

**Amendment #2 to RFP-NIH-NIAID-DAIT-08-10
Statistical & Data Coordinating Center**

This amendment provides questions submitted by potential applicants/offerors and the responses provided by NIAID. The responses are offered for information only and do not modify or become part of this solicitation. This Amendment will be updated as needed to add further questions and their related responses. All potential offerors are advised to refer back to this Amendment # 2 for additional Questions & Answers.

Amendment to Solicitation No.: NIH-NIAID-DAIT-08-10

Amendment No.: 2 (1st posting)

Issue Date: October 2, 2007

Effective Date: October 2, 2007

Proposal Due Date: November 7, 2007, at 4:00 P.M. local time

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Name and Address of Offeror: To All Potential Offerors

The above numbered solicitation is amended as set forth below. **The last date for submission of Questions regarding this RFP is October 19, 2007.** The hour and date specified for receipt of proposals **HAS NOT** been extended. Offerors must acknowledge receipt of this amendment. Failure to receive your acknowledgement of this amendment may result in the rejection of your offer. This amendment shall be acknowledged in the following manner:

- By acknowledging receipt of this amendment on each copy of the offer submitted.

Question 1: What is the average duration of an ITN trial?

Response to Question 1: The average duration of an ITN clinical trial is 2.5 years with a range from 1 to 5 years at present.

Question 2: What is the average casebook size for an ITN trial?

Response to Question 2: The average number of case report forms in a typical ITN trial “casebook” is 200 to 400 pages per participant. NIAID discourages casebooks exceeding 400 pages per participant for trials within these portfolios.

Question 3: Option 2 provides for additional SDCC support for data collection, storage, management, quality control and reporting for the AADCRCs. Please clarify the number of AADCRC studies to be considered for this option. Attachment 2 indicates multiple studies, Attachment 6 lists 10 studies and Attachment 5, page 9 indicates just one study.

Response to Question 3: **Option #2: Provision of Additional SDCC Support Services for the NIAID AADCRCs.**

A. In Attachment 5 (**Additional Business Proposal Instructions and Uniform Cost Assumptions**), Section 4 (**Options**), Page 9 of 10, NIAID requests that offerors provide a **budget proposal** for a single **Phase I clinical trial of an experimental product to be conducted at 2 study sites for a total of 40 participants**. This request is correct as written. This SDCC budget proposal will serve as **an example of projected costs** for data collection, storage, management, quality control, and reporting services to be provided by the SDCC to NIAID as a prototype “AADCRC clinical trial”.

B. This budget proposal will then be evaluated as part of NIAID’s review of projected costs for one or more of the AADCRC trials discussed under **the SOW, Part D, Option 2** of this RFP. NIAID may choose to exercise a contract modification as described for Option 2 for SDCC data management services for one or for more than one of the AADCRC studies listed in the “Additional RFP Materials” section, depending on the level of federal funding and support available at the time of the contract modification.

C. In Attachment 4 (**Additional Technical Proposal Instructions**), Section 7 (**Options, Part D**), Part A (**Option 2**), Pages 11 and 12 of 43, NIAID requests the SDCC to provide a plan and procedures needed to expand the services from the base period to include data collection, storage, management, quality control, and reporting for all of the AADCRC clinical trials under Option 2. (See details as described in Attachment #4). NIAID may choose to exercise a contract modification for Option 2 for SDCC data management services for one or for more than one of the AADCRC studies, depending on the level of federal funding and support available at the time of the contract modification. The AADCRC studies currently in development are listed in the “Additional RFP Materials” section. Additional new clinical studies may be proposed and accepted in the future for protocol development by the AADCRC Steering Committee.

Question 4: Please clarify the number of ‘other DAIT-sponsored’ studies that need to be considered for Option 3. Attachment 2 indicates multiple studies and Attachment 5, page 9 indicates just one study.

Response to Question 4: **Option #3: Provision of SDCC Support Services for Additional DAIT Clinical Trial Programs and Projects.**

A. In Attachment 5 (**Additional Business Proposal Instructions and Uniform Cost Assumptions**), Section 4 (**Options**), Page 9 of 10, NIAID requests that offerors provide a **budget proposal** based on the full range of SDCC services as specified in Part A of the SOW for a single **Phase II clinical trial of an experimental product to be conducted at 5 study sites for a total of 150 participants**. (Assume a 3-year enrollment period and a study duration of 6 years.) This request is correct as written. This SDCC budget proposal will serve as **an example of projected costs** for the full range of SDCC services to be provided by the SDCC to NIAID as a prototype “additional DAIT clinical trial”.

B. In Attachment 4 (**Additional Technical Proposal Instructions**), Section 7 (**Options, Part D**), Part B (**Option 3**), Pages 12 of 43, NIAID requests the SDCC to describe how SDCC support for **additional DAIT clinical trial programs** and projects will be accommodated. This support will be for the full range of SDCC services and include:

- i) additional scientific and technical staffing for the additional DAIT program,

ii) expanding existing or adding additional computer-based systems for collection, storage, management, quality control, and reporting of data (See details as described in Attachment #4), and

iii) modifying or augmenting the SDCC management structure to accommodate oversight responsibilities to support additional DAIT programs and projects.

C. **As described in the SOW, Part D, Option 3**, NIAID may chose to exercise a contract modification for Option 3 for one or for more than one additional DAIT program or project, depending on the level of federal funding and support available at the time of the contract modification. This will be done on a case-by-cases basis. There is no “pre-determined number” of DAIT studies that may be considered as part of Option 3.

