The Studies of Left Ventricular Dysfunction (SOLVD)

Limited Access Database

Version 2.0, August 2004

1. INTRODUCTION The Studies of Left Ventricular Dysfunction (SOLVD) was a project which evaluated the use of an angiotensin-converting enzyme (ACE) inhibitor to improve survival in patients with left ventricular dysfunction (LVD). SOLVD was sponsored by the National Heart Lung and Blood Institute, with limited support from Merck Sharp and Dohme Pharmaceutical Company. SOLVD included a pair of clinical trials. Data collection for the trials began in 1986 and was completed in 1992.

This document describes the content and structure of the Limited Access Database (LAD) created for the SOLVD Trials. This database contains all the scientifically useful data collected as part of the trial protocols, subject to minor constraints (described within) to preserve participant confidentiality.

2. STUDY OBJECTIVES The primary objectives of SOLVD were to answer the questions: (1) (Prevention Trial) In patients with LV dysfunction (resting ejection fraction <0.35) and *no history of overt CHF,* can long-term survival be improved by taking enalapril (an ACE-inhibitor)? (2) (Treatment Trial) In patients with LV dysfunction (resting ejection fraction <0.35) and *with a history of overt CHF*, can long-term survival be improved by taking enalapril?

3. STUDY DESIGN To address the study objectives, 2 separate randomized, double-masked clinical trials were conducted in 23 medical centers.

A brief description of the design of the studies, emphasizing the volume, timing, and content of data collected is presented below. A more detailed description of SOLVD can be found in the study design manuscript (SOLVD Investigators, 1990). Electronic copies of the trial protocols and operations manuals are included in this volume.

3.1. Participants The 2 basic criteria for entry into the trials are: (1) age between 21 and 80 years, inclusive, and (2) LV ejection fraction <0.35, performed within 3 months of the day of consent. Exclusion criteria fall into several broad categories: non-cardiac diseases likely to limit long-term survival, certain cardiac conditions other than primary myocardial dysfunction, intolerance to enalapril and a substantial likelihood of nonadherence to the assigned medication. The Prevention Trial is composed of participants who did not have a history of overt heart failure prior to randomization. These participants had little or no limitation of exercise tolerance due to dyspnea or fatigue and did not require treatment with digitalis, diuretics or vasodilators for heart failure at entry into the trial. The Treatment Trial is composed of participants with a

history of overt CHF, that is, participants who had clinical evidence of CHF and who, at randomization, required treatment with diuretics or inotropic drugs or vasodilators, or a combination of these, for symptomatic relief.

3.2. Study Size The study aimed to enroll 2,500 patients in the Treatment Trial and 4,600 patients in the Prevention Trial. Recruitment for the treatment trial ended ahead of schedule with 2,569 patients randomized, while recruitment was closed as scheduled in the Prevention trial with 4,228 patients randomized. Patients were randomized to enalapril or placebo in a 1:1 ratio. The actual number assigned to each treatment, by trial, is shown in Table 1, below:

Table 1. Number of Participants Randomized

	Enalapril	Placebo	Total
Prevention	2,111	2,117	4,228
Treatment	1,285	1,284	2,569
Total	3,396	3,401	6,797

3.3. Schedule and Contents of Patient Visits Table 2 lists the sequence of patient visits. The major types of data collected and the forms required are also listed.

Table 2. Schedule and Content of Patient visits

Visit	Title	Purpose	Required Forms
1	Eligibility	Evaluate Inclusion / exclusion criteria	SEF
2	Medication Tolerance	Evaluate tolerance to study medication	SMT
3	Baseline / Randomization	Evaluate placebo compliance; collect baseline data; randomize	SBF, SRF
4-20	Follow-up	Side effects; compliance; medications; CHF symptoms; hospitalizations; mortality	SFE
		Quality of Life	SQL
Any		Dose changes, hospitalizations, deaths	SDC, SHF, SFN, SFD

4. DATABASE STRUCTURE

4.1. Data Set Organization There is one table (SAS data set) in the database for each type of data collection form.

The data values from one completed paper form are stored in one record in the corresponding table (observation in the SAS data set).

Each data item on a paper form is stored as one or more columns (variables) in the data set.

Since all of the forms were revised at least once during the course of the study, the version of the paper form used to collect the data is also included on each record (e.g. versions A, B, or C). The SAS data set is a composite of the data items required to accommodate all versions of the corresponding data form. Some version specific data items will be missing in a given record depending upon which version was completed at time of data acquisition in the field.

In addition, each of the data sets contains derived variables, in place of some of the original data values. For the most part, these are transformed values, used to protect the confidentiality of individual participants. Details are contained in the table-specific documentation.

4.2. Data Set Naming Convention Each data set is named starting with a three letter mnemonic. The first letter is "S", for SOLVD; the remaining two letters identify the form type (e.g., SEF for the SOLVD Eligibility Form). This is followed, for each data set by the character string "_LAD2", for Limited Access Database, version 2.

4.3. Key Fields for Data Records The unique identification of a participant data record within a file is determined by three primary key fields for forms that can be collected once per visit (see SOLVD protocol p. VII-1), and by the use of a sequencing field for the few forms that could occur many times per visit (e.g. Dosage Change or Hospitalization forms). These items are:

1) ID_SOL: A transformed participant ID, with values that range from SOL0001 through SOL6797.
2) VISIT: Study protocol visit number, a two digit field.
3) FORMCODE: Data collection form three letter mnemonic as described above.
4) VISSEQ: Visit Sequence number, a two digit sequencing number (01-99) for multiple forms per visit (only used in the SDC and SHF files).

