OMB Survey Supporting Statement
ACAM2000® Myopericarditis Registry

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A. JUSTIFICATION

1. Circumstances That Make the Collection of Information Necessary

In the wake of the September 11, 2001 terrorist attacks, the United States (US) Government began to immunize health workers, first responders, and military personnel against smallpox in preparation for a possible terrorist attack. The Federal Government maintains a stockpile of a second-generation smallpox vaccine, ACAM2000®. ACAM2000® was developed by Acambis (now Sanofi Pasteur) under contracts with the US Centers for Disease Control and Prevention (CDC) as part of its preparations for a public health emergency. On August 31, 2007, the Food and Drug Administration (FDA) licensed ACAM2000® for persons determined to be at high risk for smallpox infection. In addition to being stockpiled for emergency use, ACAM2000® is used by the US Department of Defense (DoD) for protection of military personnel.

Several Phase IV post-licensure studies are currently underway to evaluate the long-term safety of ACAM2000® as required by the FDA. In the absence of these studies, the FDA could revoke the license for the vaccine, thus placing service members at potential risk should smallpox be used as a biological weapon. Among the required post-licensure studies is the establishment of a myopericarditis registry. The Secretary of Defense for Health Affairs accepted responsibility on behalf of the DoD to conduct these post-licensing studies, and the Deployment Health Research Department at the Naval Health Research Center (NHRC) was directed to implement the ACAM2000® Myopericarditis Registry. The ACAM2000® Myopericarditis Registry is designed to prospectively study the natural history of myopericarditis following receipt of the ACAM2000® vaccine, including evaluating factors that may influence disease prognosis.

Each of the Phase IV studies are funded by the vaccine manufacturer, Sanofi Pasteur.

2. Purpose and Users of the Information

Researchers in the Deployment Health Research Department, located at the NHRC in San Diego, California, are responsible for data collection and identified data storage. The information collected includes semiannual survey data and supportive medical records data as needed. Following receipt of informed consent, the survey can be completed online, on paper, or by phone. The survey is designed to collect contact information, basic demographic data, general health information, personal and familial cardiac risk factors, assessment of cardiac symptoms, vaccination history, and relevant behavioral histories (e.g. smoking

history). The survey was developed with the guidance of a cardiologist and as much as possible, uses pre-existing and validated survey instruments. The follow-up survey is an abbreviated version of the enrollment survey instrument.

The information collected will be used to evaluate factors that may influence myopericarditis disease prognosis. If factors are identified that suggest an elevation in risk, the information collected in this study will guide future studies and can help with the creation of policies to mitigate potential risks as further studies are conducted.

3. Efforts to Collect Information Electronically

Survey data collection includes the use of the internet as an option for survey completion and submission. Completion of a survey via the internet is faster and more cost effective than survey completion by more traditional routes, such as paper and phone survey completion. Although the preference is that participants will complete the survey online, traditional routes of completion are included in this information collection process in recognition that some individuals are not yet comfortable with an online only option.

4. Duplication and Similar Efforts

Existing data collection systems cannot adequately address the goals of this study, which are to document the natural history of confirmed, probable, suspected, and subclinical myopericarditis following ACAM2000® vaccination; and to look for potential predictive factors for the prognosis of myopericarditis following ACAM2000® vaccination. Medical records will contain diagnoses and laboratory results, but will often lack a detailed assessment of family, lifestyle, and cardiac symptom history, particularly if some or all medical care is received at a civilian care facility, thus making the data inaccessible. Existing surveys of service members do collect behavioral (e.g. smoking and drinking) histories, however these fail to collect cardiac specific information relating to symptoms, personal medical history, and family history. To ensure that the FDA licensure requirements are met in a timely fashion, it is not feasible to await future data collection tools that may or may not address the specific concerns outlined for the Phase IV Registry Study.

5. Small Business

The proposed data collection will not affect small businesses or other small entities.

6. Less Frequent Collections

The Registry will follow asymptomatic subjects for two years after enrollment. 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. While subjects are followed, they will be asked to complete a survey once every 6 months, for a maximum of 10 follow-up surveys. The survey frequency was selected following the guidance of a cardiologist and is designed to ensure adequate and timely tracking of symptoms, thus reducing recall bias and providing the most accurate assessment of the natural history and prognosis of myopericarditis. Less frequent assessments would increase recall bias and provide an incomplete view of the prognosis of the disease under investigation.

7. Special Circumstances

The Registry does not have any special circumstances that would cause information collection to be conducted that would require respondents to: report more often than quarterly, prepare a written response within 30 days of receipt, submit more than an original and two copies of any document, retain records for more than 3 years, or submit proprietary trade secrets or other confidential information. Further, the statistical analyses used in the Registry are standard descriptive analyses, and the Registry does not pledge confidentiality that is outside of the established authority.

