CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER

INFORMED CONSENT

Study Title: First-in-Human Safety and Immunogenicity Evaluation of an Intramuscular *Campylobacter jejuni* Conjugate Vaccine (CJCV2) with and without Army Liposome Formulation containing QS-21 (ALFQ)

Investigator:
Dr. Robert Frenck

Contact Info:

Industry Protocol #:
DMID 19-0003

Drug Name:
Campylobacter jejuni Conjugate Vaccine (CJCV2), Army Liposome Formulation containing QS-21 (ALFQ)

Funding:
Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)

KEY INFORMATION:

Reason for Research Study:
We are testing an experimental vaccine (CJCV2) in healthy adults against a germ called *Campylobacter*. *Campylobacter* is a common cause of diarrhea that may be severe in young children, the elderly, and people who have other health problems. Ways to prevent infection with *Campylobacter*, such as with a vaccine, are needed because the bacteria are becoming resistant to many of the antibiotics, we have to treat the infection.

A vaccine mirrors infection and causes our body to produce an immune response that may protect us from becoming sick if we were exposed to the bacteria in the future. To increase the effect of the vaccine, we also will be using an adjuvant called ALFQ. *Adjuvants* are substances that boost the body's immune response.

To date, ALFQ has been administered to people participating in a trial to evaluate a vaccine against malaria. The main reasons for this research study are to find out if CJCV2 and ALFQ are safe and see how strong of an immune response our body makes to the vaccine.

The current trial will provide additional experience with ALFQ as a vaccine adjuvant. This is the first time that CJCV2 and ALFQ will be given together in humans. The main reasons for this research study are to find out if CJCV2 and ALFQ are safe and see how strong of an immune response our body makes to the vaccine.

Your participation in the study will last for about 15 months. We will give you a handout that tells you what will happen at each study visit; but briefly, during the study you will:

- Have 17 visits: Come to the clinic for at least 9 visits, including a screening visit to see if you are eligible to be in the study (you will have a physical exam and we will review your health history) and for 8 visits you have the option to either come to the clinic or have virtual visits via the phone.
- Receive 3 vaccine shots (each about a month apart)
    - Half of the people in a cohort will receive vaccine plus ALFQ and the other half will receive vaccine alone. This will be decided randomly (like a flip of a coin)
    - If female, you will have a urine pregnancy test before each vaccine dose
- Give a blood sample 9 times and bring in a stool (poop) sample 4 times
- Will be contacted by the study staff at least 2 times after the last vaccination happens

Possible Risks from Being in This Study:
You may have some pain or bruising at the site your blood was collected. Very rarely, you could

feel faint or have a clot or infection. We take all precautions to prevent these risks.

The vaccine will be given to you as a shot. If you have a reaction to the vaccine, the things people commonly experience at the injection site are:

• Pain or tenderness • Itching or warmth	• Bruising • Pain	• Redness or swelling

Other possible reactions in the few days after receiving the vaccine include:

• Tiredness • General unwell feeling • Headache	• Body aches, muscle/joint pain • Fever, chills/shivering/sweating • Nausea, vomiting

In very rare cases, some people who have received vaccines with adjuvants have developed illnesses where their immune system harms their own body (autoimmune). These illnesses have also developed in people who have not received any vaccines. We do not know if the study vaccine or ALFQ can cause autoimmune diseases, but we will watch you very closely for this during the study.

Because the risks of the vaccine to a pregnant or nursing woman or fetus are unknown, pregnancy is an exclusion and women of childbearing potential will be counseled against becoming pregnant during their participation in the study.

Benefits to Participate:
There is no direct benefit to you for being in this study. We hope the study will teach us more about the vaccine and if further evaluation of the vaccine is warranted.

Other Options:
Your participation in this study is completely voluntary. If you decide to be in this study, you may change your mind at any time during the study and you can stop being in the study; we will still take good care of you. Take all the time you need to make your choice. You can ask questions at any time. It is also okay to ask more questions after you decide to be in the study. Refusal to participate will involve no penalty or loss of benefits you already had.

Stopping the Study Early:
If you decide to stop being in the study, we still will ask you to come for one more visit to talk with you. Certain procedures will be done if you agree.

If new information about the vaccine or adjuvant is discovered, you will be told so that you can decide if you want to remain in the study.

During the study it also is possible that, for your safety, you are removed from the study, or the study even may be stopped.

After your last visit, no additional data will be collected. However, data already collected from

you will be saved and may be included in the analysis.

