The Request For Investigation

- August 29, 1997 Congressman Jack Metcalf requested the General Accounting Office (GAO) investigate reports that the presence of antibodies for squalene had been discovered in the blood of some sick Gulf War-era veterans. The assay (test) being used to detect the antibodies had been developed at Tulane University by Dr. Robert Garry, world renowned virologist.(Appendix 1)

  At the time of Congressman Metcalf's request, the research by Drs. Garry, Asa and Cao had not yet been published in a peer-reviewed scientific journal. Their work, "Antibodies to Squalene in Gulf War Syndrome," was published in the February 2000 issue of Experimental and Molecular Pathology. (Appendix 2)

  NOTE: Squalene is a component of adjuvant formulations used in some experimental vaccines but not in any licensed vaccines. Squalene is found in shark liver oil, some vegetable oils, and the human liver and can also be manufactured through chemical engineering. (GAO/NSIAD-99-5).

Section One

The Investigation: A Pattern of Deception

September 1997 - March 29, 1999 General Accounting Office (GAO) investigators initiated their study and completed the report "GULF WAR ILLNESSES: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved" (GAO/NSIAD-99-5). The investigation was significantly slowed by government officials withholding or presenting incomplete information, ***leading GAO investigators to document their concerns questioning a "pattern of deception."*** (1) The following six dated entries are found in the background material for the GAO report. They illustrate the pattern of deception that clouded the investigation.

November 14, 1997 GAO entrance conference with Department of Defense (DOD) officials. GAO notes state,

1) "They said DOD had not performed or sponsored any research on synthetic or natural squalene or squalane until after the Gulf War. The sponsorship was through two CRADAs [Cooperative Research and Development Agreement]. However, they could not tell us who the CRADA's were with, what stage they were in, or what tests had been performed.

2) "Squalene was used in two experimental adjuvants, after the war and involving fewer than 100 subjects. These were for HIV and Malaria vaccines. They said NIH had also used in some of their research protocols. DOD officials also stated that DOD was involved after animal testing stage." (2)

In background papers, GAO investigators stated, "However, GAO found evidence of several other studies in our searches of publication databases, references and articles. ***Various DOD officials gradually acknowledged on a piece meal basis that their clinical research had started before the war,*** *that they had conducted 5 clinical studies with squalene and had planned a sixth, that the size of these studies was increasing and now has involved 572 human subjects, and that some of these studies were purely their own investigational New Drug (IND) Studies.* ***Moreover they had conducted numerous animal studies, particularly to develop a modern vaccine for anthrax. In fact, in most cases they only admitted to conducting research after we had discovered it in public records. On three occasions people attending a meeting did not report their own research on squalene adjuvants."*** *(3)*

December 10, 1997 GAO entrance conference with Food and Drug Administration (FDA) officials. GAO investigators noted that it was a very productive meeting and recorded:

1) "The purpose of developing new adjuvants, even though alum is safe, is to use fewer inoculations, get a better response, and to check unconquered antigens. Earlier adjuvant ran into problems in animal testing... Most of DOD's work has been with Ribi Detox for malaria. **Their person most interested in developing own adjuvants at WRAIR** [Walter Reed Army Institute of Research] **is Carl Alving.**

2) "Allied had concerns about the quality of our vaccines. Michigan had some manufacturing problems.

3) "Karen is sure DOD used plague vaccine. They pushed it. She confirmed that squalene was used in placebos.

4) "FDA testing of drugs and vaccines: Good Manufacturing Practices inspection every 2 years. Test each lot released. No routine random sample. For bot tox [botulism toxoid] they also checked for safety and sterility, but not the makeup of the compound. DOD should have reserve samples. Required to have them for each lot. **Squalene should not be there."** (4)

NOTE: See Appendix 25 regarding the discovery by FDA in 1999 of trace amounts of squalene found in limited testing of Anthrax Vaccine, Adsorbed in the lots tested.

