) between the MN36 and MN37 visits. Collect all Calendars mailed back for review at the MN37 visit.
3. Complete the Thirty-Six Month Follow-up Visit Form 65. Copy forms completed for the visit, and send originals to the Coordinating Center.
4. Prepare duplicate aliquots of serum as required by the Central Lipoprotein Laboratory Surveillance Procedures described in Section 4.8.4-4.
5. Send frozen serum and plasma samples to the Central Laboratory along with two copies of Form 50 and the originals of Forms 51 and 55.
6. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples. Complete Form 61 and send it to the Coordinating Center.
7. Administer two 24-hour dietary recalls to the child over the phone within two weeks of the 36-month visit.
8. Hardcopy duplicates of 24-hour recalls gathered at the 36-month visit for designated ID numbers as required by the NCC External Surveillance Procedures. Assign a pseudo-ID to the duplicate recall and send it to the NCC at least one month

after the original record has been sent. Complete the Form 62 and send it to the Coordinating Center.

9. Score Form 31, the Achenbach test booklet using your PC scoring diskette. Send the resulting printout and the original test booklet to the Coordinating Center.

10. Check physical exam and behavioral measures referral criteria and notify staff medical personnel, psychologist, or the child's parent/guardian when indicated.

11. If consent for participation in DISC II was solicited at MN36, complete the DISC II Consent Status Report.

4.9 Thirty-Seven Month Follow-Up Visit (Revised 8/24/93)

4.9.1 Before the Visit

1. If parental consent has been obtained for girls who have reached menarche, mail a Form 64 DISC Calendar to the girl every week for each consecutive week or part of a week between the MN36 and MN37 visit. Collect all Calendars mailed back for review at the MN37 visit.

2. Make an appointment for the MN37 visit.

3. Appointment reminder by telephone or letter to the parent/guardian. Include fasting instructions for the child ONLY (no food or liquid, except prescribed medications or water, for 12 hours before the venipuncture).

4.9.2 At the Visit

1. Perform venipuncture on child and record information on Form 66. See Section 4.9.4 for details on volume, preparation and labeling.

2. Administer Form 66 questions on medications to all children. Administer additional Form 66 questions on menstruation, birth control pills, and pregnancy to girls.
3. For girls who have reached menarche, review Form 64 Calendars for the preceding four consecutive full weeks or parts of a week. Complete any Calendars that have not been returned.
4. Give the female parent/guardian of girls at menarche a set of DISC Calendars (Form 64) for all of the weeks or parts of a week until the 6 week anniversary date of the MN37 visit (MN38).

4.9.3 Forms Used at the MN37 Visit

1. Form 50, DISC Serum Shipment and Report Form (Lipids).
2. Form 55, Serum Shipment Log (Hormones).
3. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only).
4. Form 66, Thirty-Seven Month Visit Summary

4.9.4 Preparation of Blood Specimens

1. Collection for children (in the order given below; vial designation on label given in brackets):
   a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins)
   b. [15] 15 ml red-top tube (hormones)
2. Aliquots for shipping vials for children (in priority given below):

a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

c. [H1] 1 ml serum in GSB for steroids (Hormone Study) (JHU).

d. [H2] 1 ml serum in GSB for bioavailable fractions (Hormone Study) (JHU).

e. [H3] 0.5 ml serum in GSB for SHBG (Hormone Study) (JHU).

3. Labels: Two for blood collections tubes, five for shipping bottles/vials, and two for shipment logs.

4. Shipment Logs for Child:

a. Original of Form 50 to go with vials labeled LI and AP.

b. Original of Form 55 to go with vials labeled H1, H2, and H3.

c. Photocopies of Forms 50 and 55 retained at the clinic.

4.9.5 Time Windows for Completing the 37-Month Visit

The window for the MN37 follow-up visit is timed in relation to the date of the MN36 visit. The acceptable time window for the 37-month visit is not sooner than one week before or later than two weeks after the one month anniversary of the MN36 visit (i.e., 3-6 weeks after the MN36 visit).

If the MN37 visit cannot be completed within this window, an attempt should be made to reschedule it for no later than one month after the one month anniversary of the MN36 visit (i.e. 3-8 weeks after the MN36 visit). Visits not made within this broader window will be labeled "missed".

4.9.6 After the Visit

1. Complete a Form 64 Calendar Cover Sheet for each girl who has reached menarche and attach ALL completed calendars. Use a separate cover sheet for Calendars to be used in the validation study.
2. For girls who have reached menarche, mail a Form 64 Calendar to the girls for each of the consecutive weeks (or parts of a week) between the MN37 and the MN38 date.
3. Collect MN38 menses calendars as they are mailed back to the clinic. One week after the MN38 date, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Form 64 Cover Sheet for each girl and attach ALL calendars returned.
4. Complete the Thirty-Seven Month Follow-up Visit Form 66. Photocopy forms completed for the visit, and send originals to the Coordinating Center.
5. Send frozen serum samples to the Central Laboratory along with two copies of Form 50 and the original of Form 55.
6. In consent for participation in DISC II was solicited at MN37 or by other contact, complete the DISC II Consent Status Report.

4.10 48-Month Follow-Up Visit

4.10.1 Before the Visit

1. COHORT 1 ONLY: Call the female parent/guardian of DISC girls not already returning DISC Calendar Form 64 (either because the girl had not reached menarche or the parent refused consent at MN36) EIGHT WEEKS BEFORE the MN48 visit and administer the Telephone Interview (Form 54). Send letters to mothers of girls who have previously completed calendars

reminding them of the menstrual cycle data collection process eight weeks before the scheduled visit. If parental consent has been obtained for a girl who has reached menarche, mail a DISC Calendar (Form 64) to the girl every week for the SIX consecutive full weeks before the MN48 visit. Collect all the calendars mailed back for review at the MN48 visit. Photocopy the Telephone Interview (Form 54) and mail the original to the Coordinating Center within one week of the last phone call.

2. Make an appointment for the MN48 visit.
3. Appointment reminder by telephone or letter to the parent/guardian. COHORT 1 ONLY: Include fasting instructions for the CHILD (no food or liquid, except prescribed medications or water, for 12 hours before venipuncture).
4. Send the Child Medical Information Follow-up Form (Form 68) to the parent/guardian.

