Investigational New Drug Application (IND)/Investigational Device Exemption (IDE) Information: Complete the following only if the protocol involves an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) under US Food and Drug Administration regulations.

IND/IDE Protocol? * (FDAAA)
Definition: Indicate if the protocol involves an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) under US Food and Drug Administration regulations (*Will not be made public - for administrative purposes only.*)

IND/IDE Grantor * (FDAAA)
Definition: FDA center to which the IND or IDE was submitted, i.e., Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER) for INDs; Center for Devices and Radiological Health (CDRH) for IDEs. Select one. (*Will not be made public - for administrative purposes only.*)

IND/IDE Number * (FDAAA)
Definition: Number assigned to an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE). (*Will not be made public - for administrative purposes only.*)
Examples: 22,333; BB1234

IND/IDE Serial Number (FDAAA)
Definition: Use the serial number from the first submission of the protocol to the IND or IDE. (*Will not be made public - for administrative purposes only.*)

Has Expanded Access? FDAAA
Definition: Indicate whether any non-protocol access is to be provided for the investigational drug or device. If so, an Expanded Access record should also be created for this IND/IDE.

Expanded Access Record FDAAA
Definition: The ClinicalTrials.gov identifier (NCT number) for the Expanded Access record associated with this study, specified if and only if "Yes" is specified for Has Expanded Access.

Human Subjects Review Submitted studies must have approval from a human subjects review board prior to the recruitment of the first patient. Appropriate review boards include an Institutional Review Board, an ethics committee or an equivalent group that is responsible for review and monitoring of this protocol to protect the rights and welfare of human research subjects. A study may be submitted for registration prior to approval of the review board so long as the study is not yet recruiting patients.

Review board information is desired but not required for trials associated with U.S. FDA Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications.

Review board information is required for internal administrative use and is not revealed to the public.

Board Approval * - provide information for only one review board, even for studies involving multiple boards

Board Approval Status *
Definition: Human subjects review board approval status. Select one.

- Request not yet submitted: review board approval is required but has not yet been requested
- Submitted, pending: review board approval has been requested but not yet granted
- Submitted, approved: review board approval has been requested and obtained
- Submitted, exempt: review board has granted an exemption in response to the approval request
- Submitted, denied: review board has denied the approval request
- Submission not required: the study does not require human subjects review

Board Approval Number * (required only if status is "Submitted, approved")
Definition: Number assigned by the human subjects review board upon approval of the protocol. May be ommitted if status is anything other than approved. If the human subjects review board does not assign numbers, please enter the date of approval in mm/dd/yyyy format.

Board Name * (required unless status is "Submission not required")
Definition: Full name of the approving human subjects review board.
Example: National Institutes of Health - NCI - IRB #1

Board Affiliation * (required only if status is "Submitted, approved" or "Submitted, exempt")
Definition: Official name of organizational affiliation of the approving human subjects review board. (Limit: 255 characters)
Example: US National Institutes of Health

Board Contact * (required only if status is "Submitted, approved" or "Submitted, exempt")
Definition: Contact information for the human subjects review board.

- Phone (or Email required): * Use the format 123-456-7890 within the United States and Canada. Otherwise, provide the country code.
- Ext: Phone extension, if needed
- Email (or Phone required): * Electronic mail address.
- Address: Mailing address for the board, including street address, city, state or province, postal code, and country.

Data Monitoring Committee?
Definition: Indicate whether a data monitoring committee has been appointed for this study. The data monitoring committee (board) is a group of independent scientists who are appointed to monitor the safety and scientific integrity of a human research intervention, and to make recommendations to the sponsor regarding the stopping of the trial for efficacy, for harms or for futility. The composition of the committee is dependent upon the scientific skills and knowledge required for monitoring the particular study.

Plan to Share Data?
Definition: Indicate whether there is a plan to make individual participant data (IPD) collected in this study available. Select Yes/No/Undecided.

Description
Definition: If IPD collected in this study are to be made available, briefly describe what participant data are to be shared, when data will be available, and how the data may be obtained. An explanation may be provided for why IPD will not be shared. (Limit: 1000 characters)

Oversight authority information is displayed on ClinicalTrials.gov. For IND/IDE protocols, Oversight Authority is filled in automatically with "United States: Food and Drug Administration."