Question 5: Please verify all new studies, ITN, AACRC and other DAIT-sponsored studies, are to be conducted using EDC (electronic data capture).

Response to Question 5: The SOW specifies the use of computer-based systems and computerized study forms for remote data entry and electronic data capture for ITN (SOW Part A.5) and AACRC (SOW Part D: Option 2) studies. For Option 3 (other DAIT-sponsored studies), this decision will be made by NIAID on a case-by-case basis.

Question 6: Attachment 2, page 8, section A #6 indicates compatibility with the systems being used by the DAIT and the ITN is required. What systems are these organizations using and do they utilize CDISC standards?

Response to Question 6: The SOW specifies the use of computer-based systems and computerized study forms for remote data entry and electronic data capture for ITN (SOW Part A.5) and compatibility with the systems being used by DAIT and the ITN (SOW Part A.5.A.6). CDISC standards are acceptable to NIAID. The incumbent (PPD) currently utilizes the following NIAID-approved systems for the databases for ITN trials:

- Oracle® Clinical Database V4.5.1 for database 1 (tracking and reporting of clinical and lab data as well as AEs),
- Oracle® Thesaurus Management System (TMS) 4.5.2 for coding of AEs and concomitant medications in database 1, and
- Oracle® AERS (Adverse Event Reporting System) Database V4.5.1.12 for comprehensive tracking and reporting of SAEs in database 2,
- SAS Software Ver 8.2 is currently in use to provide comprehensive & integrated platform for exploratory statistical data analysis and to create data tables, listings, and figures to support NIAID safety reviews within one software environment.

Question 7: Attachment 2, page 9, section C #6 indicates a computerized data query system to notify and request resolution of data issues from clinical and laboratory sites is required. Please clarify what is meant by a ‘computerized data query system’.

Response to Question 7: NIAID has requested the SDCC provide “a computerized data query system to notify and request resolution of data issues from clinical and laboratory sites” as part of new and improved technologies used in drug development to enhance the efficiency and ease of use of databases 1 and 2. Software compatible with or superior to modern systems such as “Oracle Clinical Remote Data Capture (RDC)” is requested for this set of databases. Oracle RDC (or a similar platform) allows the data to be entered electronically by participating centers and is checked “in real time” against the rules, ranges, and electronic edit checks defined in Oracle Clinical. Data errors are flagged back to the site electronically where the user can quickly correct discrepancies immediately, providing clean data with no need for additional queries. All changes are “audit trailed”, and the audit trail may be inspected in the PDF environment.

The SOW Part A.5.C [Data Quality Control] provides for the SDCC to manage quality control of all clinical and laboratory research data (database 1) and of all SAE data (database 2) collected for these clinical trials. NIAID has

requested the use of computer-based systems to provide “computerized validation and error checking (e.g. range checks, use logics, etc.” to enhance the data analysis process and reduce the data query burden on participating centers. In addition, NIAID has requested “evaluation of data derived from ongoing quality assurance checks and inclusion of summaries of quality assurance checks in Quarterly Progress Reports” when aberrant or missing data are identified.

The SDCC is required to manage the computer system servers, databases, software, and internal networking and to run internal audits each year as well as manage all software upgrades and validations in support of databases 1 and 2.

Question 8: Will medication coding require ATC coding and if so, to what level?

Response to Question 8: NIAID does not require Anatomical Therapeutic and Chemical (ATC) coding of medication use in clinical trials as part of this solicitation. (The ATC codes are divided into a 5-level hierarchical classification system that is unnecessarily complex and beyond the needs of the NIAID research mission for these studies.)

Instead, the SDCC will need to use a system compatible with that used by the incumbent data center (PPD): the Oracle® Thesaurus Management System (TMS) 4.5.2 for coding of AEs and concomitant medications in database 1. NIAID requires that the medication coding system to be used will have advanced searching and classification algorithms and will support all dictionaries (including MedDRA, COSTART, ICD9, ICD10, WHO-ART, and WHO-DRUG), as required by international regulatory authorities.

Question 9: Will medical history information or any other patient information require coding?

Response to Question 9: NIAID will collect important medical history information in dedicated case report forms; however, we do not require coding for medication history information. The incumbent SDCC (PPD) does provide coding for concomitant medications and adverse events using the Oracle® Thesaurus Management System (TMS) as part of database 1.

Question 10: Is it to be assumed that a central laboratory will be utilized for processing samples for each study and therefore the DM contractor would receive all results and normal ranges electronically on an agreed upon schedule?

Response to Question 10: In respect to ITN clinical trials, each participating center uses a combination of central and local laboratories on a case-by-case basis as required to meet the research needs of each protocol. The SDCC will develop a normal lab reference range case report form (CRF) for each protocol-specified lab result in each protocol to be completed prior to site initiation. These CRFs will be submitted to the SDCC to provide normal lab reference ranges for use in SDCC database 1.

In addition, a listing of ITN core labs (for DNA-based assays, RNA-based assays, etc.) is provided in the “Additional RFP Materials” section. Data from ITN core labs is not contained within the SDCC database. Instead, this data is collected and managed by the ITN Bioinformatics Data Center (Informatics Executive Director for ITN = David Parrish) and analyzed by the ITN Tolerance Assay and Data Analysis Group (Executive Director = Vicki Seyfert-Margolis, PhD).