4.10.2 At the Visit

1. Collect the Child Medical Information Follow-up Form (Form 68) and review with the parent/guardian.
2. COHORT 1 ONLY: Perform venipuncture on child and record information on the Forty-Eight Month Visit Summary (Form 39). See Section 4.10.4 for details on volume, preparation, and labeling.
3. COHORT 1 ONLY: Measure child's blood pressure and record results on Blood Pressure Form (Form 05).
4. After a brief physical exam, assess child's Tanner stage, measure testicular volume or areolar diameter. Ask girls about their menstrual history, birth control pill use, and information on pregnancy. Record the information on the Revised Stature-Maturity Form (Form 29).

5. Perform height and weight measurements with child in hospital gown and record on Revised Stature-Maturity Form (Form 29). COHORTS 2-6: Height should be measured by two independent observers. The second observer should be blinded to the measurements taken by the first observer.

6. COHORT 1 ONLY: For girls who have reached menarche, review Calendars (Form 64) for the preceding SIX consecutive full weeks (or parts of a week). Complete any calendars that have not been returned.

7. COHORT 1 ONLY: Administer a 24-hour dietary recall to the child covering the previous day's food intake and record on the Dietary Recall/Record (Form 22).

8. COHORT 1 ONLY: Schedule times for two or more 24-hour dietary recalls to be done by phone within two weeks of the MN48 visit.

9. COHORT 1 ONLY: Give the female parent/guardian of girls at menarche a set of DISC calendars (Form 64) to be completed for the six weeks following the visit or until the girls's next period whichever comes first (MN48).

4.10.3 Forms Used at the Visit

1. COHORT 1 ONLY:

   a. Form 05, Blood Pressure Form (Child)

   b. Form 29, Revised Stature-Maturity Form

   c. Form 39, Forty-Eight Month Visit Summary

   d. Form 50, DISC Serum Shipment and Report Form (Lipids)

   e. Form 54, Telephone Interview Form (Girls not yet returning Form 64)

   f. Form 55, Serum Shipment Log (Hormones)

g. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only)

h. Form 68, Child Medical History Follow-up Form.

2. COHORT 2+

a. Form 29, Revised Stature - Maturity Form

b. Form 30, Participant Information Form (clinic use only)

c. Form 56, DISC II Annual Visit Summary Form

d. Form 68, Child Medical History Follow-up Form

4.10.4 Preparation of Blood Specimens - COHORT 1 ONLY

1. Collection (in the order given below; vial designation on label given in brackets):

a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)

b. [15] 15 ml red-top tube (hormones)

2. Aliquots for shipping vials (in priority given below):

a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

c. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long-term storage (JHU).

d. [H1] 1 ml serum in 2 ml GSB for steroids (Hormone Study) (JHU).

e. [H2] 1 ml serum in 2 ml GSB for bioavailable fractions (Hormone Study) (JHU).

f. [H3] 0.5 ml serum in 2 ml GSB for SHBG (Hormone Study) (JHU).

3. Labels: Two for blood collection tubes, SEVEN for shipping bottles/vials, and two for shipment logs.

4. Shipment Logs:

   a. Original of Form 50 to go with vials labeled LI, AP, and ST.

   b. Original of Form 55 to go with vials labeled H1, H2, and H3.

   c. Photocopies of Forms 50 and 55 retained at the clinic.

4.10.5 Time Windows for Completing the 48-Month Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the 48-month visit is plus or minus two months from the fourth anniversary of randomization. If the 48-month visit cannot be completed within two months of the fourth anniversary date of randomization, an attempt should be made to reschedule it within six months of the fourth anniversary date. Visits not made within this broader window will be labeled "missed".

4.10.6 After the Visit

1. COHORT 1 ONLY

   a. Complete a Calendar Cover Sheet (Form 64) for each girl who has reached menarche and attach ALL completed calendars. Use a separate cover sheet for calendars to be used in the validation study.

   b. For girls who have reached menarche, mail a Calendar (Form 64) to the girl for SIX consecutive weeks (or parts of a week) after the MN48 clinic visit.

   c. Collect all menses calendars as they are mailed back to the clinic. Seven weeks after the MN48 visit, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Calendar

Cover Sheet (Form 64) for each girl and attach ALL calendars returned.

d. Complete the Forty-Eight Month Follow-Up Visit (Form 39). Copy forms completed for the visit, and send originals to the Coordinating Center.

e. Send frozen serum samples to the Central Laboratory along with originals of Forms 50 and 55.

f. Administer two 24-hour dietary recalls to the child over the phone within two weeks of the 48-month visit.

g. Check physical exam and behavioral measures referral criteria and notify staff medical personnel, psychologist, or the child's parent/guardian when indicated. Record the referral and the reason for referral on the Forty-Eight Month Visit Summary (Form 39).

2. COHORT 2+

a. Complete the DISC II Annual Visit Summary Form (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.

4.11 Year 5 (60 Months) Follow-up Visit (Revised 11/09/94)

4.11.1 Before the Visit

1. Call the female parent/guardian of DISC girls not already returning DISC Calendar Form 64 (either because the girl had not reached menarche or the parent or girl refused to participate in menses data collection) EIGHT WEEKS BEFORE the visit and administer the Telephone Interview (Form 54). Send letters to mothers of girls who have previously completed calendars reminding them of the menstrual cycle data collection process eight weeks before the scheduled visits.

If parental consent has been obtained for a girl who has reached menarche, mail a DISC Calendar (Form 64) to the girl every week for the SIX consecutive full weeks before the visit. Collect all calendars mailed back for review at the clinic visit. Photocopy the Telephone Interview (Form 54) and mail the original to the Coordinating Center within one week of the last phone call.

2. Make an appointment for the visit.
3. Appointment reminder by telephone or letter to the parent/guardian. Include fasting instructions for the PARTICIPANT (no food or liquid, except prescribed medications or water, for 12 hours before venipuncture).
4. Send the Child Medical Information Follow-up Form (Form 68) to the parent/guardian.
5. Send the Participant Information Form (Form 30) to the parent/guardian.

4.11.2 <u>At the Visit</u>

1. Collect the Child Medical Information Follow-Up Form (Form 68) and review with the parent/guardian.
2. Collect the Participant Information Form (Form 30). Retain the form at the clinic.
3. Collect the Physical Activity Assessment (Form 13) from the participant with a parent present.
4. Perform venipuncture on participant and record information on the DISC II Annual Visit Summary (Form 56). See Section 4.11.4 for details on volume, preparation, and labeling.
5. Perform height and weight measurements with participant in hospital gown and record on Revised Stature-Maturity Form (Form 29). Height measurements are to be taken by two

independent observers. The second observer should be blinded to the results of the first height measurement. (See Manual Section 10.3.1 for details.)