March 30, 1998 GAO interview with Donald Burke, Director of AIDS research for DOD during the Persian Gulf War. GAO recorded, "Burke said he was involved with AIDS trials at time of war and purposely chose not to get involved in BWD [biological weapons defense] issues at that time... In his AIDS work he experimented with MF59 [an adjuvant containing squalene] because alum was destructive to HIV proteins. He has had good cooperation with NIH [National Institutes of Health]. He recounted various studies, including a large one with 300 subjects getting MF59. . . He suggested we talk to . . . Carl Alving about DOD adjuvant research." (5))

GAO investigators noted, "Don Burke the former director of DOD's HIV research and Debbie Birx, the current director disagreed on the existence of a large early HIV trial with squalene with over 600 volunteers. She said he was thinking of an NIH trial. However, NIH reported no trials of that magnitude. (6)

April 6, 1998 GAO interview with Dr. Carl Alving, DOD's top adjuvant researcher. GAO stated,

1) **"Alving opened by saying he didn't know anything about Operations Desert Storm and Desert Shield (ODS) and the vaccines that were used. He is a researcher, and an expert, but not in the policy loop.**

2) "GAO pressed why he was not consulted about gulf war inoculations given his world class expertise. He admitted that just prior to gulf war he was asked if he could develop an anthrax vaccine on a crash basis. He stated that WRAIR has manufacturing capability, Ft. Detrick does not. He could have done it in 3-6 months but never received

a follow on phone call to formally authorize the work. If asked, he could have done it but would have recommended MF59 for anthrax because Chiron had the manufacturing capacity and the desire to market it. Ribi, Chiron and Hunter were the adjuvant leaders at the time. . . He was subsequently asked again (by DOD?) to develop an anthrax vaccine using liposomes, but it and all others. . . tested failed to protect monkeys with a single shot, which he thought was an absurd criteria. But he thought commercial considerations may have driven the criteria.

3) "He also said that as the world's foremost expert on lipids he knew quite a bit about cholesterol and its precursor, squalene. He doubted that a vaccine with squalene would produce a meaningful antibody response.

4) "Analysis: Overall, the commercial links appear to be crucial to the course of DOD vaccine R&D" (7))

GAO investigators recorded the following observation in a section titled, DOD officials were less than forthcoming about their role in Gulf War vaccine decision making: *"Carl Alving, DOD's top adjuvant researcher was not included in our meetings at WRAIR where he worked, nor even mentioned as someone we should interview. However, both NIH and FDA had said he was the person at DOD most involved with adjuvants. We subsequently met and while he acknowledged that he was probably the army's best expert on adjuvants, he at first denied having any role in the gulf war vaccine deliberations. After Kwai Chan left, Sushil Sharma pressed him on this, asking how could it be that they would discuss these issues without their principle expert. He then remembered that he had been called by someone from the army's biological warfare defense program at USAMRID [United States Army Medical Research Institute of Infectious Diseases], who asked if he could develop a new, more potent anthrax vaccine on a crash basis to use in the Operation Desert Shield. He worked on it and thought he could do it, but no one ever called him back. He wouldn't say who called from USAMRID or why he just didn't return the call." (8))*

April 19, 1998 Interview with Dr. Anna Johnson-Winegar, Director Environmental and Life Sciences, key participant in the tri-service committees advising on the science and vaccine production issues.

1) "Project Badger. [Tri-Service Task Force established prior to the Gulf War, (9/90) to investigate ways to increase production of biological warfare vaccines.] Badger was a discussion about the scientific issues involved in improving troop vaccine coverage. Discussions were wide-ranging and interesting, e.g. nonspecific immune enhancements, but there was not much data. Carl Alving was our in-house adjuvant expert, and a participant in our discussion. [Dr. Alving first told GAO he did not have any role in the gulf war vaccine deliberations, then minimized his involvement.] We discussed using liposomes, but they didn't have enough. You have to go to war with what you have, not novelties that don't have your full confidence.

2) " Adjuvants discussion and recommendations. Discussion of adjuvants was limited. Its one thing to discuss interesting phase 1 research, quite another to apply it to short term shortages. In the long run they can be of potential use. But scientific inference doesn't lead to immediate military operations. Some in the group were willing to jump out and use everything. (She refused to say who.) Our group advised the Surgeon General who in turn worked with the JCS. There was not any data on what happens to people getting the anthrax and botulism vaccines at the same time. But we had to do it.