Oversight Authorities *
Definition: The name of each national or international health organization with authority over the protocol. Use the following format for each authority:

country: organization name

Examples:
United States: Institutional Review Board
United States: Food and Drug Administration
Germany: Federal Institute for Drugs and Medical Devices
Australia: Therapeutic Goods Administration

▼ 5. Study Description

Brief Summary * **FDAAA**
Definition: Short description of the protocol intended for the lay public. Include a brief statement of the study hypothesis. (Limit: 5000 characters)

Example: The purpose of this study is to determine whether prednisone, methotrexate, and cyclophosphamide are effective in the treatment of rapidly progressive hearing loss in both ears due to autoimmune inner ear disease (AIED).

Detailed Description
Definition: Extended description of the protocol, including more technical information (as compared to the Brief Summary) if desired. Do not include the entire protocol; do not duplicate information recorded in other data elements, such

as eligibility criteria or outcome measures. (Limit: 32,000 characters)

For Patient Registries: Also describe the applicable (1) registry procedures and (2) other quality factors (e.g., third party certification, on-site audit). In particular, summarize any procedures implemented as part of the patient registry, including, but not limited to the following:

- Quality assurance plan that addresses data validation and registry procedures, including any plans for site monitoring and auditing.
- Data checks to compare data entered into the registry against predefined rules for range or consistency with other data fields in the registry.
- Source data verification to assess the accuracy, completeness, or representativeness of registry data by comparing the data to external data sources (e.g., medical records, paper or electronic case report forms, or interactive voice response systems).
- Data dictionary that contains detailed descriptions of each variable used by the registry, including the source of the variable, coding information if used (e.g., World Health Organization Drug Dictionary, MedDRA), and normal ranges if relevant.
- Standard Operating Procedures to address registry operations and analysis activities, such as patient recruitment, data collection, data management, data analysis, reporting for adverse events, and change management.
- Sample size assessment to specify the number of participants or participant years necessary to demonstrate an effect.
- Plan for missing data to address situations where variables are reported as missing, unavailable, "non-reported," uninterpretable, or considered missing because of data inconsistency or out-of-range results
- Statistical analysis plan describing the analytical principles and statistical techniques to be employed in order to address the primary and secondary objectives, as specified in the study protocol or plan.

▼ 6. Conditions and Keywords

Conditions or Focus of Study * FDAAA
Definition: Primary disease or condition being studied, or focus of the study. Diseases or conditions should use the National Library of Medicine's Medical Subject Headings (MeSH) controlled vocabulary when possible.

Keywords
Definition: Words or phrases that best describe the protocol. Keywords help users find studies in the database. Use NLM's Medical Subject Heading (MeSH) controlled vocabulary terms where appropriate. Be as specific and precise as possible. Avoid acronyms and abbreviations.

▼ 7. Study Design

Interventional Study Design * (FDAAA)
Definition: Primary investigative techniques used in the protocol. Select the most appropriate term describing the protocol from each of the following data elements.

Primary Purpose FDAAA - reason for the protocol

- Treatment: protocol designed to evaluate one or more interventions for treating a disease, syndrome or condition
- Prevention: protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition
- Diagnostic: protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition
- Supportive Care: protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects or mitigate against a decline in the subject's health or function. In general, supportive care interventions are not intended to cure a disease.
- Screening: protocol designed to assess or examine methods of identifying a condition (or risk factors for a condition) in people who are not yet known to have the condition (or risk factor).
- Health Services Research: protocol designed to evaluate the delivery, processes, management, organization or financing of health care.
- Basic Science: protocol designed to examine the basic mechanism of action (e.g., physiology, biomechanics) of an intervention.
- Other: describe in Detailed Description.

Study Phase * FDAAA

Definition: Phase of investigation, as defined by the US FDA for trials involving investigational new drugs. Use "N/A" for trials that do not involve drug or biologic products. Select only one.

N/A: for trials without phases (e.g., trials of devices or behavioral interventions)

Phase 0: exploratory trials, involving very limited human exposure, with no therapeutic or diagnostic intent (e.g., screening studies, microdose studies). See FDA guidance on exploratory IND studies for more information.