Cost to Participate:
You will not be responsible for the cost of tests performed or vaccines administered as part of the study.

Payment:
If you agree to take part in this research study, we will pay the first 6 participants in each cohort up to $1765.00 and for the main cohort (remaining 14 participants) up to $1650.00 for your time and effort. The handout you receive will show you how much you will be reimbursed for each visit. You will receive payment for this study in the form of a reloadable debit card (Clincard) that will be explained to you. Because you are being paid for your participation, you will need to complete a W-9 form for income tax reporting. As part of completing the W-9, you will need to provide your social security number (SSN). The W-9 will be given to the Cincinnati Children's business office and not kept in your study chart.

ADDITIONAL STUDY INFORMATION:

Who Should Not Be in the Study:
You cannot be in this study if you:

- Are younger than 18 years of age or already had your 51st birthday.
- Have problems fighting off infections or have Hepatitis B, C, or HIV.
- Are a female who is pregnant, breastfeeding or planning to become pregnant
- Have a personal or first-degree relative (parent or sibling) with a history of autoimmune or inflammatory conditions, such as lupus, rheumatoid arthritis, Guillain-Barre Syndrome, or inflammatory bowel disease.
- In the past 3 years, had a *Campylobacter* infection or a vaccine against *Campylobacter*.
- Have a history of allergies to compounds in the vaccine.
- Test positive for opiates on a urine drug screen.
- There are many other reasons why you cannot be in this study, and the study staff will review these with you.

To be in the study, you must sign this consent form. Also, you must be able to:

- Understand, agree, and comply with study procedures.
- Electronically complete the vaccine memory aid.
- Females need to avoid sexual relations that could result in pregnancy or use an acceptable form of birth control during the entire study.

Study staff will talk with you more about how to complete the electronic memory aid and explain what acceptable forms of birth control are.

Study Procedures:
You will get a handout so you will know what will happen at each study visit. The research staff will explain each visit to you. Study visits are briefly described below.

Screening Visit:

- We will ask questions to make sure you are healthy enough to be in the study. This may include asking your age, race, ethnic group, any past or present illnesses,

hospitalizations, surgeries, and medicines you are taking.

- We will measure your blood pressure, temperature, and heart rate.
- We will perform a physical examination.
- We will collect your blood to test for:
  - Liver and kidney function, anemia, and infection fighting cells.
  - HLA-B27 is a test that looks for a type of protein on the surface of a white blood cell. This protein may increase your risk of getting certain autoimmune conditions. *
  - Hepatitis B, Hepatitis C, and HIV infection. *

  * If any of these tests are positive, you will be counseled by a qualified study staff about the results. You will also be given information about the disease, a chance to ask questions, and a list of doctors who are experts in these diseases. If you test positive for Hepatitis B, Hepatitis C, or HIV, the law requires that we reported the results to the local health authorities.
- Urine will be collected and tested for protein (a measure of kidney health).
- Urine will be tested for opiates
- You will be given a kit and instructions on collecting a baseline stool (poop).
- Females of child-bearing potential will have urine tested for pregnancy.

Vaccination Visits:
If no concerns are noted in the Screening Visit, you will be asked to return to the clinic for vaccination. The study will have up to 3 dose levels of vaccine. You will only be in one dose level called a “cohort”. The first cohort will receive “low dose” of vaccine, the second cohort will receive a “medium dose”, and the third cohort will receive the “high dose”. Each cohort will have 20 participants. You will receive 3 doses of vaccine given about 4 weeks apart. The vaccine is given as a shot in your shoulder muscle. Half of the subjects in each cohort will receive vaccine plus ALFQ and the other half will receive vaccine alone.

As this is the first time the vaccine has been given to humans; for each cohort, initially 6 participants will be vaccinated and then we will pause for at least 7 days. After the pause, if the participants are doing well, the remaining 14 participants will be vaccinated. After each cohort, a safety review will be conducted to decide if dosing of the next cohort at the next level of vaccine may begin.

Each cohort will be divided into 2 equal groups. Half of the people in a cohort will receive vaccine plus ALFQ and the other half will receive vaccine alone. This will be decided randomly (like a flip of a coin). Neither you nor the study staff will know which group you have been assigned to. If needed for treatment of a serious reaction, your study doctor will be able to find out what you received. You will need to remain in the clinic for 30 minutes after vaccination to ensure you are doing well.

Pregnancy Test: If you are a woman and able to have children, we will test your urine before each Vaccination Visit to be sure you are not pregnant.

