

**COGA:
COLLABORATIVE STUDY ON THE
GENETICS OF ALCOHOLISM**

ASCERTAINMENT PROCEDURES

06/16/2000

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DEFINITIONS

3+: Means three or more.

18+ years old: Means eighteen years old and older. (similarly, "13+" means 13 years old and older.)

AFFECTED: For all individuals (except if otherwise noted), the word "affected" indicates:

- (a) affected with Alcohol Dependence by DSM-III-R **and** Alcoholism at the Definite level by Feighner by personal interview with SSAGA-I or SSAGA-II, OR
- (b) when a SSAGA diagnosis is not available (e.g., due to refusal, death, or an incomplete interview), affected by FHAM implications* with Alcohol Dependence by DSM-III-R **and** Alcoholism at the Definite level by Feighner, OR
- (c) when a SSAGA diagnosis is not available, affected with DSM-III-R Alcohol Dependence **and** Feighner Alcoholism--Definite based on medical records, OR
- (d) when a negative diagnosis by a SSAGA is overruled based on FHAM implications* and/or information from medical records, affected by a consensus diagnosis of DSM-III-R Alcohol Dependence **and** Feighner Alcoholism--Definite (see consensus procedure on page 12).

An individual who meets criteria for being affected in only one of the two phases is considered affected.

* The Ascertainment Committee defined the threshold for being affected by Family History (FHAM) as three implications for **both** DSM-III-R Alcohol Dependence **and** Feighner at the Definite level, without any restrictions on the relationship of the individual (implicator) to the implicatee.

BILINEALITY:

Overt: We consider a branch overtly bilineal if both parents are affected. Before December 1996, we did not recruit the offspring of overtly bilineal matings (except for obtaining the Stage I protocol on the offspring of the Proband). However, in December 1996, we started including bilineal branches in both Phase I and Phase II ascertainment. Note that overt bilineality can still prevent a Phase I:Stage I family from progressing to Phase I:Stage II (see Stage II criteria on page 6, which indicate that the three affecteds must not be offspring of bilineal matings). However, once a Phase I:Stage I family meets the Stage II criteria, all the branches of affecteds (regardless of bilineality) are to be pursued (see pages 6-7).

Non-overt: Non-overt bilineality includes all other combinations of affectation found on both sides of a mating. For example, the following family can be considered non-overtly bilineal: mother is affected, father is unaffected, paternal uncle is affected, and paternal grandmother is affected. We do not exclude the offspring of non-overt bilineal matings.

DOMESTIC PARTNER: All references to a domestic partner in this document refer to a partner of the opposite sex with whom the subject has been cohabitating for at least six months.

PROXY INTERVIEWS: When a subject is unable to be interviewed for medical reasons (e.g., due to a developmental disability, Korsakoff's syndrome, alcohol-induced psychosis, alcohol-related dementia, a head injury, or Alzheimer's disease), an interview can be conducted by proxy. In such a case, the site administers the interview to a reliable source such as a sibling, partner, adult offspring, or parent of the individual, who would respond as if s/he were the individual. At no other time is an interview done by proxy (e.g., for subjects who are deceased, who have refused, or who cannot be located). If the protocol indicates that blood is needed, the site should try to obtain blood samples from the individual only if a court-appointed surrogate gives consent (the consent of just any relative or friend is not sufficient).

PHASE I: STAGE 0

SCREENING: COGA recruits patients who are currently in a psychiatric inpatient or outpatient program for alcohol and/or chemical dependency. Detoxification must be complete before approaching the individual. (Items 1 and 2 may be administered in any order. Family structure and availability may be determined first if the site chooses to do so.)

1. **DSM-III-R/FEIGHNER SCREENER:** The interviewer scores the DSM-III-R/ Feighner Screener as it is being administered. To qualify, the potential proband must meet **both** DSM-III-R Alcohol Dependence and Feighner Alcoholism at the Definite level.

2. **SUBJECT SCREENING FORM:** The Subject Screening Form determines whether the potential proband's family structure qualifies. The following requirements must be met before s/he is invited to participate:
 - A. A potential proband must not have used intravenous drugs more than 30 times lifetime and not within six months of screening.