8. Federal Register Notice and Consultations

A notice for the collection of this data was published in the Federal Register 76 FR 13990 March 15, 2011. There have been no comments or inquiries.

The Registry was designed in conjunction with individuals from the Naval Health Research Center, the Military Vaccine Agency, and Sanofi Pasteur, and as such it was created with the varied knowledge and expertise of each of these entities. A cardiologist was consulted to help develop the survey instrument, define the optimum time between surveys, and determine the length of follow-up. Review of the survey instrument by Defense Manpower Data Center led to improvements in instructions and survey response options, thus ensuring the usefulness of the data collected.

Other consultation and oversight of the ACAM 2000® Myopericarditis Registry includes annual reviews by the NHRC internal Institutional Review Board and the Office of the Assistant Secretary of Defense (Health Affairs) TRICARE Management Activity, Human Subjects in Research Protection Office.

9. Payment/Gifts to Respondents

Individuals who join the Registry will not receive gifts or payments for their participation.

10. Confidentiality

Assurances of confidentiality are detailed in the Informed Consent Form which specifies the following: a description of the information to be used; the name of the person(s) requesting the use; the name of the person(s) who may use the requested PHI, i.e., the intended recipients; a description of each purpose of the requested use; the length of time that the data will be maintained, tied to an expiration date or an expiration event; a statement regarding the individual's right to revoke authorization for use of PHI, and whom to contact in writing to revoke the authorization; and a statement regarding the individual's right to inspect hard copies of any PHI collected, and who to contact in writing to inspect the contributed data. The informed consent also indicates where and how data are stored, details that social security numbers and other types of personal identification information are stripped from surveys prior to storing data, and that any findings will be released in an aggregate, thus preventing the identification of individuals. The Privacy Act Statement, which appears at the end of the informed consent, specifies the regulations and statutes that enable the collection of these data and the use of these data.

11. Sensitive Questions

Although some questions in the survey may be of a sensitive nature, particularly behavioral questions relating to drinking and smoking, most of the questions used in this instrument are from standardized survey instruments and cannot be omitted or modified without affecting the validity of the survey tool. Prior to selecting questions for use in this instrument, every effort was made to capture only the data that were necessary to adequately address the study objectives. None of the questions violate the Privacy Act as implemented by DoD 5400.11-R and none of the questions could implicate the respondent in violating the Uniform Code of Military Justice. Further, the Informed Consent Form, which respondents must complete prior to completing a survey, details what data are captured in the survey instrument and gives them the option of skipping any questions that they may feel uncomfortable answering.

12. Estimated Burden

This study will enroll a maximum of 200 subjects over the course of five years. Potential subjects are current or past active duty service members who received the ACAM2000® smallpox vaccine and subsequently developed signs or symptoms of myopericarditis. Over the course of the study we estimate that 10-20% of subjects will separate from the military each year, resulting in 20 to 40 civilian subjects by the end of the enrollment period. Subjects are asked to complete an initial enrollment survey, then a follow-up survey every six months, with the length of follow-up determined by the presence or absence of symptoms or positive findings for myopericarditis. 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. Therefore, except in the case when subjects were asymptomatic for two years prior to enrollment mentioned above, over the course of the study, the minimum number of surveys a subject would need to complete is five, and the maximum number of surveys is eleven.

Each survey takes approximately 30 minutes to complete, for an annual hour burden of one hour per subject, or a total annual burden time of 20 hours for the civilian component of the study.

The estimated total annualized cost to the respondents for this collection is $346.00, or $17.30 per respondent.

13. Cost to Respondents

None.

14. Cost to the Federal Government

The estimate for the total annual cost to the Federal government is zero. The manufacturer of the ACAM2000® Smallpox Vaccine, Sanofi Pasteur, has provided funds to cover the expense of this work. These funds were secured through a Navy Clinical Trials Cooperative Research and Development Agreement number NCRADA- NHRC – 09 – 3201, established between the Naval Health Research Center and Sanofi Pasteur.

15. Change in Burden

Program Change due to new collection.

16. Publication/Tabulation

The purpose of the proposed data collection system is to address FDA post-vaccine licensure requirements. Although there are no plans for publications at present, the data collected may be of interest to researchers, clinicians, or patients, thus the potential to share findings in peer reviewed journals or at scientific conferences does exist. Adverse events identified as part of this Registry will be reported to the vaccine manufacturer Global Pharmacovigilance Department and the CDC/FDA Vaccine Adverse Events Reporting System.

17. Expiration Date

Exception to displaying the expiration date is not being sought.

18. Exceptions to Certification Statement in item 19 of OMB Form 83-I

None.