Question 11: Attachment 2, section 11 A speaks to initial transition of work from the incumbent contractor to the new contractor. Please clarify whether the databases (entry screens, edit checks, etc.) for ongoing studies are to be migrated to the new contractor for use in continuing work on the ongoing studies or the new contractor is expected to develop new databases and populate them with data received in datasets from the incumbent contractor.

Response to Question 11: In the event of a new SDCC contractor, the awardee of this RFP is required to plan and implement an orderly, efficient, and secure transition of all data (active and archived) from the incumbent (PPD). (See SOW Part A.11 [Initial and Final Transitions]). A draft initial transition plan prepared by the new SDCC contractor is required for NIAID Project Officer review within 14 days of the effective date of the contract. The NIAID PO will review and provide comments on the draft initial transition plan within 7 calendar days back to the SDCC contractor. The new SDCC contractor will be expected to plan and develop new databases for each of the active and enrolling trials (on a priority basis) and to populate them with data transferred from the incumbent (PPD) using SAS transport (XPORT) files using a reasonable timeline to allow database building and validation.

Question 12: Please verify that during the development of the transition plan the new contractor will be able to review and comment on all draft transition plans developed.

Response to Question 12: A draft initial transition plan prepared by the new SDCC contractor is required for NIAID Project Officer review within 14 days of the effective date of the contract. The NIAID PO will review and provide

comments on the draft initial transition plan within 7 calendar days back to the SDCC contractor. (See SOW Part A.11 [Initial and Final Transitions]).

Question 13: Attachment 5, #8: Regarding the 21 active ITN trials a new DM provider would need to assume responsibility for:

- a. are all of these currently being conducted using eDC and if so, which eDC tool?
- b. If not all are being conducted using eDC how many are paper-based?
- c. Can the project specific parameters (e.g. number of sites, number of patients, number of CRFs/completed patient, Last Patient In date, expected database lock dates, etc.) for each of these studies be provided at this time to assist in proposal preparation?

Response to Question 13:

- A. In respect to ITN clinical trials, the current method of data collection is using paper case report forms (CRFs). NIAID is migrating from a paper CRF system to the use of electronic (remote) data capture as part of this solicitation. Oracle RDC (or a similar platform) will be selected for use with the SDCC contractor as part of the next generation of the SDCC for these studies.
- B. All of the current ITN clinical trials are currently using a paper CRF system.
- C. Many of the “project specific parameters” (e.g. the number of sites and the number of patients to be enrolled) are provided in the “Additional RFP Materials” section. Other project specific parameters (such as number of CRFs/completed patient, last patient in date, expected database lock dates, etc) will be provided for each of these studies at the initial meetings following contract award.

Question 14: The RFP specifies that type must be 10 to 12 points and not exceed 6 lines per inch or 15 characters per inch. Times 11 does not exceed 6 lines per inch, but whether it exceeds 15 characters per inch depends on whether one counts spaces as characters. Does the character-count requirement include spaces as characters? Is Times New Roman 11 considered acceptable for the proposal body text?

Response to Question 14: The NIAID Office of Acquisitions can not provide a pre-proposal submission acceptability determination with regard to specific font types for potential offerors under a competitive acquisition, but does recognize that most standard fonts within their 10 to 12 point range are acceptable per the requirements of the RFP.

Question 15: Will the Contractor be responsible for submitting expedited cases to the Regulatory Authorities and CECs in Europe and in rest of world countries?

Response to Question 15: Yes, the SDCC will be responsible for reporting of foreign suspected unexpected serious adverse reactions (SUSAR) to the appropriate Competent Authority (CA)/Ethics Committee, to the Eudravigilance database for EU member states, and to regulatory authorities for applicable clinical trials supported by this contract with NIAID as described in SOW Part A, 5.B.3) regarding compliance with the European Union (EU) Clinical Trial Directive for notification of SUSARs.

Question 16: Please provide the country/regional distribution for these studies.

Response to Question 16: A list of specific countries for the clinical trials covered in this RFP cannot be provided at this time. Please assume a global application of the reporting for suspected unexpected serious adverse reactions (SUSARs).

Question 17: What is the estimated number of SAEs (in current safety database) that will need to be migrated to the Contractor's new safety database at project startup?

Response to Question 17: There are approximately 423 INITIAL SAE reports in our SAE database at present. Each INITIAL SAE has multiple follow-up SAE reports.

Question 18: Attachment 5 contains the travel assumptions for the budget and provides two columns of information. It is noted that at times the information in the first column is repeated in the second column -- does that mean that the travel is considered the same and so we should only use the assumption in the first column or does it mean that with the addition of new work that the travel will double?

Response to Question 18: The assumptions provided in the **Uniform Cost Assumptions** (See Section 3 of the Additional Business Proposal Instructions) are arranged into **three columns**:

- i. Column 1 = “**Activity**” (Name or Function),
- ii. Column 2 = “**Ongoing Activities at Contract Award**”, and
- iii. Column 3 = “**New Work for Contract Period of Performance**”.

This contract will be funded for a base period of six (6) years. NIAID intends for offerors to use these assumptions as guidelines for establishing their budgets for tasks as described in the Statement of Work (SOW). Column 2 describes **the upper limit of work or travel** to be performed at start-up (within 6 mos of award) for this contract. Column 3 then goes on to describe **the upper limit of work or travel** to be performed each year of the base contract period of performance (Years 1 – 6).