Electronic Memory Aid: Starting on the day you receive the vaccine; you will be asked to record how you are feeling every evening for 7 days after each vaccination. Your information will be entered into a web-based computer program called an electronic memory aid. Study staff will teach you how to use the electronic memory aid. A digital thermometer and measuring ruler will be given to you. In case you experience problems with the electronic memory aide, you will also be given a paper copy of the form. The paper copy is to be completed only if you are unable to

use the electronic form.

During the 7 days, you will be asked to immediately call the study team if you;

- Have a severe reaction
- Need to seek medical care or are hospitalized
- Become pregnant, or
- Have any concerns

Post-Vaccination Visits:
At 7 days after each vaccine you will return to the clinic.

- We will ask questions about your health and medicines you are taking.
- We will collect blood to check your health and response to the vaccine.
- We will collect a stool sample from you and tell you about stool samples needed at future visits (as shown in the study handout).
- We will review your electronic memory aid information with you.

At 3 days (±1) and 15 days (±2) after each vaccine, you will either return to the clinic or have a post-vaccination visit virtually.

If visit is in the clinic:

- We will ask questions about your health and medicines you are taking.
- We may collect blood to check your health and response to the vaccine.
- We may collect a stool sample from you at certain visits (we will tell you).
- We will review your electronic memory aid information with you.

If visit is virtual:

- We will ask questions about your health and medicines you are taking.
- We will review your electronic memory aid information with you.

Blood and stool will be collected throughout the study. The blood and stool collection schedule, including the amounts of blood to be collected, are listed on your study handout.

ADDITIONAL RISKS OF PARTICIPATION:

Besides those listed previously, other potential risks are described below. Additionally, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Vaccine and Study Product Administration Risks:
Since this vaccine and adjuvant have not been tested together in humans, we do not know all the possible side effects. However, in a previous study that tested a very similar vaccine in 48 adults, there were no significant safety problems. The adjuvant is being tested in humans at another place. Because the testing just started, we do not know all the possible side effects. In another study, an adjuvant similar to the one we will use in this study was well-tolerated and the side effects were redness, swelling, pain, and tenderness at the injection site. There may be risks and side effects we do not know about right now.

A potential rare side effect of vaccines can be the development of Guillain-Barré syndrome (GBS). GBS is a rare neurological disease that can range from a very mild case with brief weakness to a severe case that could leave you paralyzed. Fortunately, most people recover completely, but some people can be paralyzed for a long time. Some strains of Campylobacter can also cause GBS. However, special care has been taken to ensure that the parts of *Campylobacter* associated with causing GBS are not in the vaccine.

Very rarely, people who have received vaccines with adjuvant have developed illnesses, sometimes serious, called autoimmune diseases, where their immune system harms their own body. These illnesses have also developed in people who have not received these vaccines. We do not know if the study vaccine can actually cause autoimmune diseases.

Rarely, vaccines and adjuvants can cause a severe allergic reaction within a few minutes to a few hours after vaccination. Signs of a severe allergic reaction can include hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, and weakness. We will observe you for reactions for 30 minutes after each vaccine and there will be medicines available to treat allergic reactions.

If I Have Questions About:

- This study, a study emergency, any research-related concerns, or complaints of injuries, you may call Dr. Frenck, the study doctor, or the Study Nurse Coordinator at

- Your rights as a research participant, you may call the Institutional Review Board (IRB) at . The IRB is a group of scientists and community members who make sure research meets legal and ethical standards.

Privacy:
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

You will be registered in the Cincinnati Children's Hospital Medical Center's (CCHMC) computer system as a research patient. We will keep a copy of this consent form in your research chart. To keep your information private and confidential, CCHMC and/or the study doctor will:

- Use code numbers instead of your name in your study chart
- Limit the people who can see your study records
- Not identify you in any records or articles published about the study findings

By signing this consent form, you are giving permission for parts of your medical and research records related to this study to be reviewed by:

- Cincinnati Children's Hospital Medical Center (CCHMC)
- The study doctor and CCHMC research staff who are part of the study
- The CCHMC Institutional Review Board and the Office for Research Compliance and Regulatory Affairs
- The sponsor: National Institutes of Health (NIH) or authorized representative
- The Department of Defense (DOD) or their representatives
- Your personal healthcare provider

The Food and Drug Administration (FDA) may review your records since they are in charge of studies of experimental, unapproved vaccines.

To help us protect your privacy, we have a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers can use this Certificate to legally refuse to give information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except for reporting of communicable diseases to State and local health departments.