 - B. A potential proband must not have any life-threatening illness other than alcohol-related terminal illnesses such as cirrhosis or Korsakoff's.

 - C. A potential proband must not be infected with the HIV virus.
(At the SUNY COGA site, a potential proband must also not have TB.)

 - D. A potential proband and his/her first-degree relatives must speak English.

 - E. A potential proband must live within one of the following six COGA catchment areas:
 - 1) CONNECTICUT: All of New England, except northern Maine
 - 2) INDIANA: 150 mile radius around Indianapolis
 - 3) IOWA: 150 mile radius around Iowa City
 - 4) NEW YORK: 150 mile radius around New York City
 - 5) ST. LOUIS: 150 mile radius around St. Louis
 - 6) SAN DIEGO: 150 mile radius around San Diego

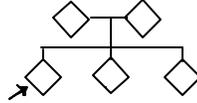
 - F. A potential proband must have at least two first-degree relatives aged 18 or older (13 or older at the SUNY COGA site) living in one of the COGA catchment areas. These relatives may, but are not required to, belong to the nuclear family that enabled entrance into COGA (see point G).

G. A potential proband must have one of the following family structures:

(Arrow points to the potential proband.)

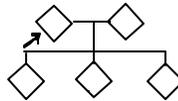
1) Two living parents and at least two living full siblings aged 18 or older*.

For example:



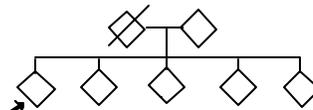
2) At least three living offspring aged 18 or older* by the same living partner.

For example:



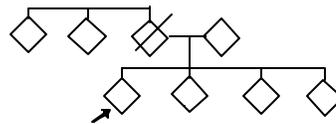
3) One living parent and at least four living full siblings aged 18 or older*.

For example:



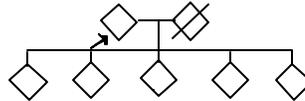
4) One living parent and at least three living full siblings aged 18 or older* **and** at least two additional living first-degree relatives of the deceased parent.

For example:



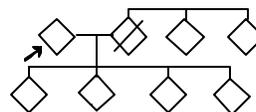
5) At least five living offspring aged 18 or older* by same deceased partner.

For example:



6) At least four living offspring aged 18 or older* by same deceased partner **and** at least two additional first-degree relatives of the deceased partner.

For example:



* Across all family structures, the SUNY COGA site is recruiting families with children/siblings aged 13 and older, rather than 18 and older. For the IRPG protocol, all sites will recruit families with children/siblings aged 13 and older.

H. The potential proband must consent to participate, which includes consent to be interviewed, consent for the release of medical records, and consent for the staff to contact other family members. All sites, except the St. Louis COGA site, require that at least two first-degree relatives also agree to participate before a family is invited.

If the above requirements are met, the potential proband is invited to participate in the study, consent is obtained, the SSAGA-I is administered (either self or proxy), and the individual becomes a Proband. If the Proband is affected by both DSM-III-R (Dependence) and Feighner (Alcoholism -- Definite level), his/her family becomes a Stage I family. If the Proband is not affected by both DSM-III-R and Feighner, or the site discovers that the family structure does not meet the Stage 0 requirements, the family becomes a Pilot family. The decision to pursue or discontinue a Pilot family is at the discretion of the site Principal Investigator.

PHASE I RECRUITMENT OF MINORITY POPULATIONS

In December of 1996, COGA limited Phase I recruitment to a few minority populations, including only potential probands who met the Stage 0 requirements described above and who are also members of the following groups:

- C men and women of African-American, African-Caribbean, and African descent
- C men and women of Hispanic or Latino ethnicity (which may include, but is not limited to, being of Puerto Rican, Mexican, Cuban, Central American, South American, and/or Spanish descent)
- C Caucasian women who have a family that is likely to meet the Phase I:Stage II criteria. (To determine if their families may be good candidates for Stage II, the Caucasian female potential probands are asked during screening if any of their first degree relatives have had problems with alcohol.)