6. After a brief physical exam, assess participant's Tanner stage, measure testicular volume or areolar diameter. Ask girls about their menstrual history, birth control pill use, and information on pregnancy. Record the information on the Revised Stature - Maturity Form (Form 29).
7. For girls who have reached menarche, review Calendars (Form 64) for the preceding SIX consecutive full weeks (or parts of a week). Complete any calendars that have not been returned.
8. Administer a 24 hour dietary recall to the participant covering the previous day's food intake and record on the Dietary Recall/Record (Form 22).
9. Schedule times for two more 24 hour dietary recalls to be done by phone within two weeks of this visit.
10. Give the female parent/guardian of girls at menarche a set of DISC calendars (Form 64) to be completed for the six weeks following the visit or until the girl's next period whichever comes first.

4.11.3 Forms Used at the Visit

1. Form 13, Physical Activity Assessment
2. Form 29, Revised Stature-Maturity Form
3. Form 30, Participant Information Form (clinic use only)
4. Form 50, DISC Serum Shipment and Report Form (Lipids)
5. Form 54, Telephone Interview Form (Girls not yet returning Form 64)
6. Form 55, Serum Shipment Log (Hormones)
7. Form 56, DISC II Annual Visit Summary Form

8. Form 61, Central Lipoprotein Laboratory External Surveillance Form.

9. Form 62, Nutrition Coding Center External Surveillance Form.

10. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only)

11. Form 68, Child Medical Information Follow-up Form

4.11.4 Preparation of Blood Specimens

1. Collection (in order given below; vial designation on label given in brackets):

   a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)

   b. [10] 10 ml red top tube (lipids, lipoproteins, apoproteins, permanent storage)

   c. [15] 15 ml red-top tube (hormones)

2. Aliquots for shipping vials (in priority given below):

   a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

   b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU)

   c. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).

   d. [H1] 2 ml serum in 5 ml GSB for steroids (Hormone Study) (JHU).

   e. [H2] 2 ml serum in 5 ml GSB for bioavailable fractions (Hormone Study) (JHU).

   f. [H3] 1 ml serum in 2 ml GSB for SHBG (Hormone Study) (JHU).

   Do not discard excess serum. Include it in H1, and H2, and H3 aliquots.

3. Labels: Three for blood collection tubes, seven for shipping bottles/vials, and two for shipment logs.

4. Shipment Logs:

   a. Original of Form 50 to go with vials labeled LI, AP, and ST.

   b. Original of Form 55 to go with vials labeled H1, H2, and H3.

   c. Photocopies of Forms 50 and 55 retained at the clinic.

4.11.5 Duplicate Quality Control Samples for the Central Laboratory:

Collect an extra 25 ml of blood (15 ml and 10 ml red-top tube) from children (or two 15 ml and two 10 ml red top tubes from a fasting volunteer with total cholesterol in the 170-220 mg/dl range). Aliquot as in 4.11.4.2 above and label with assigned pseudo-ID number(s). Freeze samples with pseudo-ID numbers. Labels have been provided by the Coordinating Center for quality control purposes.

4.11.6 Time Windows for Completing the Year 5 Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the Year 5 (60 month) visit is plus or minus two months from the fifth anniversary of randomization. If the visits cannot be completed within two months of the anniversary date of randomization, an attempt should be made to reschedule the visit within six months of the anniversary date. Visits not made within this broader window will be labeled "missed".

4.11.7 After the Visit

1. Complete a Calendar Cover Sheet (Form 64) for each girl who has reached menarche and attach ALL completed calendars. Use a separate cover sheet for calendars to be used in the validation study.

2. For girls who have reached menarche, mail a Calendar (Form 64) to the girl for SIX consecutive weeks (or parts of a week) after the clinic visit.
3. Collect menses calendars as they are mailed back to the clinic. Seven weeks after the visit, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Calendar Cover Sheet (Form 64) for each girl and attach ALL calendars returned.
4. Complete for DISC II Annual Visit Summary (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.
5. Send frozen serum samples to the Central Laboratory along with originals of Forms 50 and 55.
6. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples. Complete Form 61 and send it to the Coordinating Center.
7. Administer two 24 hour dietary recalls to the child over the phone within two weeks of the visit.
8. Check physical exam and behavioral measures referral criteria and notify staff medical personnel, psychologist, or the child's parent/guardian when indicated. Record the referral and the reason for referral on the DISC II Annual Visit Summary (Form 56).
9. File Form 30, Participant Information Form, locally and update local database. Do not return Form 30 to the Coordinating Center.

4.12 Year 6 (72-Month) Follow-Up Visit (Revised 10/13/94)

4.12.1 Before the Visit

1. Make an appointment for the Year 6 visit.
2. Appointment reminder by telephone or letter to the parent/guardian.
3. Send the Participant Medical Information Follow-up Form (Form 68) to the parent/guardian.

4.12.2 At the Visit

1. Collect the Participant Medical Information Follow-up Form (Form 68) and review with the parent/guardian.
2. Collect the Participant Information Form (Form 30). Retain the form at the clinic.
3. Perform height and weight measurements with the participant in hospital gown and record on Revised Stature-Maturity Form (Form 29). Height should be measured by two independent observers. The second observer should be blinded to the measurements taken by the first observer. (See Manual Section 10.3.1 for details.)
4. After a brief physical exam, assess participant's Tanner stage, measure testicular volume or areolar diameter. Ask girls about their menstrual history, contraceptive medications, and information on pregnancy. Record the information on the Revised Stature-Maturity Form (Form 29).

4.12.3 Forms Used at the Visit

1. Form 29, Revised Stature - Maturity Form
2. Form 30, Participant Information Form (clinic use only)
3. Form 56, DISC II Annual Visit Summary Form
4. Form 68, Participant Medical History Follow-up Form

4.12.4 Time Windows for Completing the Year 6 (72-Month) Follow-up Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the Year 6 visit is plus or minus two months from the sixth anniversary of randomization. If the Year 6 visit cannot be completed within two months of the sixth anniversary date of randomization, an attempt should be made to reschedule it within six months of the sixth anniversary date. Visits not made within this broader window will be labeled "missed".