3) "Safety issues. There was little discussion of long term safety issues. They were thinking short term and immediate. Generally inactive vaccines don't have a problem. They used inactive antigens. But there were a lot of discussions regarding GMP [Good Manufacturing Practice] issues. For instance, they had trouble finding the exact same fermenter. Getting approval for a new one could take FDA 30 months. They went ahead started production with it and got retroactive approval. Anthrax vaccine is stable for up to 20 years if kept at right cool temperature." (DI-9)

NOTE: In a DOD Badger document File 120396_sep96_decls10_0002.txt, Subject: Desert Shield Biological Warfare HOC Working Group, the following statement is found: "It was reported that the individuals from logist___ USAMRIID, were expected back from theater today with the ___ anthrax and botulinum vaccines, antitoxin, ribavirin and centoxin. While in theater the items were under refrigeration; however, there was a report that the refrigerator failed to operate for a period of time and possibly these items

were damaged. The items will be re___ to USAMRIID and a determination made with regard to the disposition." (Appendix 3)

GAO notes state, "Anna Johnson-Winnegar played a major role in Project Badger, leading the effort seeking the urgent assistance of vaccine manufacturers. She sat in on most of the Project Badger meetings addressing BW defenses. Our interview with her revealed several contradictions. At first she said they had limited discussion about adjuvants, but then added that discussions were wide ranging and interesting, e.g. nonspecific immune enhancements, but there was not much data to base a decision. Alving, she said, was their in-house adjuvant expert, and a participant in their discussions. Some in the group felt is was one thing to discuss interesting Phase 1 research, quite another to apply it to short term shortages, ***but others were willing to jump out and use everything. She declined to tell us who advocated pushing forward the use of experimental vaccines."*** *(10)*

April 23, 1998 GAO meeting with General Ronald Blanck, Surgeon General of the Army, a discussion on the deliberations, decision making of DOD on vaccine production and administration for the Persian Gulf War. GAO summarized Gen Blanck's recollection:

1) "One manufacturer, Michigan for both botulism and anthrax vaccine. We had a fair amount of anthrax vaccine but only a small amount for botulism (BT). However, we found Iraqis might have F and G strains so we contracted with Porton to make them. To best of his knowledge none were administered. We got it but didn't use it. Everything we used was from Michigan. Salk at Swiftwater had the capacity to help produce, but got nothing from them. He got NIH to approve NCI use.

2) "Novel Adjuvants Use. Blanck recalled no discussion of boosting immunogenicity with novel adjuvants. He was certain nothing was added to the products at Michigan. They decided to not do anything outside of the FDA. The anthrax vaccine used alum as an adjuvant.

3) "Who else should GAO interview. We should talk to Winnegar and Collis as planned. **Collis headed oversight for Badger and vaccine efforts**..." (11)

The following GAO statement summarized the failed attempts to interview Peter Collis. ***"Peter Collis, the chairman of the tri-service task force, Project Badger, repeatedly declined to talk to us.*** *First he said he could not meet unless he had the classified project summary to ensure his recall was accurate. We said we could provide those. Then he said as a civilian without a clearance he could not look at the notes. [GAO could proceed with process to obtain a temporary clearance for him.] Then he called declining one last time saying he really didn't know much. However, the Project Badger notes clearly show him to be at the hub of all the discussions, and that he conducted the briefings about the committees recommendations."* (12)

September 11, 1998 GAO exit Conference with DOD officials. GAO investigators record:

1) "We presented a summary our principal findings of our job on Squalene and Gulf War Illnesses, 713014. DOD officials stated that **if the independent researchers have developed a good test for squalene antibodies, there was no reason to wait for publication. The researchers could share it with DOD and they could cooperate on further research and development concerning squalene and Gulf War illness.** This could be done through a CRADA which would protect the rights of the independent researchers. DOD would like to validate the test, particularly its specificity.