Phase 1: includes initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients

Phase 1/Phase 2: for trials that are a combination of phases 1 and 2

Phase 2: includes controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks

Phase 2/Phase 3: for trials that are a combination of phases 2 and 3

Phase 3: includes expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate

the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling

Phase 4: studies of FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use

Intervention Model (FDAAA) (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - intervention assignments

- Single Group: single arm study
- Parallel: participants are assigned to one of two or more groups in parallel for the duration of the study
- Cross-over: participants receive one of two alternative interventions during the initial phase of the study and receive the other intervention during the second phase of the study
- Factorial: two or more interventions, each alone and in combination, are evaluated in parallel against a control group

Number of Arms (FDAAA)
Definition: Number of intervention groups (enter 1 for single-arm study).

Masking (FDAAA) (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - knowledge of intervention assignments

- Open: no masking is used. All involved know the identity of the intervention assignment.
- Single Blind: one party, either the investigator or participant, is unaware of the intervention assignment; also called single-masked study.
- Double Blind: two or more parties are unaware of the intervention assignment

If Single Blind or Double Blind is selected, check the role(s) that are to be masked: Subject, Caregiver, Investigator or Outcomes Assessor.

Allocation (FDAAA) (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - participant assignment to intervention group

- N/A: single arm study
- Randomized Controlled Trial: participants are assigned to intervention groups by chance
- Nonrandomized Trial: participants are expressly assigned to intervention groups through a non-random method, such as physician choice

Study Classification (formerly Endpoint) - type of primary outcome or endpoint that the protocol is designed to evaluate. Select one.

- N/A: not applicable

- Safety: show if the drug is safe under conditions of proposed use
- Efficacy: measure of an intervention's influence on a disease or health condition
- Safety/Efficacy
- Bio-equivalence: scientific basis for comparing generic and brand name drugs
- Bio-availability: rate and extent to which a drug is absorbed or otherwise available to the treatment site in the body
- Pharmacokinetics: the action of a drug in the body over a period of time including the process of absorption, distribution and localization in tissue, biotransformation, and excretion of the compound
- Pharmacodynamics: action of drugs in living systems
- Pharmacokinetics/dynamics

Enrollment (Target or Actual Number of Subjects) FDAAA
Definition: Number of subjects in the trial. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected enrollment, updating the number as needed over the course of the study. Upon study completion, change Type to Actual and update the enrollment if necessary.

Observational Study Design

Observational Study Model * - primary strategy for subject identification and follow-up. Select one.

- Cohort: group of individuals, initially defined and composed, with common characteristics (e.g., condition, birth year), who are examined or traced over a given time period
- Case-control: group of individuals with specific characteristics (e.g., conditions or exposures) compared to group(s) with different characteristics, but otherwise similar
- Case-only: single group of individuals with specific characteristics
- Case-crossover: characteristics of case immediately prior to disease onset (sometimes called the hazard period) compared to characteristics of same case at a prior time (i.e., control period)
- Ecologic or community studies: geographically defined populations, such as countries or regions within a country, compared on a variety of environmental (e.g., air pollution intensity, hours of sunlight) and/or global measures not reducible to individual level characteristics (e.g., health care system, laws or policies median income, average fat intake, disease rate)
- Family-based: studies conducted among family members, such as genetic studies within families or twin studies and studies of family environment
- Other - explain in Detailed Description

Time Perspective * - temporal relationship of observation period to time of subject enrollment. Select one.

- Prospective: look forward using periodic observations collected predominantly following subject enrollment
- Retrospective: look back using observations collected predominantly prior to subject selection and enrollment
- Cross-sectional: observations or measurements made at a single point in time, usually at subject enrollment
- Other - explain in Detailed Description

Biospecimen Retention - select one

- None Retained - no samples retained
- Samples With DNA - samples retained, with potential for extraction of DNA from at least one of the types of samples retained (e.g., frozen tissue, whole blood)
- Samples Without DNA - samples retained, with no potential for DNA extraction from any retained samples (e.g., fixed tissue, plasma)

Biospecimen Description
Definition: Specify all types of biospecimens to be retained (e.g., whole blood, serum, white cells, urine, tissue). (Limit: 1000 characters)

Enrollment (Target or Actual Number of Subjects) *
Definition: Number of subjects in the trial. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected enrollment, updating the number as needed over the course of the study. Upon study completion, change Type to Actual and update the enrollment if necessary.