4.12.5 After the Visit

1. Complete the DISC II Annual Visit Summary Form (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.
2. Check clinical monitoring referral criteria (see Manual of Operations Chapter 26) and start a Clinical Monitoring Form 69 when indicated.
3. File the Participant Information Form (Form 30) locally and update your local database. Do not send the Form 30 to the Coordinating Center.

4.13 Year 7 (84 Months) Follow-up Visit

4.13.1 Before the Visit

1. Call the female parent/guardian of DISC girls not already returning DISC Calendar Form 64 (either because the girl had not reached menarche or the parent or girl refused to participate in menses data collection) EIGHT WEEKS BEFORE the visit and administer the Telephone Interview (Form 54). Send letters to mothers of girls who have previously completed calendars reminding them of the menstrual cycle data

collection process eight weeks before the scheduled visits. If parental consent has been obtained for a girl who has reached menarche, mail a DISC Calendar (Form 64) to the girl every week for the SIX consecutive full weeks before the visit. Collect all calendars mailed back for review at the clinic visit. Photocopy the Telephone Interview (Form 54) and mail the original to the Coordinating Center within one week of the last phone call.

2. Make an appointment for the visit.
3. Appointment reminder by telephone or letter to the parent/guardian. Include fasting instructions for the PARTICIPANT (no food or liquid, except prescribed medications or water, for 12 hours before venipuncture).
4. Send the Participant Medical Information Follow-up Form (Form 68) to the parent/guardian.
5. Send the Participant Information Form (Form 30) to the parent/guardian.

4.13.2 <u>At the Visit</u>

1. Collect the Participant Medical Information Follow-Up Form (Form 68) and review with the parent/guardian.
2. Collect the Participant Information Form (Form 30). Retain the form at the clinic.
3. Collect the Physical Activity Assessment (Form 13) from the participant.
4. Perform venipuncture on participant and record information on the DISC II Annual Visit Summary (Form 56). See Section 4.13.4 for details on volume, preparation, and labeling.
5. Perform height and weight measurements with participant in hospital gown and record on Revised Stature-Maturity Form

(Form 29). Height measurements are to be taken by two independent observers. The second observer should be blinded to the results of the first height measurement. (See Manual Section 10.3.1 for details.)

6. If the participant was not at Tanner Stage 5 at the last visit, assess participant's Tanner stage and measure testicular volume or areolar diameter. Ask girls about their menstrual history, contraceptive medications, and information on pregnancy. Record the information on the Revised Stature - Maturity Form (Form 29).
7. For girls who have reached menarche, review Calendars (Form 64) for the preceding SIX consecutive full weeks (or parts of a week). Complete any calendars that have not been returned.
8. Administer a 24 hour dietary recall to the participant covering the previous day's food intake and record on the Dietary Recall/Record (Form 22).
9. Schedule times for two more 24 hour dietary recalls to be done by phone within two weeks of this visit.
10. Give the female parent/guardian of girls at menarche a set of DISC calendars (Form 64) to be completed for the six weeks following the visit or until the girl's next period whichever comes first.

4.13.3 Forms Used at the Visit

1. Form 13, Physical Activity Assessment
2. Form 29, Revised Stature-Maturity Form
3. Form 30, Participant Information Form (clinic use only)
4. Form 50, DISC Serum Shipment and Report Form (Lipids)
5. Form 54, Telephone Interview Form (Girls not yet returning Form 64)

6. Form 55, Serum Shipment Log (Hormones)

7. Form 56, DISC II Annual Visit Summary Form

8. Form 60, Blood Spot Sample Shipment Log and Report Form (DNA Ancillary Study) One-time collection at an annual or final visit.

9. Form 61, Central Lipoprotein Laboratory External Surveillance Form.

10. Form 62, Nutrition Coding Center External Surveillance Form.

11. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only)

12. Form 68, Participant Medical Information Follow-up Form

4.13.4 Preparation of Blood Specimens

1. Collection (in order given below; vial designation on label given in brackets):

   a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)

   b. [10] 10 ml red top tube (lipids, lipoproteins, apoproteins, permanent storage)

   c. [15] 15 ml red-top tube (hormones)

   d. [5] 5 ml purple-top tube with EDTA (DNA blood spots) (JHU). One-time collection at an annual or final visit.

2. Aliquots for shipping vials (in priority given below):

   a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

   b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU)

   c. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).

   d. [Hl] 5 ml serum in 10 ml GSB for hormone analyses (Hormone Study) (JHU).

Do not discard excess serum. Include it in the H1 aliquot.

e. [DN] Four whole blood spots (about 20 drops) on filter paper for DNA analyses (DNA Ancillary Study) (JHU).

3. Labels: Maximum of four for blood collection tubes, six for shipping bottles/vials/bags, and three for shipment logs.

4. Shipment Logs:

a. Original of Form 50 to go with vials labeled LI, AP, and ST.

b. Original of Form 55 to go with vials labeled H1.

c. Original of Form 60 to go with DNA blood spot samples labeled DN. (One-time collection at an annual or final visit.)

d. Photocopies of Forms 50, 55, and 60 retained at the clinic.

4.13.5 Duplicate Quality Control Samples for the Central Laboratory: Collect an extra 25 ml of blood (15 ml and 10 ml red-top tube) from children (or two 15 ml and two 10 ml red-top tubes from a fasting volunteer with total cholesterol in the 170-220 mg/dl range). Aliquot as in 4.13.4.2 above and label with assigned pseudo-ID number(s). Freeze samples with pseudo-ID numbers. Labels have been provided by the Coordinating Center for quality control purposes.

4.13.6 Time Windows for Completing the Year 7 Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the Year 7 (84 month) visit is plus or minus two months from the seventh anniversary of randomization. If the visits cannot be

completed within two months of the anniversary date of randomization, an attempt should be made to reschedule the visit within six months of the anniversary date. Visits not made within this broader window will be labeled "missed".

If a participant's 18th birthday is within 2 months 0 days before and 3 months 29 days after the Year 7 visit, perform the FV01 final visit instead of the Year 7 visit. If a participant's 18th birthday is between 4 months 0 days and 10 months 0 days after the Year 7 visit, then perform the Year 7 visit as usual and perform the FV01 final visit within the appropriate time window for the FV01 final visit. After the FV02 final visit is performed, no other visits will be necessary.