We recruit the Phase I African-American and Hispanic/Latino families the standard way we have recruited throughout Phase I, that is, inviting all who qualify, even if they do not seem to be good candidates for Stage II. These families are designated Stage I, II, III, and IV, as applicable. However, because we “accelerate” the recruitment of Caucasian women by recruiting only those families that will most likely meet Stage II criteria, the accelerated families are designated Stage A-I, A-II, A-III, and A-IV as applicable. Stage A-I families are assessed with the Standard Protocol for Stage I (see page 5), and Stage A-II families are assessed with the Standard Protocol for Stage II (see page 6). Families of African-American and Hispanic/Latino female probands will not be accelerated.

PHASE I: STAGE I

A family becomes Stage I if they met the Stage 0 criteria and the Proband's SSAGA diagnosis is affected by both DSM-III-R (Alcohol Dependence) and Feighner (Alcoholism at the Definite level).

Standard Stage I Protocol: Standard Stage I protocol should be administered to (a) the Proband; (b) the Proband's first-degree relatives aged 7 and older (i.e., offspring, full siblings, and parents); and (c) the Proband's mate(s) with whom s/he produced offspring. If the Proband has not produced offspring with his/her current spouse or domestic partner and the female partner is under age 45 (i.e., is still of child-bearing age), then also recruit this spouse/domestic partner.

- 1) SSAGA (Adult interview administered to ages 18+) OR
CSSAGA-C (Child interview administered to ages 7-12) OR
CSSAGA-A (Adolescent interview administered to ages 13-17) and
CSSAGA-P (Parent interview, administered to a parent of children aged 7-17,
whether or not the child/children is/are able to be interviewed)
- 2) Tridimensional Personality Questionnaire (TPQ), administered to ages 18+.
(The Indiana and St. Louis COGA sites use the TCI instead.)
- 3) Sensation Seeking Scale-V (SSS-V), administered to ages 18+
- 4) Family History Assessment Module (FHAM), which includes updating the pedigree
and administering the Individual Assessment Module (IAM), the FHAM worksheets,
and the Tobacco FHAM, administered to ages 18+. (The St. Louis COGA site also
administers Dr. Van Eerdewegh's FHAM addendum.)
- 5) Pedigree Structure Form (PSF), administered to the Proband and his/her mate(s), or
to a knowledgeable informant.

Stage I Special Extension Protocol: In addition to the standard Stage I protocol described above, we administer the following Stage I Special Extension protocol to the branches of the Proband's siblings and offspring who are **affected** by SSAGA **and** who have one or more interviewable children aged 7-17:

- 1) CSSAGAs, to the children aged 7-17
- 2) CSSAGA-P, to a parent (about the children aged 7-17)
- 3) SSAGAs, FHAMs, TPQ(TCI), and SSS-Vs, to the offspring aged 18+
- 4) SSAGA, FHAM, TPQ(TCI), and SSS-V, and PSF to the co-parent

If necessary, any Stage I interview can be conducted over the telephone for an individual who lives outside one of the catchment areas.

If a CSSAGA-C or CSSAGA-A is unobtainable (e.g., the child is too young for a telephone interview, or a parent refused to let the child participate), a C-SSAGA-P still should be administered to a parent about that child.

PHASE I: STAGE II

To become a Stage II family, the Proband and at least two first-degree adult relatives*:

- C must be **affected by personal interview with the SSAGA-I** (The only time a proxy interview can turn a family Stage II is when the individual's medical problem is likely to be alcohol-related. See Proxy Interviews, page 1), AND
- C must not be offspring of overtly bilineal matings (i.e., both parents are affected) AND
- C must have agreed to have their blood drawn, AND
- C must not have used an intravenous drug more than 30 times lifetime and not within 6 months of contact, AND
- C must not have a life-threatening illness, other than an alcohol-related illness, AND
- C must not be known to be HIV-positive.

* These additional first-degree relatives need not belong to the nuclear family that enabled entrance into the study.

To help avoid later refusal and failure to cooperate, the site should attempt to move a family from Stage I to Stage II as quickly as possible.

Standard Stage II Protocol: The standard Stage II protocol listed below should be administered to (a) all Stage II affecteds and leapfrogees (see discussion on next page); (b) the first-degree relatives aged 7 and up of those affecteds/leapfrogees; and (c) the mates who have produced offspring with the affecteds and leapfrogees. Current childless spouses and domestic partners should be recruited if the female partner is under age 45 (i.e., still of childbearing age).