Duplications of work or travel listings between Columns 2 and 3 simply indicate that meetings, teleconferences, etc. will be performed both at the time of the award (Column 2) and again during each year of the base contract period of performance (Column 3). In these cases please consider the meetings, teleconferences, etc. in Column 3 as work to be performed for each year of the six year contract.

Question 19: Second, sometimes the first column and second column may have duplicated information but then the second column will also include an additional type of trip (e.g: see #5 Clinical Trial Investigator Meetings: the first and the last items are the same but column 2 additionally has Interim Investigator Meetings) -- does that mean that all repeated trips mean that the travel will remain the same regardless of the added work and the only additional work will be the added Interim Meetings?

Response to Question 19: Duplications of work (in row #5 - Clinical Trial Investigator Meetings) listed in Columns 2 and 3 simply indicate redundant meetings will occur. Some meetings, teleconferences, etc. will be performed both at the time of the award (Column 2) and again later during each year of the base contract period of performance (Column 3). In these cases please consider the meetings, teleconferences, etc. as additional work (**i.e., they are additive**) **for each year** of the six year contract. Interim Investigator Meetings are listed in Column 3 to indicate they will be performed each year of the base contract period of performance.

Question 20: And lastly, occasionally the first and second column do not match but rather will have 5 trips in the first column and 10 trips in the second column -- does that mean that there will be a total of 15 trips of that specific activity or does it increase just to 10 trips with the addition of the new work?

Response to Question 20: The assumptions provided in the Uniform Cost Assumptions (See Section 3 of the Additional Business Proposal Instructions) may be different for work to be performed at start-up (within 6 months of award), (**See details in Column 2**) as compared to later during each year of the base contract period of performance (**See details in Column 3**). Please account for all meetings, travel, teleconferences, etc. as described in Column 3 to occur yearly for each year during years one through six of the base contract period of performance as **the upper limit of work or travel** for this SDCC contract. If there are 5 trips listed in Column 2 and 10 trips per year listed in Column 3, then the total upper limit of travel indicated =

For example:

5 trips in Column 2 (At Contract Award) + [10 trips /year * 6 yrs in Column 3] = upper limit of ~ 65 trips total over six years base period of contract performance.

Question 21: Sharing Research Data: RFP Section L (Page 48), Section M Item 3 (Page 62), and Item 2 in Section 8 of the Additional Technical Proposal Instructions specify that the offeror must submit a plan in the technical proposal for data sharing. Essentially all of the data for which the SDCC will be responsible will be generated by the ITN and AACRRC research networks. Does either of these networks have data sharing policies or procedures in place that should be considered in the Data Sharing Plan to be developed by the SDCC?

Response to Question 21:

A. In reference to the ITN, there are two helpful documents related to this issue for your review:

i.Attachment #1.: ITN Draft Clinical Data Transfer Policy

ii.Attachment #2: ITN Publications Policy and Procedures

B. In reference to the AADCRCs, there are no data sharing policies yet established for the AADCRC's. These clinical studies are all single-site studies. However, data generated by AADCRC trials will be reported in abstracts and journal publications or presented to the public through oral presentations. Data may also be shared among investigators during the AADCRC Steering Committee meetings.

Question 22: The SOW Technical Requirements introductory paragraph indicates that “SDCC staff members shall serve as members of Study Management Teams established for each ITN-approved clinical trial. . .” Does the ITN have in place policies or procedures that define the specific roles of SDCC staff on these teams or should those roles be proposed as a part of this solicitation?

Response to Question 22: The SDCC staff roles for both the ITN and the AADCRC should be proposed as part of the response to the RFP according to all of the contractor’s internal SOPs, in support of NIAID’s clinical research mission, and in compliance with current Good Clinical Practice guidelines for the conduct of human clinical trials. (FDA cGCP Reference site: <http://www.fda.gov/oc/gcp/regulations.html>).

It is NIAID’s intention that the SDCC will provide comprehensive support and experienced staff to assure the safe and efficient conduct of human clinical trials in the areas of protocol development; statistical design and analysis of clinical protocols; database support; mechanistic and surrogate/biomarker trials; data collection, storage, and management; project management to coordinate contract-related activities, as well as safety oversight and SAE reporting for domestic and international trials.

Question 23: The Part A of the SOW Technical Requirements Item 1.A.1) indicates that the SDCC will perform feasibility assessments of Concept Proposals and Full Applications from ITN and non-ITN investigators. Is the information collection needed for these feasibility assessments the sole responsibility of the SDCC or are the investigators primarily responsible for information collection as directed by the SDCC in concert with NIH?

Response to Question 23: The information needed for these statistical feasibility assessments is the responsibility of the investigators (and their pharma partners when applicable). A detailed scientific summary (including background, summary of previous pre-clinical and clinical data, objectives, rationale, scientific significance, proposed sample size, eligibility criteria, description of the intended treatment regimen, selected endpoints, a description of the proposed clinical trial study design, and the proposed statistical analysis plan, as well as any mechanistic or surrogate biomarker studies) is submitted by the investigators for review to the Network Steering Committee (or a similar body) and to the data center staff in parallel. These proposals are reviewed periodically each year of the contract at Network Steering Committee meetings for ITN projects.

