# Request for Approval for Registration of Individuals with Amyotrophic Lateral Sclerosis (ALS) in the National ALS Registry

Part B

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## B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

The ALS Registry coordinator and statistician will conduct periodic statistical analyses on the data in the system. An annual registry report will be generated using SAS (SAS Institute, Cary, NC).The annual report will include information from both individuals who self-register and those from administrative data. Evaluation of the representativeness of those self-registering will be conducted (see description below). This information will be part of the annual report. It is anticipated that the annual report will include information on:

- Number of people identified with ALS
- Number of individuals who self-identified vs those obtained from existing data
- Mean age of case
- Sex distribution of the cases
- Racial distribution of the cases
- Geographic distribution of the cases by region
- Distribution of other characteristics such as cigarette use, alcohol use, occupation, service in the military, physical activity, and family history.

The ALS registry coordinator may employ the following methodology:

- Data transformation
- Case classification
- Baseline estimation

Registry reports will include data both from those individuals identified using existing datasets and those who self-register. ATSDR evaluated the feasibility of using existing administrative data to identify cases of ALS in four geographically diverse pilot projects including tertiary care facilities for ALS, HMOs, and state based organizations. These four pilot projects matched data from Medicare, Medicaid, the Veterans Health Administration, and Veterans Benefits Administration to data available within the four pilot project sites administrative and clinical databases for a 5-year time period (January 1, 2001 – December 31, 2005). ATSDR provided the pilot projects with individual encounters with an ICD-9 code for any MND (335.2-335.29) for the specific project catchment area. Pilot projects completed a standardized spreadsheet for each individual found in any database indicating in which database(s) a record was located, ICD-9 code recorded for the encounter, as well as the years and types of providers seen. Medical records were abstracted and diagnoses verified. A deidentified dataset was sent to ATSDR for analysis. All individuals who were identified with a possible ALS diagnosis, as indicated by ICD-9 code for any MND, and had their medical record reviewed by a neurologist from the four pilot projects were combined. Approximately 4400 medical records were reviewed. It was possible to develop an algorithm using variables from the administrative data that identified true cases of ALS (verified by a neurologist). The best algorithm had sensitivity of 85% and specificity of 85%. Similar results were found in the individual pilot project analyses.

Basic demographic variables such as age, race, and sex will be available on all individuals regardless of how they were identified, although these are not verified and race will not have all of the approved categories.

The representativeness of the survey data will be evaluated by determining the number of individuals who self-register compared with those who were identified from existing datasets. That is, we will determine if those who self-register have already been identified in an existing dataset. If those who self-register are distributed between those who were already identified from existing datasets and newly identified, the survey data should be representative of ALS patients in general.

**1. Respondent Universe and Sampling Methods**

This activity is surveillance; respondents are not sampled. Furthermore, no sample selection is involved in this registry. The registry will identify individuals from existing data and will allow cases to self-identify. The primary purpose of the registry is to calculate the incidence and prevalence of ALS and provide basic demographic information including, age, race, sex and geographic area. The tabulation of risk factor information required by Congress is for descriptive purposes only. We consider it surveillance rather than etiologic research because no hypotheses will be tested. As the registry matures and more individuals self-register, the information could be used for research, however research activities are not planned for this current OMB submission but will be considered for the OMB renewal. If there is overwhelming registration of ALS patients and the data are determined to be representative of ALS patients in general (see description above), ATSDR will request an amendment to the current OMB package to allow these additional analyses.

ATSDR has a multi-pronged approach for publicizing the existence of the registry. First, ATSDR will promote the information on their ALS website. Second, ATSDR is working with two advocacy groups, the ALS Association (ALSA) and the Muscular Dystrophy Association, ALS Division, to promote the registry with their constituents and on their respective websites. Third, ATSDS is working with the Office of Communication to develop a media campaign which will include presentation at conferences, advertisements, and social media.

**2. Procedures for the Collection of Information**

ALS patients will be allowed to voluntarily register for the registry. Case status will be validated using six questions standardized by the Veterans Administration and shown to correctly identify cases 93% of the time (Attachment 4). Once an individual passes validation, he will be permitted to register. To enable the collection of additional information from registrants who volunteer, a series of short survey modules will be available for completion via a secure web portal (Attachment 6). We are using a survey validated by the ALS Consortium of Epidemiologic Studies (ACES). The survey has been divided in to short modules because of the physical limitations of the study population. All surveys are designed to be answered only once except for the symptoms survey which can be answered every 6 months. It is anticipated that most participants would complete the symptom survey 3-4 times at most because the average life expectancy of an individual diagnosed with ALS is 2-3 years and the disease is quite debilitating.

For the symptoms survey we will use the ALS Functional Rating Scale-Revised (ALSFRS-R), a standard set of questions used by physicians to measure function overtime. Researchers have developed and tested a self-administered version of the ALSFRS-R which showed excellent reliability to change over time. This test is scored in a standard fashion. (Attachment 10) The published version of the self-administered ALSFRS-R was slightly modified to make the question responses more user friendly. Changes to the questions were only grammatical and were reviewed by two ALS researchers to assess impact. It was decided that because the changes were only grammatical no additional cognitive or reliability testing was needed. Below are some examples of changes with the added words bolded.

| Original | Change |
|---|---|
| Need to be fed | **I** need to be feed |
| Use PEG without assistance or difficulty | **I** use **a** PEG without assistance or difficulty |
| Not all words are legible | Not all **my** words are legible |

Individuals will be consented prior to registering with the National ALS Registry and completing any survey modules. Participants will not be contacted to take surveys. For all surveys the individual will have to visit the website and log in to his/her personal account. Therefore, if a participant doesn't want to take part any longer, he/she just doesn't log in

**3. Methods to Maximize Response Rates and Deal with Non-response**

There is not a method to deal with non-response because it is unknown who has ALS. We will attempt to maximize the response rate by partnering with ALS advocacy groups and neurologists to publicize the registry.

**4. Tests of Procedures or Methods to be Undertaken**

The web site has been tested and will continue to be tested until deployment. No further procedures or methods are needed at this time.

**5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data**

Individuals consulted on statistical aspects:

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## List of Attachments