- 1) SSAGA, CSSAGA-C, CSSAGA-A, CSSAGA-P
- 2) TPQ(TCI) and SSS-V, administered to ages 18+
- 3) FHAM, administered to ages 18+
- 4) PSF, administered to affecteds and their mate(s)
- 5) Neuropsychological Battery, administered to ages 7-70 (The St Louis COGA site omits the WISC-R/WAIS-R from the neuropsychological battery.)
- 6) Event-Related Potentials (ERP), administered to ages 7-70 (see ERP Testing Pre-Screener)
- 7) Blood, drawn for DNA, Cell lines, and Biochemistry, ages 7+ (We will not draw a subject's blood if we know a subject is HIV+.)

Stage II Special Extension Protocol: In addition to the standard Stage II protocol described above, we will pursue the following from the branches of the Proband's siblings and offspring who are **not affected** by SSAGA **and** who have one or more interviewable children aged 7-17:

- 1) CSSAGA, ERP, and blood (for DNA/Cell lines/biochems), to children aged 7-17 (no neuropsychological testing)
- 2) CSSAGA-P, to a parent (about the children aged 7-17)
- 3) SSAGA, FHAM, TPQ(TCI), SSS-V, ERP, and blood (for DNA/Cell lines/biochems), to the offspring aged 18+ (no neuropsychological testing)
- 4) SSAGA, FHAM, TPQ(TCI), SSS-V, PSF, ERP, and blood (for DNA/Cell lines/biochems), to the co-parent (no neuropsychological testing) (Note: We will not draw a subject's blood if we know a subject is HIV+.)

If necessary, Stage II individuals who live outside the catchment areas may be interviewed over the telephone and have blood drawn at a local clinic or doctor's office.

Stage II Extensions and Leapfrogs: We extend through all affecteds, alive and dead, which means the standard Stage II protocol is administered to all first-degree relatives of all affecteds. If any of these relatives is affected, then we extend to his/her first-degree relatives, and continue if any of them are affected. (No stopping rules exist at the present time.)

Extension examples:

C Proband's deceased brother has 3+ FHAM implications

He is considered affected by definition (see page 1), so we proceed with standard Stage II protocol on his offspring and the mate(s) with whom he produced offspring.

C Proband's mother refused to participate and has 3+ FHAM implications, and the Proband's father is not affected

Extend through Proband's mother to her first-degree relatives.

We also extend by leapfrogging. Extension by **leapfrogging** occurs over a living or dead unaffected into a branch containing at least two first-degree relatives of the “leapfroggee” who have 3+ FHAM implications. Extension by leapfrog proceeds by administering the standard Stage II protocol to all first-degree relatives of the unaffected leapfroggee. Leapfrogging should be done only once per branch, although there is no restriction on the number of extensions through affecteds done before or after a leapfrog. All leapfrogging situations should be reviewed by the Ascertainment Committee.

Leapfrogging examples:

C Unaffected sibling of Proband has two offspring that are affected by FHAM.

Complete the standard Stage II protocol on all first-degree relatives of the unaffected sibling (the leapfroggee).

C Both parents of a Proband are unaffected, and one of them has a parent and sibling, or two siblings who are affected by FHAM.

Complete standard Stage II protocol on all first-degree relatives of the unaffected parent.

PHASE I: STAGE III

In Phase I, Stage II families become Stage III families when they are available for genotyping, such as when all the protocol has been completed or the site has decided to no longer pursue the family. Before a family is moved from Stage II to Stage III, the pedigree must be reviewed for completeness. Families that are deemed inappropriate for genotyping after the Committee’s review remain in this category.

PHASE I: STAGE IV

Families chosen by the Ascertainment Committee for genotyping (i.e., sent to panel) are designated Stage IV.

PHASE I: CONTROL FAMILIES

Each COGA site will have recruited 40 Control families consisting of two living parents and three or more full siblings, aged 14 or older (aged 10 or older at SUNY). The Control Probands and families will be ascertained via random consecutive sampling from either HMOs or dental clinics. They are to be representative of the general population and do not have to be unaffected individuals. Therefore, a Control family should not be eliminated if alcoholism is present among any of its members.