2) " DOD officials again acknowledged that they had the know how to develop such an assay and could have tested for squalene antibodies but did not... They stated that DOD could do the screening for antibodies to squalene for veterans who are ill along with a larger battery of tests, but they would have to think through the health administration consequences because they didn't want to do screening if they were not prepared to act on the results. Colonel Takafuji concluded that the questions raised by the independent researchers are going to come back to DOD." (13)

Section Two

The Stonewalling and Obfuscation

March, 1999 GAO presented to Metcalf their findings (GAO/NSIAD-99-5). GAO recommended DOD not wait for the peer-review and publication process, but take immediate action to: **"conduct research designed to replicate or dispute the independent research results** that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans." Surprisingly, DOD's comments regarding the GAO recommendations, contained in the report, **accused GAO of being "scientifically and fiscally irresponsible," even though their own officials had stated there was no reason to wait for publication.** (14) The GAO report stated, "Safety concerns have been cited regarding the use of novel adjuvant formulations in vaccines, including squalene, and the associated adverse reactions. It has also been suggested that the safety of vaccines containing these formulations must be evaluated in conservative ways." (GAO/NSIAD-99-5 Page 3)

May 13, 1999 Congressman Metcalf wrote Secretary of Defense William Cohen challenging DOD's refusal to carry out the GAO recommendations, and encouraging DOD to get to the truth by doing the research necessary to validate or dispute the Tulane test results. (Appendix 4)

May 24, 1999 Dr. Carl Alving called Dr. Robert Garry of Tulane, and indicated his "purely scientific" interest in Dr. Garry's work. Dr. Alving also asked to review a draft of the manuscript on anti-squalene antibodies which was subsequently published. Dr. Garry agreed to fax him a copy of the in progress work for his personal review, requesting that he not circulate the copy. **Dr. Garry was not made aware of Dr. Alving's intent to circulate the paper and publicly subject it to scathing reviews as published on the DOD website prior to publication.** (Appendix 5)

May 25, 1999 Dr. Russell Wilson of Autoimmune Technologies, Tulane's exclusive licensee for the anti-squalene antibodies technology, sent a letter to Dr. Carl Alving sharing information, and offering to provide information regarding the ASA (anti-squalene antibody) assay and research with DOD. (Appendix 6)

May 28, 1999 Dr. Sue Bailey, Assistant Secretary of Defense for Health Affairs, provided GAO the DOD's final response to the March, 1999 report. She stated, "Our position and the concerns expressed in our comments to the draft report have not changed . . . The test methods proposed by the investigators at Tulane University need to be reviewed and validated by other scientists." ***DOD would not take action until the peer-reviewed publication process was complete.*** (Appendix 7)

Summer 1999 An anonymously written DOD memo was obtained by the defense team representing five young Marines at Twenty-Nine Palms who were being court-martialed for their refusal of the anthrax vaccine.

The six page document entitled, "Issues Relating to Antibodies to Squalene" was a scathing review by Dr. Carl Alving and Dr. Matyas of the unpublished work of Dr. Garry and his colleague Dr. Pamela Asa. It discussed the phone calls of May 24 and 25 between Dr. Alving and Drs. Garry and Wilson. With absolutely no proof, it accused Drs. Garry and Asa of an apparent anti-military agenda. **It concluded by stating "There is an obvious need for independent in-house research by the Army to examine the issues and implications, if any, of antibodies to squalene." Attached was a chart detailing a three year study, with a total cost of $1,260,834.00.** (Appendix 8)

July 23, 1999 Dr. Bailey responded to Metcalf's May 13, 1999 letter to Secretary Cohen. Once again she commented, " The Department's position and concerns have not changed from those published as Appendix VI of the GAO report." (Appendix 9)

September 27, 1999 Metcalf letter to Secretary Cohen. Metcalf replied, " . . . because of your department's years of research in this area, I ask that you reconsider and proceed with the GAO recommendations. Your current position of waiting for the completion of the peer review and publication process does not recognize the vast amount of research that the DOD has already accomplished regarding adjuvant formulations containing squalene. **The men and women who served honorably and are suffering from Gulf War Illnesses deserve truthful answers and *immediate action.*"**(Apdx. 10)

October 25, 1999 Because of DOD's refusal to cooperate with GAO recommendations, Congressman Metcalf asked for congressional intervention. With the help of Congressman George Nethercutt, the House Report to H.R. 2561, the Fiscal Year 2000 Department of Defense Appropriations Bill, included language instructing DOD to develop and/or validate the assay to test for the presence of squalene antibodies. This legislative action was signed into law by the President on October 25. (Appendix 11)