4.13.7 <u>After the Visit</u>

1. Complete a Calendar Cover Sheet (Form 64) for each girl who has reached menarche and attach ALL completed calendars. Use a separate cover sheet for calendars to be used in the validation study.
2. For girls who have reached menarche, mail a Calendar (Form 64) to the girl for SIX consecutive weeks (or parts of a week) after the clinic visit.
3. Collect menses calendars as they are mailed back to the clinic. Seven weeks after the visit, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Calendar Cover Sheet (Form 64) for each girl and attach ALL calendars returned.
4. Complete the DISC II Annual Visit Summary (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.

5. Send frozen serum samples to the Central Laboratory along with originals of Forms 50 and 55.
6. Send blood spot samples to the Central Laboratory along with the original of Form 60. (One-time collection at an annual or final visit.)
7. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples. Complete Form 61 and send it to the Coordinating Center.
8. Administer two 24 hour dietary recalls to the child over the phone within two weeks of the visit.
9. Check physical exam and behavioral measures referral criteria (See Manual of Operations Chapter 26) and start a Clinical Monitoring Form 69 when indicated. Record the referral and the reason for referral on the DISC II Annual Visit Summary (Form 56).
10. File Form 30, Participant Information Form, locally and update local database. Do not return Form 30 to the Coordinating Center.

4.14 Year 8 (96-Month) Follow-Up Visit (10/13/94)

4.14.1 Before the Visit

1. Make an appointment for the visit.
2. Appointment reminder by telephone or letter to the participant and parent/guardian.
3. Send the Participant Medical Information Follow-up Form (Form 68) to the parent/guardian.

4.14.2 At the Visit

1. Collect the Participant Medical Information Follow-up Form (Form 68) and review with the parent/guardian.
2. Collect the Participant Information Form (Form 30). Retain the form at the clinic.
3. Perform height and weight measurements with the participant in hospital gown and record on Revised Stature-Maturity Form (Form 29). Height should be measured by two independent observers. The second observer should be blinded to the measurements taken by the first observer. (See Manual Section 10.3.1 for details.)
4. If the participant had not reached Tanner stage 5 at the last visit, assess the participant's Tanner stage and measure testicular volume or areolar diameter. Ask girls about their menstrual history, contraceptive medications, and information on pregnancy. Record the information on the Revised Stature-Maturity Form (Form 29).

4.14.3 Forms Used at the Visit

1. Form 29, Revised Stature - Maturity Form
2. Form 30, Participant Information Form (clinic use only)
3. Form 56, DISC II Annual Visit Summary Form
4. Form 68, Participant Medical History Follow-up Form

4.14.4 Time Window for Completing the Year 8 (96-Month) Follow-up Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the Year 8 visit is plus or minus two months from the eighth anniversary of randomization. If the Year 8 visit cannot be completed within two months of the eighth anniversary date of

randomization, an attempt should be made to reschedule it within six months of the eighth anniversary date. Year 8 visits not made within these broader windows will be labeled "missed".

If a participant's 18th birthday is within 2 months 0 days before and 3 months 29 days after the Year 8 visit, perform the FV01 final visit instead of the Year 8 visit. If a participant's 18th birthday is between 4 months 0 days and 10 months 0 days after the Year 8 visit, then perform the Year 8 visit as usual and perform the FV01 final visit within the appropriate time window for the FV01 final visit. After the FV02 final visit is performed, no other visits will be necessary.

4.14.5 After the Visit

1. Complete the DISC II Annual Visit Summary Form (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.
2. Check clinical monitoring referral criteria (see Manual of Operations Chapter 26) and start a Clinical Monitoring Form 69 when indicated.
3. File the Participant Information Form (Form 30) locally and update your local database. Do not send the Form 30 to the Coordinating Center.

4.15 Year 9 (108 Months) Follow-up Visit (11/10/94)

4.15.1 Before the Visit

1. Call the female parent/guardian of DISC girls not already returning DISC Calendar Form 64 (either because the girl had not reached menarche or the parent or girl refused to participate in menses data collection) EIGHT WEEKS BEFORE the visit and administer the Telephone Interview (Form 54). Send

letters to mothers of girls who have previously completed calendars reminding them of the menstrual cycle data collection process eight weeks before the scheduled visits. If parental consent has been obtained for a girl who has reached menarche, mail a DISC Calendar (Form 64) to the girl every week for the SIX consecutive full weeks before the visit. Collect all calendars mailed back for review at the clinic visit. Photocopy the Telephone Interview (Form 54) and mail the original to the Coordinating Center within one week of the last phone call.

2. Make an appointment for the visit.
3. Appointment reminder by telephone or letter to the parent/guardian. Include fasting instructions for the PARTICIPANT (no food or liquid, except prescribed medications or water, for 12 hours before venipuncture).
4. Send the Participant Medical Information Follow-up Form (Form 68) to the parent/guardian.
5. Send the Participant Information Form (Form 30) to the parent/guardian.

4.15.2 <u>At the Visit</u>

1. Collect the Participant Medical Information Follow-Up Form (Form 68) and review with the parent/guardian.
2. Collect the Participant Information Form (Form 30). Retain the form at the clinic.
3. Collect the Physical Activity Assessment (Form 13) from the participant.
4. Perform venipuncture on participant and record information on the DISC II Annual Visit Summary (Form 56). See Section 4.15.4 for details on volume, preparation, and labeling.

5. Perform height and weight measurements with participant in hospital gown and record on Revised Stature-Maturity Form (Form 29). Height measurements are to be taken by two independent observers. The second observer should be blinded to the results of the first height measurement. (See Manual Section 10.3.1 for details.)
6. If the participant was not at Tanner Stage 5 at the last visit, assess the participant's Tanner stage and measure testicular volume or areolar diameter. Ask girls about their menstrual history, contraceptive medications, and information on pregnancy. Record the information on the Revised Stature - Maturity Form (Form 29).
7. For girls who have reached menarche, review Calendars (Form 64) for the preceding SIX consecutive full weeks (or parts of a week). Complete any calendars that have not been returned.
8. Administer a 24 hour dietary recall to the participant covering the previous day's food intake and record on the Dietary Recall/Record (Form 22).
9. Schedule times for two more 24 hour dietary recalls to be done by phone within two weeks of this visit.
10. Give the female parent/guardian of girls at menarche a set of DISC calendars (Form 64) to be completed for the six weeks following the visit or until the girl's next period whichever comes first.