Target Follow-Up Duration *
Definition: For Patient Registries, the anticipated time period over which each participant is to be followed. Provide a number and select a unit of time (years, months, weeks, days).

Number of Groups/Cohorts *
Definition: Number of study groups/cohorts. Enter 1 for a single-group study. Many observational studies have one group/cohort; case control studies typically have two.

▼ 8. Arms, Groups and Interventions

Arms: For interventional studies specify the arms, corresponding to Number of Arms specified under Study Design (for single-arm studies, the following data elements are optional).

Arm Label * (FDAAA) - the short name used to identify the arm. (Limit: 62 characters)
Examples:

- Metformin
- Lifestyle counseling

- Sugar pill

Arm Type * (FDAAA) - select one

- Experimental
- Active Comparator
- Placebo Comparator
- Sham Comparator
- No intervention
- Other

Arm Description (FDAAA) - brief description of the arm. This element may not be necessary if the associated intervention descriptions contain sufficient information to describe the arm. (Limit: 999 characters)

Groups: For observational studies specify the predefined participant groups (cohorts) to be studied, corresponding to Number of Groups specified under Study Design (for single-group studies, the following data elements are optional). Do not use this section to specify strata (Detailed Description can be used for that purpose, if desired).

Group/Cohort Label * - the short name used to identify the group. (Limit: 62 characters)
Examples:

- Statin dose titration
- Chronic kidney disease, no anemia
- No treatment

Group/Cohort Description Definition: Explanation of the nature of the study group (e.g., those with a condition and those without a condition; those with an exposure and those without an exposure). Note that the overall study population should be described under Eligibility. (Limit: 1000 characters)

Interventions: For all studies, and for expanded access records, specify the associated intervention(s). For interventional studies, at least one intervention must be specified. For observational studies, specify the intervention(s)/exposure(s) of interest, if any.

Intervention Type * FDAAA - select one per intervention

- Drug (including placebo)
- Device (including sham)
- Biological/Vaccine
- Procedure/Surgery
- Radiation
- Behavioral (e.g., Psychotherapy, Lifestyle Counseling)
- Genetic (including gene transfer, stem cell and recombinant DNA)
- Dietary Supplement (e.g., vitamins, minerals)
- Other

Intervention Name * FDAAA - for drugs use generic name; for other types of interventions provide a brief descriptive name. (Limit: 200 characters)

For investigational new drugs that do not yet have a generic name, a chemical name, company code or serial number may be used on a temporary basis. As soon as the generic name has been established, update the associated protocol records accordingly.

For non-drug intervention types, provide an intervention name with sufficient detail so that it can be distinguished from other similar interventions.

> **Other Names** - list other names used to identify the intervention, past or present (e.g., brand name for a drug). These names will be used to improve search results in ClinicalTrials.gov. (Limit: 200 characters per name)

Intervention Description (FDAAA) - cover key details of the intervention. Must be sufficiently detailed to distinguish between arms of a study (e.g., comparison of different dosages of drug) and/or among similar interventions (e.g., comparison of multiple implantable cardiac defibrillators). For example, interventions involving drugs may include dosage form, dosage, frequency and duration. (Limit: 1000 characters)
Example:

> 50 mg/m2, IV (in the vein) on day 5 of each 28 day cycle. Number of Cycles: until progression or unacceptable toxicity develops.

[Arm or Group]/Intervention Cross-Reference * (FDAAA) - if multiple Arms/Groups have been specified for the study, edit the Cross-Reference, checking boxes to indicate which of the Interventions are to be administered under each Arm/Group of the study.

▼ 9. Outcome Measures

NOTE: When Results are added to a record, outcome measures are transferred from the protocol section to the results section.

Primary Outcome Measure FDAAA [* Required by ClinicalTrials.gov for records first released on or after December 1, 2012]
Definition: Specific key measurement(s) or observation(s) used to measure the effect of experimental variables in a study, or for observational studies, to describe patterns of diseases or traits or associations with exposures, risk factors or treatment.

- **Title** * - A concise name for the specific measure that will be used to determine the effect of the intervention(s) or, for observational studies, related to core objectives of the study and receiving the most emphasis in assessment. (Limit: 254 characters)
- **Time Frame** (FDAAA) [* Required by ClinicalTrials.gov for records first released on or after December 1, 2012] - Time point(s) at which outcome measure is assessed. (Limit: 254 characters)