November 5, 1999 Metcalf received a reply to his September 27 letter from Secretary Cohen. While stating: "The Department's position has been consistent and remains unchanged," he went on to inform Congressman Metcalf that **a DOD investigator** has been funded to "pursue a study to determine the feasibility of developing a test for antibodies to squalene." (Appendix 12)

Although Secretary Cohen did not identify the DOD investigator, GAO discovered that DOD had awarded the study to Dr. Carl Alving. The project was not designed to replicate or dispute theTulane findings as had been recommended by GAO, but to develop a different means of testing for antibodies to squalene. (Appendix 13)

January 2000 DOD provided some members of Congress a report titled, "Development and Validation of an Assay to test for the Presence of Squalene Antibodies." It stated, "This Report has been prepared in response to a requirement of the 106th Congress, House of Representatives, Report 106-244, 2000 Department of Defense Appropriations Bill." It acknowledged that DOD had funded a DOD researcher to "determine the feasibility of developing a test for antibodies to squalene." **It did not suggest a collaborative effort with Dr. Garry and his colleagues at Tulane to save valuable time for those who are suffering from Gulf War Illnesses, even though the researchers at Tulane had expressed their willingness to assist.** (Appendix 14)

January 31, 2000 Congressman Metcalf was joined by nine colleagues requesting DOD do an objective analysis of "Antibodies to Squalene in Gulf War Syndrome" - the peer-reviewed article published in the February 2000 issue of *Experimental and Molecular Pathology* by Drs. Asa, Cao and Garry. **The question from Congress was**

clear, "Given the published article, it seems prudent to use the assay if it could help sick Gulf War era veterans. Do you agree?" (Appendix 15)

February 25, 2000 Congressman Metcalf sent a strong letter to Secretary Cohen asking for immediate action to remove misleading information from the DOD's official Anthrax Vaccination Inoculation Program (AVIP) website regarding the peer-reviewed, published article on squalene antibodies. Earlier in the week, the information had been discovered, prior to receipt of the DOD's official reply to the January 31 letter. (Appendix 16)

February 28, 2000 The official DOD response to the January 31 letter was delivered to Congressman Metcalf's office. *Most of the information provided was based on a review of the early draft,* not the published study which included significant changes. The half-page critical analysis of the peer-reviewed article was anonymously written, with no indication of the author's professional credentials to conduct and provide the review. DOD did not address the congressional question regarding the potential use of the assay to help sick Gulf War era veterans. (Appendix 17)

March 3, 2000 Congressman Metcalf challenged Secretary Cohen to halt the obfuscation campaign that DOD was waging concerning the issues surrounding antibodies to squalene research. Metcalf provided ample evidence to demonstrate his conclusion. (Appendix 18)

March 27, 2000 On behalf of Secretary Cohen, Dr. Sue Bailey responded to Congressman Metcalf's February 25 and March 3 letters. She acknowledged needed modifications on the DOD AVIP website to more objectively reflect the Tulane research. She also informed Metcalf that the Armed Forces

Epidemiological Board (AFEB) would convene a subcommittee of experts to review and critique the published article in response to Congressman Metcalf's March 3 letter. (Appendix 19)

June 2000 An exchange of letters in *Experimental and Molecular Pathology*. Dr. Carl Alving and Dr. John Grabenstein submitted a critique of the Tulane research, and Drs. Asa, Cao and Garry co-authored the response. The journal Editorial Note made the

following statement: "New findings require confirmation within the bounds of comparability. This is as true for methodology as it is for the data produced from a particular study. This exchange of letters ...relates to methodology. **Drs. Alving and Grabenstein offer no data against the conclusions of Asa et al.** (Appendix 20)

August 10, 2000 Congressman Metcalf was presented the DOD ' objective analysis' of the article "Antibodies to Squalene in Gulf War Syndrome" by an Armed Forces Epidemiological Board subcommittee of experts. They concluded unanimously that the research reported in the paper does not support its claim that the laboratory test created by Dr. Garry at Tulane may identify persons ill with Gulf War Syndrome. **However, on the last page of the report, they state, " Whatever the paper's flaws and since the AFEB cannot exclude the remote possibility that the authors have identified a laboratory means of distinguishing persons with possible Gulf War Syndrome (GWS) from all others, replicability becomes the major unresolved issue...Therefore we recommended that a suitable test of replicability be done in cooperation with the authors..."** They go on to state, **" ... we are trying to ... get quickly and inexpensively to a more meaningful bottom line: does the ASA assay clearly, reliably and unequivocally distinguish people with GWS from all others, and, if so, with what specificity and sensitivity?"** (Appendix 21)