Once the detailed scientific summary is obtained, then the SDCC staff will provide a statistical feasibility assessment of all items outlined in the SOW Technical Requirements [Item 1 (Statistical Design and Analysis). Part A. (Statistical Design), #1) Concept Proposals and Full Applications (items a – e)] to NIAID, the investigators, and to the Network. This feasibility assessment is then used by NIAID and the Network to evaluate, prioritize, and recommend which concept proposals and/or full applications for clinical trials should go forward to formal protocol development, which should be re-designed, and which should be declined all together.

In reference to the AADCRCs, a parallel process for statistical feasibility assessments provided by the SDCC staff regarding a limited number of concept proposals submitted by AADCRC Principal Investigators for evaluation by the AADCRC Steering Committee is described in Part B of the SOW, Item 1 (Statistical Design), a. Concept Proposals. The SDCC will provide statistical feasibility assessments of these concept proposals on an as-needed basis to NIAID and to the AADCRC investigators directly with attention to study design, sample size, eligibility criteria, statistical analysis plan, etc. It is expected that these will occur less frequently for the AADCRCs than for the ITN. It is expected that the AADCRC investigator who will require SDCC support will be providing the SDCC with the information on availability of study populations and on the variance of primary outcomes to help the SDCC with the feasibility assessment.

Question 24: The SOW Technical Requirements Item 1.B3) “Electronic Data Transfers” contains the following statement: “These files shall include associated text documents (e.g., cover memoranda) and programmed data files (e.g., tables, listings and figures) per protocol and shall be transferred regularly 2-3 times per month, using software compatible with SAS software (version 8.2 or higher) and transferred in SAS transport (XPORT) files.” While it is possible to format text documents and tables and listings as SAS transport files, such files are typically hard to view and to manipulate for many

users. We expect that only the actual data files are to be sent as SAS transport files and that other files will be transferred electronically in more useable formats. Is our assumption correct, and if so, are specific formats expected for the text files and the actual table, listing, and figure files?

Response to Question 24: NIAID, the incumbent data center (PPD), and the investigators from ITN use password-protected “WinZIP® data compression files” for easy transport of data files within the “Microsoft Windows” environment. In addition, NIAID and ITN have developed standard templates for DSMB summary memos, SAE narratives, and responses to NIAID DSMB comments in Microsoft Office Word 2003 and more recent versions of this software. These will be shared with the awardee of this RFP within 90 days of the award. We agree that MS Office Excel data files will be sent as SAS Transport files from the data center to the ITN Bioinformatics Group, and that other files will be transferred electronically in the most useable formats.

Question 25: The SOW Technical Requirements Part A, Item 5.a.3) contains the following requirement: “Central computerized registration and randomization of the majority of subjects on ITN protocols, and non-computerized methods on a limited basis for selected study sites. In addition, a system for off-line data entry for sites with intermittent internet connection shall be provided. Data may be transmitted at a later time when internet connection is available.” Is the statement about a system for off-line data entry only applicable to the computerized registration and randomization system? If not, that is if it is applicable also to the clinical database, we have concerns that a client-side data entry system can be made 21 CFR Part 11 compliant in the absence of a dedicated client-side computer, and this RFP precludes the purchase of such computers. Can we assume that NIH will provide sites with intermittent access dedicated data entry machines to allow reasonable 21 CFR Part 11 validation, or is the offeror expected to implement a compliant system with off-line capability that does not rely on dedicated client-side computers?

Response to Question 25: The NIH will not provide sites with intermittent access dedicated data entry machines. The SOW Technical Requirements, Part A.10 [Facilities, Equipment, and Other Resources], clearly states that “*The Government will not provide any government-furnished equipment nor funds from this contract to purchase government-furnished equipment.*”

The SOW Technical Requirements Part A, Item 5.a.3) refers to two systems: one for registration and randomization of candidates as subjects in ITN studies (with a back-up telephonic system) and the other for remote data entry and capture:

- i. A central computerized registration and randomization system provided by the SDCC: The incumbent (PPD) currently uses an interactive voice recognition system to allow 24 hour access for registration and randomization of new subjects entering ITN studies. A “back-up” to the current IVR computerized system exists at PPD using a telephonic system for randomization of candidates onto ITN studies to prevent delays with randomization of new subjects. This is a high priority back-up system that functions even when the remote electronic system or the internet is not functioning properly.
- ii. Remote Data Entry and Transmission/Capture (RDC) system: For use of the RDC system, the site must simply wait for the internet service to come back on line in order to submit protocol-specified clinical and lab data to the SDCC database via the remote data capture network provided by the SDCC.

Question 26: Relative to SOW Technical Requirements in Part A, Item 7.A.12) for “real-time” queries of the data, must the system provide true dynamic reporting from the on-line data system or are off-line reports based on periodic snapshots from the data system adequate?

Response to Question 26: The clinical study internet-based collaboration portal NIAID is hoping to use will provide true dynamic reporting from the on-line data system as our preference. Alternatively, a less desirable system could provide “off-line reports” based on “periodic snapshots” from the data system. However, such a system may be viewed as less advantageous to NIAID and its investigators.

Question 27: Relative to SOW Technical Requirements in Part A, Item 8.A.1), can NIH provide more information on the data that the SDCC must download from the DAIT Regulatory Management Center to reconcile with site-specific ranges?

Response to Question 27: The DAIT Regulatory Management Center receives the Normal Lab Reference Ranges provided by each lab from each participating site in a NIAID-sponsored clinical trial as part of an essential document checklist for clinical studies supported by NIAID funds. In some cases, these normal lab values were not properly collected at the start

of the trial directly by the SDCC. The DAIT Regulatory Management Center shares these ranges with the SDCC on a periodic basis as a way to confirm their accuracy and to enable the collection of these results for all studies covered by this solicitation.