4.4: Common Variables Across Data Sets Three additional variables appear in every data set, which are often helpful in identifying particular subsets of the data:

5) FORMVER: Version of the data collection form. A one character field recording which version of the paper form was used to collect the data record. Possible values are "A", "B", and "C".
6) TRIAL: a one character variable with values of "P" or "T".
7) HOSPCODE: A two character variable with values "01" – "74" which uniquely identifies the recruitment source (e.g., hospital) at which a participant was treated and followed.

4.5. Data Item Naming Conventions The mapping of individual data items from a SOLVD data collection form to the corresponding table field uses standard naming conventions. The key field and sort variables used in common across all forms have the same name on each SAS record type (ID_SOL, VISIT, FORMCODE, etc.). To predictably and uniquely link data items to table field names, a combination of the form code mnemonic and question number is used. For example, question 1 on the Eligibility form, "today's date", is named SEF1 on the corresponding SAS file. Similarly, question 13.1, "qualifying ejection fraction", from the Eligibility form is named SEF13Z1. Note that because SAS does not allow "." to be used in variable names all "." were replaced by a "Z" in creation of SAS data sets.

4.6. Status Bytes Status bytes were created by the data entry and edit programs used in keying the SOLVD data collection forms. Each question on the paper forms was edited with the results of that edit contained in the value of the associated status byte. The naming convention used for status bytes parallels the standard variable names. SAS variable SEF1 from question 1 has the companion status byte SB1 (note status byte names are not unique across forms). Likewise, question 13.1 has the accompanying status byte SB13Z1. Status byte values and their interpretation are:

Table 3. Data Item Status Bytes

Value	Meaning
#	Value is "clean". Includes values that have passed all edits and values that are appropriately missing.
C	Value has been confirmed as correct by an authorized person. These values were investigated, usually because of failed edits, occasionally because a person questioned them.
Q	The value is wrong or suspicious, but could not be confirmed or corrected.
(blank)	Data item was not collected in this version of the data form.

Note that the possible values of status bytes have been combined and transformed from those described in the protocol and operations manual to reflect the fact that all data management activities have been completed.

5. DESCRIPTION OF DATA COLLECTION FORMS / DATABASE TABLES

5.1. Eligibility Form (SEF) Participants thought to be eligible for the SOLVD trials have primary eligibility and identifying information obtained at this first visit and recorded on this form.

5.2. Medication Tolerance Form (SMT) After the participant undergoes a medication tolerance period to test for a potential toxic reaction to the study drug, this second visit form records a standard battery of laboratory data to monitor specific hematologic and biochemical abnormalities, and adverse reactions.

5.3. Baseline Form (SBF) At the third visit the participant's adherence to the placebo run-in was evaluated along with continuing to meet the study eligibility inclusion criteria. A collection of medical history questions, current signs and symptoms, and medication use are contained in this form.

5.4. Randomization Form (SRF) This form contains the primary linking information between the pre and post-randomization data collection periods of a SOLVD participant. The date of randomization is also important in defining the start of a participant's follow-up.

5.5. Follow-up Examination Form (SFE) This form records the ongoing general physical status of a participant, study drug side effects, adherence to study drug, and nonstudy medication profile. Dose titration is also recorded on this form.

5.6. Quality of Life Form (SQL) A self administered form completed by the participant at baseline, 6 weeks, and 12 months of follow-up.

5.7. Alteration in Study Drug Dose Form (SDC) For those cases in which the study physician wishes to change the dose of the study drug between visits, this form records the reason, and if any side effects were associated with the change in medication.

5.8. Hospitalization Form (SHF) Whenever a participant is admitted to hospital this form detailing the primary and secondary reasons for hospitalization is completed.

5.9. First Notification of Death Form (SFN) This initial notice of a participant death is completed immediately following ascertainment of the death of a study participant, and documents only the date of death.

5.10. Final Designation of Death Form (SFD) Once the actual cause of death is determined, this form is completed. Each death is classified as cardiovascular or noncardiovascular by the study physician using available information.

6. ENDPOINTS DATA SET (SEP)

The Endpoints data set is not directly associated with any particular CRF. It has one record per participant. It consists almost entirely of "derived variables" whose values are defined based on combinations of data items, primarily from the follow-up, hospitalization and death forms. Primary and secondary endpoints (outcomes) specified in the SOLVD protocol (see p. II-2) are coded into a series of 0/1 indicator variables (corresponding to no/yes). Times from randomization to the first occurrence of primary outcomes are also computed and included.

The endpoints data set is the only data set in the database that contains the variable TRTMENT, which identifies which treatment group a participant was randomized to. The values "PLAC" and "ENAL" specify the participant as being assigned to the placebo or enalapril groups, respectively.

IMPORTANT NOTE: In a few cases, inconsistencies or omissions in the information required to define these variables could not be corrected on the original data forms (and corresponding files in this database). These idiosyncratic cases were adjudicated by the SOLVD Executive Committee and their resolutions are included in this file. This file contains the endpoint definitions used for all the primary SOLVD publications, and should be considered the "gold standard" for analyses of clinical events from SOLVD.