Equivalent center-specific protocols may be substituted for this type of ascertainment; however, sites should avoid samples of convenience obtained by advertising. A family is chosen only if both parents and at least three full siblings aged 14+ (or 10+ for SUNY) agree to participate. The parents and all siblings aged 7 and up should have the following protocol administered to them:

Control Protocol:

- 1) SSAGA, CSSAGA-C, CSSAGA-A, CSSAGA-P
- 2) FHAM, administered to ages 18+
- 3) PSF, administered to both parents
- 4) TPQ(TCI) and SSS-V, administered to ages 18+
- 5) ERP, administered to ages 7-70 (see ERP Testing Pre-Screener)
- 6) Blood, drawn for DNA and Biochemistry (unless we know the subject is HIV+)

Neuropsychological testing is not required in Control families; however, it is encouraged.

If necessary, individuals who live outside the catchment areas may be interviewed by telephone and have blood drawn at a local clinic or doctor's office.

If a Control family meets the Stage II criteria, then the family can be designated CL-II (see SPECIAL FAMILY DESIGNATIONS below) and proceed to CL-III and CL-IV as applicable.

SPECIAL FAMILY DESIGNATIONS

There are four additional family types:

I-S-II, I-S-III, I-S-IV: Families who met ascertainment criteria in Phase I for Stage I but not for Stage II. They are pursued because of their informativeness for linkage analysis. Stage I-S-II families are assessed with the Standard Stage II protocol (see page 6).

L-II, L-III, L-IV: Families who did not meet Phase I: Stage I requirements, but are good families to be followed for linkage analysis. Segregation analysis will not be performed on these families. Stage L-II families are assessed with the Standard Stage II protocol (see page 6).

CL-II, CL-III, CL-IV: Families who were originally recruited as Controls, but may be used for linkage analysis because they met Stage II criteria. Stage CL-II families should be assessed with the Standard Stage II protocol (see page 6), so some subjects may have to be recontacted to provide blood for cell lines.

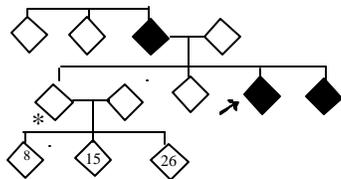
A-I, A-II, A-III, A-IV: Families with a female proband who were ascertained in Phase I at an accelerated pace (see page 4). These families were invited to participate only if they seemed like good candidates for meeting Stage II criteria. The family starts at Stage A-I, and once the family has met Stage II criteria, the family proceeds to Stage A-II and is assessed with the Standard Stage II protocol (see page 6).

PHASE II RECRUITMENT AND PROTOCOL

Phase II is the follow-up phase for COGA. In Phase II, the following individuals will be recruited approximately five years after the nuclear family was interviewed in Phase I:

- C all Probands (excluding Pilot families)
- C all Stage I and III (including I-S-III, L-III, CL-III, and A-III) Probands' offspring aged 7-25 and the co-parents of those offspring (excluding Pilot families). Childless mates, mates whose offspring are all younger than 7 or all older than 25, and all offspring younger than 7 or older than 25 will not be recruited.
- C all Stage IV (including I-S-IV, L-IV, CL-IV, and A-IV) affecteds/leapfrogees and their first-degree relatives aged 7 and older (including mates who have produced offspring with the affecteds/leapfrogees). Current childless spouses and domestic partners should only be recruited if the female partner is under 45 (i.e., still of child-bearing age). Include subjects who were not interviewed in Phase I (for example, refusals or subjects who have aged up during the interval). Half-siblings of the proband and their co-parents should be recruited only if at least one half-sibling is fully affected by FHAM.
- C any new extensions in the Stage IV families (including I-S-IV, L-IV, CL-IV, and A-IV) which result from information gained at follow-up, such as new affecteds. We will follow the same extension and leapfrogging rules used in Phase I:Stage II (see page 6-7).
- C all Control nuclear family members (i.e., the two parents and all of their biological offspring aged 7 and older, even if not interviewed in Phase I)
- C all subjects whose blood was selected for genotyping in Phase I (i.e., blood that was sent to panel), including ex-mates without offspring.
- C any Stage I-IV (including I-S, L, CL) Probands' nieces, nephews, and grandchildren who are 7-25 years old and their parents, regardless of the parents' affection. (Exclude Control and Pilot families).