In addition, the SDCC will prospectively collect the Normal Lab Result ranges directly via (NLR) case report forms (CRFs) for all new clinical trials prior to site initiation at the beginning of each study.

The sites will submit a set of NLRs to the DAIT Regulatory Management Center each year or whenever these ranges change throughout the conduct of the trial. These ranges include tables for normal lab results for hematology, chemistry, immunology, metabolic-endocrine, and other labs as per the schedule of events for each protocol.

Question 28: Relative to SOW Technical Requirements in Part A, Item 8.C., can NIH clarify the role of the SDCC relative to the DAIT Drug Distribution Center in establishing drug accountability?

Response to Question 28: The main responsibility of the SDCC in this case is to communicate effectively with the DAIT Drug Distribution Center in regard to the development of a randomization schedule for participants in a blinded or double-blinded NIAID-sponsored clinical trial and to enable rapid responses to study drug unblinding requests for participants in NIAID-sponsored clinical trials as requested from the NIAID medical monitor or the site investigator for medical safety reasons.

NIAID expects the SDCC to be responsible for developing and communicating the randomization schedule and handling unblinding of participants for medical safety reasons rapidly via communications with the project team, protocol chair, NIAID medical monitor, and representatives from the DAIT Drug Distribution Center within 24 hrs of an unblinding request.

Question 29: Relative to SOW Technical Requirements in Part A, Item 9/B.2), can NIH clarify the roles of the SDCC and the DAIT Clinical Site Monitoring Contractor in assessing the capability of a site to conduct a study in compliance with GCP?

Response to Question 29: In reference to SDCC clinical site assessments for ITN protocols, NIAID will require the SDCC to evaluate and to support each site's ability to successfully interact with the centralized computer-based systems, servers, and databases operated and maintained by the SDCC as well as the password-protected clinical study internet-based collaboration portal for each protocol. The SDCC evaluation will focus on computer equipment, internet access, facilities, systems, plans, and procedures for data quality control and safety (AE/SAE) reporting, as well as site personnel.

The DAIT Clinical Site Monitoring (DCSM) contractor and the NIAID Project Manager will work at the site itself, relaying information to the SDCC and whether or not each site has met the regulatory and technical requirements needed to meet GCP and individual study needs. Once a study has opened the SDCC will coordinate CRF development and receive data from individual sites participating in each clinical trial. The DCSM contractor will review and compare data entered on CRFs with primary source data from each site to run a comparison between data sets looking for errors, abnormal lab results, protocol deviations, and/or missing data or missing visits. When finished, the DCSM monitor then reports his/her findings to the SDCC, thereby generating data queries.

Question 30: Can NIH clarify what (if any) role the SDCC PI has within the AADCRC Steering Committee?

Answer to Question 30: In reference to SOW Part B, Item 1 (Statistical Design for the AADCRCs), the SDCC statisticians will provide statistical feasibility assessments of concept proposals submitted to the AADCRC Steering Committee (item 1a) and will review study designs and statistical analysis plans for final draft protocols approved for implementation by the AADCRC Steering Committee (item 1b) to ensure the appropriateness of the proposed overall study design, entry criteria, sample size and power estimates, primary and secondary endpoints, statistical analysis plan, and randomization/stratification/blocking methods. The SDCC PI will not be a voting member of the AADCRC Steering Committee and will not be required to attend all AADCRC Steering Committee meetings or teleconferences. However, SDCC PI may be asked to attend a teleconference or a meeting of the AADCRC Steering Committee where a project in which the SDCC is involved is to be discussed.

Question 31: Relative to SOW Part C, Item 1.B.3) can NIH provide more information on the types of compounds and manufacturing operations for which the SDCC will be expected to provide CMC support under this contract?

Response to Question 31: In reference to SOW Part C, Item 1.B.3) (Chemistry, Manufacturing, and Control Personnel), NIAID cannot provide a specific list of study compounds for future clinical trials in the ITN or AACRC studies as there is no fixed list. However, please refer to the section on “Additional RFP Materials” for a list of NIAID’S on-going studies with ITN (item #2) and planned studies for the AACRC (item #3), which names some of our investigational agents. Many of these agents are categorized as biological products (human cells or tissues, monoclonal or polyclonal antibodies, peptides, allergenic extracts, etc.) or drugs (Sirolimus, Atorvastatin, etc.).

Question 32: On page 22 of Attachment 2 in the RFP, weekly protocol status teleconferences are mentioned. Is it the responsibility of the SDCC to arrange, pay for, and provide agendas for these meetings?

Response to Question 32: NIAID expects the SDCC staff to participate in an advisory role on these weekly teleconferences, and not as a planner for each week’s call. The DAIT Project Managers (PMs) and ITN Clinical Operations Managers (COMS) will schedule and plan all of the weekly protocol status teleconferences. The SDCC staff will provide input on protocol development, study design, study implementation, data collection/management/& analysis, as well as on DSMB support and safety oversight considerations. However, the NIAID PMs and study investigators will determine agendas for these teleconferences.

Question 33: A larger question is that it is not clear which group will respond to site clinical issues (such as questions about subjects meeting inclusion/exclusion criteria). Are these activities the responsibility of the SDCC?