4.15.3 Forms Used at the Visit

1. Form 13, Physical Activity Assessment
2. Form 29, Revised Stature-Maturity Form
3. Form 30, Participant Information Form (clinic use only)
4. Form 50, DISC Serum Shipment and Report Form (Lipids)

5. Form 54, Telephone Interview Form (Girls not yet returning Form 64)
6. Form 55, Serum Shipment Log (Hormones)
7. Form 56, DISC II Annual Visit Summary Form
8. Form 61, Central Lipoprotein Laboratory External Surveillance Form.
9. Form 60, Blood Spot Sample Shipment Log and Report Form (DNA Ancillary Study). One-time collection at an annual or final visit.
10. Form 62, Nutrition Coding Center External Surveillance Form.
11. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls who have reached menarche only)
12. Form 68, Participant Medical Information Follow-up Form

4.15.4 Preparation of Blood Specimens

1. Collection (in order given below; vial designation on label given in brackets):
   a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)
   b. [10] 10 ml red top tube (lipids, lipoproteins, apoproteins, permanent storage)
   c. [15] 15 ml red-top tube (hormones)
   d. [5] 5 ml purple-top tube with EDTA (DNA blood spots) One-time collection at an annual or final visit.
2. Aliquots for shipping vials (in priority given below):
   a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).
   b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU)
   c. [ST] Two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).
   d. [H1] 5 ml serum in 10 ml GSB for hormone analyses (Hormone Study) (JHU).

Do not discard excess serum. Include it in the H1 aliquot.

e. [DN] Four whole blood spots (about 20 drops) on filter paper for DNA analyses. (DNA Ancillary study.) (JHU) One-time collection at an annual or final visit.

3. Labels: Maximum of four for blood collection tubes, six for shipping bottles/vials/bags, and three for shipment logs.

4. Shipment Logs:

a. Original of Form 50 to go with vials labeled LI, AP, and ST.

b. Original of Form 55 to go with vials labeled H1.

c. Original of Form 60 to go with DNA blood spot sample labeled DN. (One-time collection at an annual or final visit.)

d. Photocopies of Forms 50, 55, and 60 retained at the clinic.

4.15.5 Duplicate Quality Control Samples for the Central Laboratory:

Collect an extra 25 ml of blood (15 ml and 10 ml red-top tube) from children (or two 15 ml and two 10 ml red-top tubes from a fasting volunteer with total cholesterol in the 170-220 mg/dl range). Aliquot as in 4.15.4.2 above and label with assigned pseudo-ID number(s). Freeze samples with pseudo-ID numbers. Labels have been provided by the Coordinating Center for quality control purposes.

4.15.6 Time Windows for Completing the Year 9 (108 month) Follow-Up Visit

Windows for the follow-up visits are timed in relation to each participant's randomization date. The acceptable time window for the Year 9 (108 month) visit is plus or minus two months from the

ninth anniversary of randomization. If the visits cannot be completed within two months of the anniversary date of randomization, an attempt should be made to reschedule the visit within six months of the anniversary date. Visits not made within this broader window will be labeled "missed".

If a participant's 18th birthday is within 2 months 0 days before and 3 months 29 days after the Year 9 visit, perform the FV01 final visit instead of the Year 9 visit. If a participant's 18th birthday is between 4 months 0 days and 10 months 0 days after the Year 9 visit, then perform the Year 9 visit as usual and perform the FV01 final visit within the appropriate time window for the FV01 final visit. After the FV02 final visit is performed, no other visits will be necessary.

4.15.7 <u>After the Visit</u>

1. Complete a Calendar Cover Sheet (Form 64) for each girl who has reached menarche and attach ALL completed calendars. Use a separate cover sheet for calendars to be used in the validation study.
2. For girls who have reached menarche, mail a Calendar (Form 64) to the girl for SIX consecutive weeks (or parts of a week) after the clinic visit.
3. Collect menses calendars as they are mailed back to the clinic. Seven weeks after the visit, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Calendar Cover Sheet (Form 64) for each girl and attach ALL calendars returned.
4. Complete the DISC II Annual Visit Summary (Form 56). Copy forms completed for the visit, and send originals to the Coordinating Center.

5. Send frozen serum samples to the Central Laboratory along with originals of Forms 50 and 55.
6. Send blood spot samples to the Central Laboratory along with the original of Form 60. (One-time collection at an annual or final visit.)
7. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples. Complete Form 61 and send it to the Coordinating Center.
8. Administer two 24 hour dietary recalls to the child over the phone within two weeks of the visit.
9. Check physical exam and behavioral measures referral criteria (See Manual of Operations Chapter 26) and start a Clinical Monitoring Form 69 when indicated. Record the referral and the reason for referral on the DISC II Annual Visit Summary (Form 56).
10. File Form 30, Participant Information Form, locally and update local database. Do not return Form 30 to the Coordinating Center.

4.16 Final Visit 01 (Revised 10/13/94)

4.16.1 Before the Visit

1. Call the female parent/guardian of DISC girls not already returning DISC Calendar Form 64 (either because the girl had not reached menarche or the parent or girl refused to participate in menses data collection) EIGHT WEEKS BEFORE the visit and administer the Telephone Interview (Form 54). Send letters to mothers of girls who have previously completed calendars reminding them of the menstrual cycle data

collection process eight weeks before the scheduled visits. If parental consent has been obtained, mail a Form 64 DISC menses calendar to the girl every week for the SIX consecutive full weeks before the FV01 visit. Collect all calendars mailed back for review at the FV01 visit.

2. Make an appointment for the final visit 01.
3. Appointment reminder by telephone or letter to the participant and parent/guardian. Include fasting instructions for the PARTICIPANT (no food or liquid, except prescribed medications or water, for 12 hours before the venipuncture). Remind the parent or participant to bring all medications and a copy of the participant's birth certificate (to document birth weight) to the visit.
4. Send Final Visit 01 Medical Information Follow-up Form (Form 78) to the parent/guardian.