EXAMPLE:



For this Stage IV family, we would recruit the first-degree relatives of the affecteds (the affecteds are shaded; the arrow points to the Proband). We would also recruit the offspring age 7-25 of the unaffected subject who is marked with an asterisk, as well as the co-parent of those offspring. In this example, the offspring who are 8 and 15 would be recruited, but not the offspring who is 26.

- C for association studies, we will collect DNA and cell lines from the parents of the Stage I and Stage III Probands only if **both** parents are available and willing to have their blood drawn (regardless of affection). We will not administer any other Phase II protocol to these parents.

Phase II Protocol: Interviewers should be blind to an individual's Phase I diagnoses before interviewing him/her in Phase II. All Phase II subjects, regardless of family status, will be administered the full Phase II protocol, except the parents of Stage I and Stage III Probands, who will only be asked to provide blood samples for DNA and cell lines:

- 1) SSAGA-II (18+), CSSAGA-C-II (7-12 year olds), CSSAGA-A-II (13-17 year olds), CSSAGA-P-II (to a parent of child/children 7-17 year olds) [**A five year interval should be attempted between the participant's first and second interview, especially between child and adolescent interviews. There must be a minimum interval of three years.**]
- 2) FHAM (includes pedigree updates, IAM, FHAM worksheets, Tobacco FHAM) for subjects aged 18+
- 3) Adult ADHD section for subjects aged 18+
- 4) Adult self-report forms for subjects aged 18+ (completed in any order):
 - Alcohol Expectancy Questionnaire (AEQ)
 - SRE (if ever tried alcohol) (UCSD has the SRE administered by an interviewer during the SSAGA-II, after question E5. Others give as a self-report form.)
 - Daily Hassles and Uplifts
 - Perceived Social Support -- Family
 - Perceived Social Support -- Friends
 - NEO Five Factor Inventory of Personality (NEO-FFI)
 - Craving Scale (if ever tried alcohol)
 - Dependence Scale (if ever tried alcohol)
 - Childhood and Adult Behavior Checklist
- 5) Child self-report forms for subjects aged 7 to 12 [read aloud to 7-10 year olds]:
 - Harter Self-Perception Profile for Children
 - Harter Importance Rating Scale for Children
 - Harter Social Support Scale for Children
 - Sensation Seeking Scale for Children (SSSC)
- 6) Adolescent self-report forms for subjects aged 13 to 17 (completed in any order):
 - Alcohol Expectancy Questionnaire -- Adolescent Form (AEQ)
 - SRE (if the adolescent has ever used alcohol) (Interviewer-administered at UCSD)
 - Harter Self-Perception Profile for Adolescents
 - Harter Importance Rating Scale for Adolescents
 - Dimensions of Temperament Scale (DOTS-R)
 - Perceived Social Support -- Family
 - Perceived Social Support -- Friends
 - NEO Five Factor Inventory of Personality (NEO-FFI)
 - Craving Scale (if ever tried alcohol)
 - Dependence Scale (if ever tried alcohol)
 - Childhood and Adult Behavior Checklist (childhood portion only)

Note: The type of self-report administered, i.e. child or adolescent, should match the type of interview administered. For example, if a subject is administered a C-SSAGA-A at age 17, but does not complete the self-reports until after turning 18, that subject would still be administered the adolescent self-reports.