Response to Question 33: Matching of potential study subjects to inclusion and exclusion criteria falls to study site coordinators and the site investigators for each trial. The NIAID Medical Monitor and Project Manager will review and confirm questions regarding clinical issues with the site.

The SDCC’s role will include comprehensive support of the central computerized registration and randomization system (See SOW Technical Requirements Part A, Item 5.a.3); managing database 1 [for AEs., clinical, and laboratory research] and database 2 [for SAEs] (SOW Technical Requirements Part A, Item 5), and coordinating with monitors from the DAIT Clinical Site Monitoring (DCSM) contractor on study site audit findings. The SDCC will report any potential inclusion/exclusion errors to the NIAID PM and the NIAID Medical Monitor for that specific protocol.

Question 34: Can you clarify which group is responsible for overall coordination among contractors?

Response to Question 34: NIAID appoints a Project Officer (PO) to serve as a scientific/medical/technical advisor to the NIAID Contract Officer (CO) for each awarded NIAID contract. The NIAID PO will have expertise in the conduct of clinical trials and will work together with the SDCC on a daily/weekly basis over the life of the contract to support NIAID’s research mission. The NIAID PO will attend teleconferences, working sessions, and ITN Network Steering Committee meetings with SDCC staff.

The NIAID PO and Contracting Officer (CO) may elect to conduct one or more site visit(s) at the SDCC facilities or to request reverse site visits at any time during the contract. (SOW Part C.2.B.3 Meetings and Teleconference – Site Visits). In addition, the NIAID PO and CO will review & approve monthly invoices as well as quarterly and annual progress reports provided by the SDCC as per RFP Attachment #2 (Reporting Requirements and Deliverables).

Coordination of the SDCC contract will fall to the NIAID PO and CO with input from Senior DAIT/NIAID staff. The Division Director of DAIT, NIAID provides supervisory administration of all project officers in DAIT, NIAID.

Question 35: Participation by the SDCC in site initiation visits is mentioned a number of times in both the main RFP and its attachments: Criterion 1.4) c. on page 64; Item 9.B.2) on pg 16 of the SOW; and Section M. 2) of the Additional Technical in Proposal Instructions (Attachment 4, pg 9). There is no corresponding reference to site initiation visits in the Uniform Cost Assumptions detailed in Attachment 5. Site assessment visits are mentioned, however. Because the aforementioned examples of the site initiation requirement appear under a heading addressing site assessment and all instructions specify that the intention of the initiation visit is “to assess the capabilities of study sites,” we are assuming that the terms “site initiation” and “site assessment” are interchangeable in this proposal. Please confirm this assumption.

Response to Question 35: The assumptions provided in the **Uniform Cost Assumptions** (See Section 3 of the Additional Business Proposal Instructions) that address item 12 [**Clinical site training, Assessment, and Technical Assistance**] are **correct as written** in regard to the total number of site assessments, web casts, and meetings at contract award and during the contract period of performance. These terms are used interchangeably in the RFP document. Offerors who respond to this RFP should use the assumptions as stated in the Uniform Cost Assumptions section regarding the total numbers of site assessments, web casts, and meetings for cost estimates.

NIAID uses the terms “site initiation” and “site assessment” to work in conjunction; however, the two terms do not imply the same specific set of tasks to NIAID. A site initiation is performed prior to screening or enrolling the first participant in an ITN or AADCRC clinical trial. A site assessment may occur at any time during the clinical trial. NIAID and/or the SDCC may need to perform a site assessment following an unexpected severe or life-threatening adverse event, a significant protocol deviation, or at the request of local, national, or international health authorities for safety reasons.

NIAID will require the SDCC to assist the NIAID PM and the DAIT Clinical Site Monitoring (DCSM) contractor as *part of* the site initiation process. The SDCC will teach the site how to submit data to the centralized computer systems, via servers and databases provided and maintained by the SDCC.

The SDCC will answer questions from the site and evaluate the capabilities of each site to meet the comprehensive needs of a cGCP, 21CFR, and local IRB - compliant clinical trial. The SDCC will evaluate the site’s ability to do the following prior to site initiation:

- To access and use the electronic registration and randomization system provided by the SDCC;
- To interact with the centralized computer-based systems, servers, and databases operated and maintained by the SDCC to enter data using the electronic CRFs and the remote data entry and capture system provided by the SDCC;
- To interact with the password-protected clinical study internet-based collaboration portal for each protocol.

The NIAID PM and the DCSM contractor will evaluate the site’s ability to follow the IRB-approved version of the protocol in compliance with cGCP standards, 21 CFR, and local IRB standards. The role of the SDCC in performing clinical site assessments is described in response to question 9 (See above).

Question 36: Attachment 5, Item 1) A.7. Regulatory Submissions of the Uniform Cost Assumptions includes information about the number of meetings in this category: 1 meeting and 1 teleconference in the first 6 months; 5 meetings or teleconferences with regulatory health authorities per year; and 5 pre-IND, IND or other regulatory meetings with health authorities per year. The Meetings and Travel section includes another set of assumptions about these meetings under item 2) A.7. This latter set of assumptions does not match what was detailed in the earlier section. Please indicate which set of instructions should be used.