Section Three

FDA Testing Reveals Squalene in Anthrax Vaccine

For over a year, the DOD has been contracting with SRI International to test for squalene in vials of the anthrax vaccine preparations which have been and are being given to military personnel. For some time, DOD documents have made two claims regarding squalene:

1) The FDA verified that none of the vaccines used during the Gulf War contained squalene as an adjuvant; and

2) they have found NO squalene in their testing of anthrax vaccine lots. (Appendix 13 and 22)

Documents on the DOD AVIP website from SIR International confirm their tests revealed no squalene in the anthrax vaccine sent to them for analysis. (Example: Appendix 23)

January 31, 2000 Congressman Metcalf wrote the FDA asking them to confirm the following DOD statement made to Congress, "The FDA verified that none of the vaccines used during the Gulf War contained Squalene as an adjuvant." (Appendix 24)

March 20, 2000 The FDA responded to Congressman Metcalf and provided their official position. "In fact FDA did verify to the Senate Special Investigations Unit on July 23, 1997, in a telephone conversation with Committee staff of the SIU, not with DOD, **that neither the licensed vaccines known to be used in the Gulf War, nor the one investigational product known to have been used,** contained squalene as an adjuvant in the formulations on file with FDA."

Most importantly, the FDA closed their letter with the following statement: "Very limited testing of Anthrax Vaccine, Adsorbed, conducted by CDER in 1999 determined that there were only trace amounts of squalene in the lots tested ... (Appendix 25)

Dr. Dorothy Lewis of Baylor College of Medicine sent a letter to Congressman Metcalf explaining that the test used by FDA which found low levels of squalene in Anthrax vaccine samples is a "much more sensitive technique" than the one used by DOD. ***(Why would DOD use a less sensitive test procedure?)***

Dr. Lewis determined, ***"The real issue is whether squalene in parts per billion was added to the vaccine preparations given to the military, as well as whether this concentration of squalene could alter the immune response."***

While acknowledging the need for research to respond to the findings, she stated, ***"it is possible that very small amounts of a biologically active product could induce an immune response, either to the molecule itself or it could boost immune responses to other agents in the mixture."*** (Appendix 26)

CONCLUSION

1. Despite numerous denials by the Department of Defense, FDA has found squalene in the Anthrax Vaccine in limited testing. This vaccine is still being forced upon our active military duty personnel. Immediate action must be taken to halt the current AVIP (Anthrax Vaccination Immunization Program) until this matter is resolved. Aggressive research must be undertaken to determine the source of the squalene, if it could alter the immune response, and the potential health consequences to those who have been vaccinated, both during the Gulf War, and as a result of the mandatory, force-wide AVIP.

2. The recommendation of the Armed Forces Epidemiological Board subcommittee that, "...a suitable test of replicability be done in cooperation with the authors..." mirrors the findings of the GAO over eighteen months ago- - "DOD should conduct research designed to replicate or dispute the independent research results that revealed the presence of squalene antibodies in the blood of ill Gulf War-era veterans."

3. Congress should take immediate action to review the findings of the GAO and the Armed Services Epidemiological Board, and provide independent oversight for the immediate implementation of their recommendations. The Department of Defense has wasted years in their determined effort to stonewall this issue. The researchers at Tulane are willing to work with DOD to pursue answers for those suffering from Gulf War Illnesses. Within a few months, and for a small investment of money, important knowledge will be acquired that may offer real hope. For the men and women who honorably serve this nation, there is no valid reason for further delay.

All footnotes are references to General Accounting Office (GAO) background working documents for GAO final report "Gulf War Illnesses: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved, (GAO-NSIAD-99-5)March 1999.

1. DI-23
2. DI-2
3. DI-23
4. F-5
5. DI-20
6. DI-23
7. DI-7
8 DI-23
9. DI-9
10. DI-23
11. DI-8
12. DI-23
13. DI-13
14. DI-13

Bolding and italics added for emphasis.

Appendices can be requested from the office of:
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