4.16.2 <u>At the Visit</u>

1. <u>For the DISC Participant:</u>
   a. Perform venipuncture on participant and record information on the Final Visit 01 Summary (Form 71). See Section 4.16.4 for details on volume, preparation, and labeling.
   b. Measure participant's blood pressure and record results on Blood Pressure Form (Form 05).
   c. Perform anthropometric measurements (i.e. height, weight, girths, and skinfolds) with participant in hospital gown, and record on Final Visit 01 Physical Exam Form (Form 72). Height should be measured by two independent observers. The second observer should be blinded to the

measurements taken by the first. (See Manual Section 10.3.1 for details).

d. Perform physical exam on participant (optional). Assess participant's Tanner stage if participant was less than Tanner stage 5 at the last visit. Measure testicular volume or areolar diameter. Ask girls about their menstrual history, contraceptive use, and information on pregnancy. Record information on Final Visit 01 Physical Exam Form (Form 72).

e. For girls, review Calendars (Form 64) for the preceding six consecutive full weeks. Complete any Calendars that have not been returned.

f. Administer Participant History Form (Form 67) to the participant when the parents are not present.

g. Administer a 24-hour dietary recall to the participant covering the previous day's food intake and record on the Dietary Recall/Record (Form 22).

h. Schedule times for two more 24-hour dietary recalls to be done by phone within two weeks of the FV01 visit.

i. Administer the Physical Activity Assessment (Form 13) to the participant.

j. Administer the psychosocial battery (Forms 32, 73, 76 and 77 to the participant. Remember to administer the Woodcock-Johnson Math and Reading Tests early in the visit before the participant becomes fatigued.

k. Administer the Confidence Rating Form I (Form 79) to all participants.

l. Schedule a visit to draw a second blood specimen on the participant at FV02.

2. For the Parent/Guardian(s):

   a. Collect Final Visit 01 Medical Information Follow-up Form (Form 78) and review with the parent/guardian(s).

   b. Administer Achenbach Child Behavior Checklist (Form 31) to parent/guardian(s). If only one parent is present, an attempt should be made to schedule the other parent/guardian to complete the Achenbach at a convenient time.

   c. Administer the Family Environment Form (Form 35) to both parents if present.

   d. Administer the Participant Information Form (Form 30) to at least one parent/guardian. Retain the form at the clinic.

   e. Give or send female parent/guardians of girls a set of DISC Calendars (Form 64) for ALL of the weeks (or parts of a week) until the girl's FV02 visit.

4.16.3 Forms Used at the FV01 Visit

1. Form 05, Blood Pressure Form (Participant)
2. Form 13, Physical Activity Assessment Form
3. Form 30, Participant Information Form
4. Form 31, Achenbach CBCL
5. Form 32, Woodcock-Johnson Math and Reading Clusters
6. Form 35, Family Environment Form
7. Form 50, DISC Serum Shipment and Report Form (Lipids)
8. Form 51, Serum Shipment Log and Report Form (CDC)
9. Form 54, Telephone Interview
10. Form 55, Serum Shipment Log (Hormones)
11. Form 60, Blood Spot Sample Shipment Log and Report Form (DNA Ancillary Study) If not collected at an annual visit.

12. Form 61, Central Lipoprotein Laboratory External Surveillance Form
13. Form 62, Nutrition Coding Center External Surveillance Form
14. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls)
15. Form 67, Participant History Form
16. Form 71, Final Visit 01 Summary
17. Form 72, Final Visit 01 Physical Exam Form
18. Form 73, Youth Self-Report Form
19. Form 76, Beck Form
20. Form 77, Self-Evaluation Form
21. Form 78, Final Visit 01 Medical Information Follow-up Form
22. Form 79, Confidence Rating Form I

4.16.4 Preparation of Blood Specimens

1. Collection for participants (in order given below; vial designation on label given in brackets):
    (1) [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage)
    (2) [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins, permanent storage and non-lipids)
    (3) [BL] 7 ml royal blue-top (zinc and copper)
    (4) [PR] 2 ml purple-top tube with EDTA (CBC, red cell folate)
    (5) [15] 15 ml red-top tube (hormones)
    (6) [5] 5 ml purple-top tube with EDTA (DNA blood spots) If not collected at an annual visit.
2. Aliquots for shipping vials or samples for participants (in priority given below):
    (1) [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

(2) [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

(3) [FE] 1 ml serum in plastic vial (PV) for ferritin (CDC).

(4) [FO] 0.1 ml whole blood plus 1 ml of a 1 gm/dl solution ascorbic acid in PV for red cell folate -- from purple-top tube (CDC).

(5) [ZN] 2 ml serum in PV for zinc and copper -- from royal blue-top collection tube (CDC).

(6) [VA] 1 ml serum in PV for vitamin A, tocopherol, and carotenoids (CDC).

(7) [CB] 0.5 ml whole blood for CBC from 2 ml purple-top tube (local laboratory).

(8) [ST] two 0.5 ml aliquots of serum in 2 ml GSBs for long term storage (JHU).

(9) [H1] 5 ml serum in 10 ml GSB for hormone analyses (Hormone Study) (JHU).

Do not discard excess serum. Include it in the H1 aliquot.

(10) [DN] Four whole blood spots (about 20 drops) on filter paper from 5 ml purple-top tube (DNA Study) (JHU). If not collected at an annual visit.

c. Labels: Maximum of six for blood collection tubes, 12 for shipping bottles/vials/bags, one for sample CBC locally and four for shipment logs.

3. Shipment Logs for Participants and Parents:

a. Original of Form 50 to go with vials labeled LI, AP, ST.

b. Original of Form 60 to go with blood spot samples labeled DN. (If not collected at an annual visit.)

c. Original of Form 51 to go with vials labeled FE, ZN, FO, and VA.

d. Original of Form 55 to go with vials labeled H1.

e. Photocopies of Forms 50, 51, 55, and 60 retained at the clinic.

4. Duplicate Quality Control Samples for the Central Laboratory: Collect an extra 25 ml of blood in 15 ml and 10 ml red-top tubes from participants (or two 15 ml and two 10 ml red top tubes from a fasting volunteer with total cholesterol in the 170-220 mg/dl range). Aliquot as in 4.16.4.2 above and label with assigned pseudo-ID number(s). Freeze samples with pseudo-ID numbers. Labels have been provided by the Coordinating Center for quality control purposes.

4.16.5 Time Windows for Completing the Final Visit 01

Windows for the final visit 01 are timed in relation to each participant's 18th birthday. The acceptable time window for the Final Visit 01 is 2 months before and 2 months after the participant's 18th birthday. If the final visit 01 cannot be completed within the time window, an attempt should be made to reschedule it within six months of the participant's 18th birthday.

For the final visit 01, if the participant cannot be seen within the visit window, the final visit 01 information should be obtained at any time the participant is seen subsequent to the missed visit. Under these circumstances, the Coordinating Center should be contacted as to the appropriate forms to use.

