OMB Survey Supporting Statement
ACAM2000® Myopericarditis Registry

Principal Investigator: Ava Marie S. Conlin, DO, MPH

Institution: Naval Health Research Center
Deployment Health Research Department – Dept 164
140 Sylvester Road
San Diego, California 92106-3521

Phone: (619) 767-4489 Email: ava.conlin@med.navy.mil

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

1. Describe (including a numerical estimate) the potential respondent universe and any sampling or other respondent selection method to be used. Data on the number of entities (e.g. establishments, State and local governmental units, households, or persons) in the universe and the corresponding sample are to be provided in tabular form. The tabulation must also include expected response rates for the collection as a whole.

This study will enroll a maximum of 200 participants. To be eligible for participation, individuals must be current or past members of the active duty military, Reserve, or National Guard, in any branch of service, who received the ACAM2000® smallpox vaccine and subsequently met the case definition for confirmed, probable, suspected, or subclinical myopericarditis. During the course of the study we anticipate that 10% - 20% of subjects will separate from the military for an estimated total of 20-40 civilian subjects.

A power calculation is not indicated for this study because all participants have the exposure and the outcome of interest, myopericarditis, following receipt of the ACAM2000® vaccine. As described previously, the purpose of this study is to follow the natural course of disease and identify possible predictive factors for the prognosis of myopericarditis following ACAM2000® vaccination. The estimate of no more than 200 subjects is based on the expected number of vaccine recipients who will develop myopericarditis over five years, the length of time required by the FDA for the Registry enrollment phase.

Using response rates to another vaccine registry managed by personnel at the Deployment Health Research Department which also relies on referrals, the anticipated response rate for self and physician referrals is 95-100%. The response rate for referrals from other sources is more difficult to estimate, but this population, many of whom have had or are currently experiencing symptoms that may be related to their vaccine, is likely to be highly motivated to join a registry designed to elucidate the natural history of myopericarditis experienced subsequent to receipt of the smallpox vaccine and potential risk factors for disease prognosis. Therefore, we conservatively estimate a 70-75% response rate for all other routes of referral.

2. **Describe the procedures for the collection, including: the statistical methodology for stratification and sample selection; the estimation procedure; the degree of accuracy needed for the purpose described in the justification; any unusual problems requiring specialized sampling procedures; and any use of periodic (less frequent than annual) data collection cycles to reduce burden.**

   Subject recruitment for the Registry is passive, relying on the referral of potential cases to the Registry team, and will continue until the maximum number of participants is reached. A cardiologist was consulted to define the optimum time between surveys and determine the length of follow-up, thus ensuring adequate time for symptoms to develop or resolve, while still keeping the window narrow enough to reduce recall bias, but not so narrow as to overburden participants.

3. **Describe the methods used to maximize response rates and to deal with nonresponse. The accuracy and reliability of the information collected must be shown to be adequate for the intended uses. For collections based on sampling, a special justification must be provided if they will not yield "reliable" data that can be generalized to the universe studied.**

   Efforts to maximize response rates and reduce non-response include having three separate modes for survey completion via the phone, on paper, or web-based. Further, contact follows a modified Dillman technique, a method often employed by researchers because of its demonstrated ability to yield the highest response rate. After completing the initial survey instrument, subjects will be asked to complete subsequent surveys every six months, with a length of follow-up that varies depending on the subjects' clinical course. The Registry will follow asymptomatic subjects for two years after enrollment, unless the subject was asymptomatic for two years prior to enrollment, in which case the subject would complete an enrollment survey and one follow-up survey (two surveys total). Any subject with symptoms or positive findings will be followed for two years after last occurrence of symptoms or positive findings. Notwithstanding the foregoing, follow-up will continue for a maximum of five years after initial enrollment. Active follow-up in the Registry will terminate at the five year mark even if symptoms or positive findings persist.

   The enrollment and follow-up surveys for this study utilize several standardized survey instruments, many of which have undergone extensive testing to reduce respondent burden and improve the utility of the instrument. Other studies, such as the Millennium Cohort Study, have utilized many of the instruments employed in this study, and demonstrate excellent reliability and an absence of survey fatigue (tapering off of responses towards the end of the survey due to survey length).

4. **Describe any tests of procedures or methods to be undertaken. Tests are encouraged as effective means to refine collections, but if ten or more test respondents are involved OMB must give prior approval.**

   Data collection will be performed in the Deployment Health Research Department, located at the Naval Health Research Center, San Diego, CA. Analyses will be performed by Sanofi Pasteur, or their designated agents, using databases stripped of personal identifiers. NHRC and collaborator/sponsor study teams may also contribute to analyses, or supplementary analyses as needed.

Statistical analyses will include descriptive evaluations of population characteristics of ACAM2000® immunized military members who meet the study definition for subclinical, suspected, probable, or confirmed myopericarditis. Univariate analyses, including chi-square, t-tests, and exact tests will be performed to assess the significance of unadjusted associations between variables of interest, including demographic, family history, and medical history characteristics. Exploratory analyses will assess regression diagnostics, adjusted associations, multiplicative interactions, and possible confounding, while simultaneously adjusting for all other variables in the models.

Statistical modeling producing unadjusted and adjusted odds ratios and relative risks (RRs), and associated 95% confidence intervals will be performed using SAS® software (Version 9.0, SAS Institute, Inc., Cary, NC).

5. Individuals Contacted on Statistical Aspects of Design

Analyses will be performed by Sanofi Pasteur or their designated agents. Personnel consulted in the statistical aspects of the design are coordinated through Sanofi Pasteur, and can be contacted through the Clinical Trials Manager:

David Powell, Clinical Trials Manager, Sanofi Pasteur,
Email: David.Powell@sanofipasteur.com
Phone: (570) 957-5939