- 7) Teacher reports for subjects aged 7 to 12, including the CBCL Teacher Report Form, Iowa Conners, and the Harter Teacher Rating Scale

- 8) Event-Related Potentials (ERP) for subjects aged 7 to 70 (See ERP Testing Pre-Screener)
- 9) Blood drawn for DNA for subjects aged 7+ **only** if the DNA blood was not collected during Phase I (unless the subject is known to be HIV+)
- 10) Blood drawn for Cell lines for subjects aged 7+ **only** if Cell lines were not collected or did not grow during Phase I (unless subject is known to be HIV+)
- 11) Neuropsychological Battery for subjects aged 7 to 17 **only** if it was not administered during Phase I (including children who have aged-up since Phase I)
- 12) PSF for all affecteds and their mates if not completed in Phase I

Notes about Phase II Recruitment:

While we have active families in both Phase I and Phase II, it is important to keep the two protocols straight. For the time being, we will continue to use the Phase I protocol for all Phase I subjects (including the newly recruited African-American families, Hispanic/Latino families, and the families of Caucasian female probands; see page 4). Likewise, we will use the Phase II protocol for **all** Phase II subjects (including those who were not assessed in Phase I).

In Phase II, we will pursue the family even if we find out that we cannot locate some family members, including the proband.

When making decisions about extensions, we will consider a subject affected if s/he is affected in either Phase I or Phase II. (See definition of affected on page 1.)

During Phase II, families will not proceed from a Stage I status to a Stage II status as they did in Phase I even if, after Phase II interviews, they have three affecteds by SSAGA.

Our goal is to have the family's average Phase II interview be approximately five years after the average Phase I interview. Subjects will be recruited according to their nuclear family's anniversary date. **A five year interval between the participant's first and second interview should be the goal, especially with children. There must be a minimum of three years between the participant's first and second interview.**

If a C-SSAGA-C or C-SSAGA-A is unobtainable, a C-SSAGA-P should still be administered to the parent about that child.

CONSENSUS DIAGNOSIS

The information obtained from interview with a SSAGA is assumed to be the most reliable and valid with respect to a positive diagnosis. **A consensus is required if a negative SSAGA diagnosis is in conflict with a positive diagnosis by FHAM or documented evidence, such as medical records.** Note that in Phase I, a positive consensus diagnosis will not allow a family to move from Stage I to Stage II, because only the affectation status obtained from personal interview with SSAGA is used for family classification (see page 6). A consensus diagnosis can, however, prevent a family from moving to Stage II if any of the three affecteds (including the proband) that are required for a Stage II family turns out to be the offspring of a bilineal mating after a consensus diagnosis. Consensus diagnoses can also determine if particular branches within a pedigree need to be ascertained.

The following rules apply for consensus diagnosis:

RULE 1: If three or more FHAM* interviews suggest a diagnosis not supported by SSAGA, a consensus diagnosis must be performed.

RULE 2: Data obtained from a SSAGA-I or SSAGA-II can be overridden by a consensus diagnosis based on documented contrary evidence (e.g., court, police, or medical records). If the archival record provides a diagnosis different from that obtained from a SSAGA interview, the archival record must also report a sufficient number of symptoms to enable the rater to determine both DSM-III-R Alcohol Dependence and Feighner Alcoholism at the Definite level diagnoses.

Whenever available, documented evidence from medical/other records should take precedence over family history. If records are unavailable or inconclusive, family history and/or other information should be pursued.

Consensus Procedure : At least two site clinicians will independently review all possible information, including the SSAGA, audio tapes of the interview, FHAM* reports about the individual, medical records, and, if necessary, discussions with the editor and interviewer. The clinicians must be blind to the consequence of their decisions, particularly when consensus is being performed that will affect family progress (e.g., preventing a family from moving to Stage II, or determining an extension into a branch). **To be considered affected by consensus, the clinicians must each assign both DSM-III-R Alcohol Dependence and Feighner Definite for Alcoholism to the individual.** A narrative should be written describing the rationale for the diagnostic decisions made by each of the clinicians, and these narratives should be forwarded to the Ascertainment Committee Chairman. Diagnostic disagreements should be resolved by either a consensus between the two clinicians or a third independent clinician rating. When any disagreement cannot be resolved by consensus among the clinicians, that case will be reviewed by one or more members of the Ascertainment Committee for resolution.

* The FHAM covers seven diagnostic categories (alcohol dependence, drug dependence, depression, mania, schizophrenia, ASPD, and unspecified psychiatric disorder). Since neither schizophrenia nor unspecified psychiatric disorder are SSAGA diagnostic categories, they should be excluded from Rule 1. The consensus FHAM diagnoses should, in general, be limited to alcohol dependence, drug dependence, and depression.