4.16.6 After the Visit

1. Complete a Form 64 Calendar Cover Sheet for each girl and attach ALL completed calendars. Use a separate cover sheet for Calendars to be used in the validation study.
2. For girls, mail a Form 64 Calendar for each of the consecutive weeks (or parts of a week) between the FV01 and FV02 visits. Collect all Calendars mailed back for review at the FV02 visit.
3. Complete the Final Visit 01 Summary (Form 71). Copy forms completed for the visit, and send originals to the Coordinating Center.
4. Prepare duplicate aliquots of serum as required by the Central Lipoprotein Laboratory Surveillance Procedures described in Section 4.16.4-4.
5. Send frozen serum/plasma samples to the Central Laboratory along with two copies of Form 50 and the originals of Forms 51 and 55.
6. Send blood spot samples to the Central Laboratory along with the original of Form 60. (If not sent at an annual visit.)
7. Send serum samples with pseudo-ID numbers to the Central Laboratory about one week after primary samples have been sent. Use the same shipping procedures as used with primary samples. Complete Form 61 and send it to the Coordinating Center.
8. Administer two 24-hour dietary recalls to the participant over the phone within two weeks of the FV01 visit.
9. Hand copy duplicates of 24-hour recalls gathered at the FV01 visit for designated ID numbers as required by the NCC External Surveillance Procedures. Assign a pseudo-ID to the

duplicate recall and send it to the NCC at least one month after the original record has been sent. Complete the Form 62 and send it to the Coordinating Center.

10. Score Form 31, the Achenbach test booklet, using your PC scoring diskette. Send the original test booklet to the Coordinating Center.
11. Check physical exam and behavioral measures clinical monitoring criteria and start a Clinical Monitoring Form 69 when indicated.

4.17 Final Visit 02

4.17.1 Before the Visit

1. If parental consent has been obtained for girls, mail a Form 64 DISC Calendar to the girl every week for each consecutive week or part of a week between the FV01 and FV02 visits. Collect all Calendars mailed back for review at the FV02 visit.
2. If the Form 78, Final Visit 01 Medical Information Follow-up was not collected at FV01, mail another copy to the parent.
3. Make an appointment for the FV02 visit.
4. Appointment reminder by telephone or letter to the participant and parent/guardian. Include fasting instructions for the participant (no food or liquid, except prescribed medications or water, for 12 hours before the venipuncture). Remind the participant or parent to bring all medications to the FV02 visit.

4.17.2 At the Visit

1. Perform venipuncture on participant and record information on Form 74. See Section 4.17.4 for details on volume, preparation and labeling.
2. Administer Form 74 questions on medications to all children. Administer additional Form 74 questions on menstruation, contraceptive medications, and pregnancy to girls.
3. If the Form 13, Physical Activity Assessment, was not collected at FV01, administer it to the participant.
4. For girls, review Form 64 Calendars for the preceding six consecutive full weeks or parts of a week. Complete any calendars that have not been returned.
5. Give the female parent/guardian of girls a set of DISC Calendars (Form 64) for all of the weeks or parts of a week until the six week anniversary date of the FV02 visit (FV03).

4.17.3 Forms Used at the FV02 Visit

1. Form 50, DISC Serum Shipment and Report Form (Lipids).
2. Form 55, Serum Shipment Log (Hormones).
3. Form 60, Blood Spot Sample Shipment Log and Report Form (DNA Ancillary Study) If not collected at an annual visit or FV01.
4. Form 64, DISC Calendar Cover Sheet and DISC Calendars (Girls)
5. Form 74, Final Visit 02 Summary

4.17.4 Preparation of Blood Specimens

1. Collection for participants (in the order given below; vial designation on label given in brackets):
   a. [15] 15 ml red-top tube (lipids, lipoproteins, apoproteins)

b. [10] 10 ml red-top tube (lipids, lipoproteins, apoproteins)

c. [15] 15 ml red-top tube (hormones)

d. [5] 5 ml purple-top tube with EDTA (DNA blood spots) If not collected at an annual visit or FV01.

2. Aliquots for shipping vials/bags for participants (in priority given below):

a. [LI] 5 ml serum in GSB for lipids/lipoproteins (JHU).

b. [AP] 0.5 ml serum in 2 ml GSB for apoproteins (JHU).

c. [H1] 5 ml serum in 10 ml GSB for hormone analyses (Hormone Study) (JHU).

Do not discard excess serum. Include it in the H1 aliquot.

e. [DN] Four whole blood spots (about 20 drops) on filter paper from 5 ml purple-top tube for DNA analyses. (DNA Ancillary Study) (JHU) If not collected at an annual visit or at FV01.

3. Labels: Maximum of four for blood collections tubes, five for shipping bottles/vials/bags, and three for shipment logs.

4. Shipment Logs for Child:

a. Original of Form 50 to go with vials labeled LI and AP.

b. Original of Form 55 to go with vials labeled H1.

c. Original of Form 60 to go with blood spot samples labeled DN. (If not collected at an annual visit or FV01.)

d. Photocopies of Forms 50, 55, and 60 retained at the clinic.

4.17.5 Time Windows for Completing the Final Visit 02

The window for the FV02 follow-up visit is timed in relation to the date of the FV01 visit. The acceptable time window for the

FV02 visit is no sooner than one week before or later than two weeks after the one month anniversary of the FV01 visit (i.e., 3-6 weeks after the FV01 visit).

If the FV02 visit cannot be completed within this window, an attempt should be made to reschedule it for no later than one month after the one month anniversary of the FV01 visit (i.e. 3-8 weeks after the FV01 visit). Visits not made within this broader window will be labeled "missed".

4.17.6 <u>After the Visit</u>

1. Complete a Form 64 Calendar Cover Sheet for each girl and attach ALL completed calendars. Use a separate cover sheet for Calendars to be used in the validation study.
2. For girls, mail a Form 64 Calendar for each of the consecutive weeks (or parts of a week) between the FV02 and the FV03 date.
3. Collect FV03 menses calendars as they are mailed back to the clinic. One week after the FV03 date, review the calendars returned for completeness. Follow-up missing or unclear information by phone. Complete a Form 64 Cover Sheet for each girl and attach ALL calendars returned.
4. Complete the Final Visit 02 Summary Form 74. Photocopy forms completed for the visit, and send originals to the Coordinating Center.
5. Send frozen serum samples to the Central Laboratory along with two copies of Form 50 and the original of Form 55.
6. Send blood spot samples to the Central Laboratory along with the original of Form 60. (If not sent at an annual visit or FV01.)