The Certificate of Confidentiality:

- Will not be used to prevent disclosure to state or local authorities for information required by local or state law.
- Cannot be used for information in your medical records.
- Does not prevent disclosure of your information to the NIH, Food and Drug Administration (FDA), or federal funding agency.
- Does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research.

If you give your consent to release information to a medical care provider, an insurer, or other person to receive research information, then the researchers will not withhold that information.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov/ as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. The clinicaltrials.gov identifier is NCT#.

If you give your consent to release information to a medical care provider, an insurer, or other person to receive research information, then the researchers will not withhold that information. The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

If Injured While in the Study:
If you believe that you have been injured as a result of this research, you should contact Dr. Frenck as soon as possible to discuss the concerns. Treatment for injuries is available at Cincinnati Children's. If you go to the Emergency Room or to another hospital or doctor, it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form.

Cincinnati Children's follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government.

Return of Results:
Most tests done on samples or images obtained in research studies are only for research and have no clear meaning for healthcare. If the research with your information or samples gives results that do have meaning for your health, the researchers will contact you and ask you if you would like to know what they have found. You can say 'no' to hearing about the results at that time if you desire.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this research study, you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What Protected Health Information Will be Used and Shared During this Study?
Cincinnati Children's Hospital Medical Center (Cincinnati Children's) will need to use and share your PHI as part of this study. This PHI will come from:

- Your Cincinnati Children's medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnoses, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports

Who Will Share, Receive, and/or Use Your Protected Health Information in This Study?

- Staff at all the research study sites (including Cincinnati Children's)
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs

How Will You Know That Your PHI is Not Misused?
People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can You Change Your Mind?
You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI, you need to notify the study doctor in writing. Your request will be effective immediately and no new PHI about you will be used or shared. However, data and PHI that already have been shared, are in the process of

being shared, or are needed to maintain the integrity of the research at the time you withdraw your permission, still will be used.

Will This Permission Expire?
Unless you notify the study team, your permission will not expire.

Will Your Other Medical Care be Impacted?
By signing this document, you agree to participate in this research study and give permission to Cincinnati Children's to use and share your PHI for the purpose of this research study. If you refuse to sign this document, you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan, or eligibility of benefits will not be affected.

Storage and Use of Samples or Data in Other Research Studies (Future Research):
As part of this study, we are obtaining samples and information from you. We will collect and store extra samples of blood and stool for future research, Future research is research that is not part of this study and we do not know specifically the research that will be done. We collect these samples during this study so that the researchers may continue to study the body's responses to the vaccine, and to develop better vaccines or lab tests.

You are free to choose whether you want to participate in the Future Research, however, if you do not agree to extra samples for Future Research, you will not be eligible to take part in the vaccine trial.

These samples will be stored indefinitely at Cincinnati Children's or another facility that the National Institutes of Health chooses.

Samples and/or data may be shared with other collaborators at Cincinnati Children's, and possibly with outside collaborators who may be at another institution or for-profit company. Your samples and data will be coded, but researchers outside the institution will not be given information that can identify you. The code key with your ID number and name is kept in a secure (database/locked cabinet) by the investigator and study staff.

If information that could identify you is removed from your information or samples collected during this research, that information or those samples could be stored and used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

If you do not want your extra tubes of blood and stool to be collected and stored, you should not take part in this study. Samples will be used for research only. They will not be sold or used to make new cell lines. They may be used to help develop new vaccines, used in new or different laboratory tests, or used to study other infections. There will be no identifying information used in reporting or publications of any future testing results. The results of this testing will not be reported to you or your doctor and will not benefit you. Tissues or body fluids collected for this research may result in the development of a product that could be patented/licensed and sold. You will not be paid if this happens.

Genetic Testing:
At this time, we have no plans to do genetic research in this study. However, in the future this plan may change, and we would do genetic testing on your blood and/or stool samples. Any

genetic testing would be performed on samples from which your identity has been removed, and the study team will not provide the code to the people receiving your samples. The de-identified genetic testing information may be shared.

We may share your genetic information (data) through a “closed” database, also called a restricted data repository. NIH gives permission to other researchers to use your genetic information for research. To qualify, researchers must receive approval from NIH to access and use the research information. Types of secondary research using your data may be related to the research in this study or other types of research. Your individual data will not contain information that can easily identify you.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research, you will document your permission by signature below.

You will receive a copy of this signed document for your records.

_____
Printed Name of Research Participant

_____ _____
Signed Name of Research Participant Date

_____ _____
Signature of Individual Obtaining Consent Date