Response to Question 36: Please use the **Uniform Cost Assumptions** as stated in Attachment 5, Item 1) (Technical Cost Assumptions).A.7 “Regulatory Submissions”:

- 1 meeting and 1 teleconference with US or Non-US regulatory health authorities and clinical investigators within 6 months of contract effective date.
- 5 meetings or teleconferences with US or Non-US regulatory health authorities and clinical investigators per year of the contract.
- Prepare for and attend 5 (five) Pre-IND, IND or other regulatory meetings or teleconferences with US or Non-US regulatory health authorities each year of the contract.

Question 37: Item 1) A.9. Safety Oversight and Reporting of the Uniform Cost Assumptions includes information about a number of meetings in this category. Though pg. 12 of the Statement of Work indicates that contractor staff will give oral presentation at meetings and teleconferences of NIAID safety oversight, the Meeting and Travel section does not include any instructions as to how many meetings and attendees we should include in our budget. Please provide further information.

Response to Question 37: Please use the same assumptions as described in item 1).A.9. “Safety Oversight and Reporting” from Attachment #5, (Technical Cost Assumptions) in preparing your budget for meetings and/or teleconferences in support of NIAID Safety Oversight reviews by data and safety monitoring committees and/or boards.

Question 38: Items 1) A.11 and 12 of the Uniform Cost Assumptions include information about training visits requiring SDCC preparation and/or participation. These meetings are addressed again in the Meetings and Travel section under item 2) A.6. Details in these sections do not match. Please indicate which set of instructions should be used.

Response to Question 38: Please use the same assumptions as described in the UNIFORM COST ASSUMPTIONS, Attachment 5, items 1).A. rows 11 and 12.

Question 39: On pg. 5 of Attachment 2, under Regulatory Submissions D. Annual Reports to Health Authorities, the RFP notes that the SDCC will “assist in the preparation of . . . clinical documents required for Annual IND Reports for health authority review.” Does this sentence mean that the SDCC will be responsible for preparing and submitting IND reports to the FDA and for preparing and submitting Annual Safety Reports to the EU authorities?

Response to Question 39: The SDCC will act in a supporting role for IND (or other) regulatory agency submissions “in the preparation of statistical and clinical documents required for Annual IND Reports for health authority review for all ITN clinical trials conducted under IND applications”. The SDCC statistical group will attend working group teleconferences for each clinical trial and will provide data tables, line listings, and/or figures (as needed) describing data observed in ITN clinical trials as per the standard outline for annual reports as provided in SOW Part A, Item 4.D [Annual Reports to Health Authorities] to the DAIT Regulatory Affairs group. DAIT Regulatory Affairs works with the DAIT Regulatory Management Center (Social & Scientific Systems) to develop and submit formal IND applications and other reports and/or briefing packages to FDA and other health authorities for ITN studies. Please refer to Attachment #7 (Additional RFP Materials) for a description of the DAIT Regulatory Management Center.

The SDCC for ITN and AADCRC clinical trials will not fall under the direct purview of DAIT Regulatory Affairs. NIAID will, however, require the SDCC to assist NIAID to locate and summarize data as requested by health authorities or to assist in reconciling mistakes or errors found in regulatory submissions before NIAID delivers the final documents to the health authorities.

Question 40: The SOW Technical Requirements Items 6.C.3) and 6.C.4) seem somewhat inconsistent in that item 3 requires 8 a.m. to 6 p.m. support M-F, while Item 4 requires SAE processing within 24 hours of receipt. Does NIH require 24 hours completion of these reports if they are received via the Electronic System on weekend or holiday days, or is 1 business day reporting adequate? The difference in these processing time requirements is likely to have cost and budget implications.

Response to Question 40: Please see the last sentence of section 6.C.3., where it states, “And maintain one trained person to be on-call after working hours, on weekends, and on all holidays to respond to inquiries.” Twenty-four hour reporting holds true, regardless of holidays or weekends.

Question 41: On pg. 8 of Attachment 2, under Safety Data Collection and Reporting, part 3) the RFP states that the SDCC SAE procedures and systems must meet the FDA and non-domestic health authority guidelines regarding notification of health authorities and participating investigators in EU member states of suspected serious and unexpected life-threatening or fatal adverse reactions. Will the SDCC be responsible for foreign SUSAR reporting to the appropriate Competent Authority (CA)/Ethics Committee, including electronic submission of SUSARS to the Eudravigilance database for EU member states?

Response to Question 41: Yes, the SDCC will be responsible for reporting of foreign suspected unexpected serious adverse reactions (SUSAR) to the appropriate Competent Authority (CA)/Ethics Committee, to the Eudravigilance database for EU member states, and to regulatory authorities for applicable clinical trials supported by this contract with NIAID as described in SOW Part A, 5.B.3) regarding the European Union (EU) Clinical Trial Directive for notification of SUSARS.

The reporting of SUSARs is a time-sensitive process, driven by regulations and guidelines from countries, regions, standards organizations, oversight committees and company practices. It requires the immediate attention of healthcare professionals adhering to standard operating procedures (SOPs) and good clinical practices (GCPs). When an SAE is reported, rapid communication between sponsor and investigator is required to determine if SUSAR reporting is required. Medical opinions on causality and expectedness must be agreed upon, affecting whether regulatory authorities need to be notified within timelines as short as seven calendar days.

In case of a SUSAR event, regulatory guidelines recommend the unblinding of the patient’s study medication to help oversight committees determine if it is ethical for the trial to continue; and blinding data ideally should be hidden from the clinical analysis team to avoid bias. This RFP is seeking an SDCC with capabilities and resources to meet these

international safety reporting requirements. The current incumbent SDCC (PPD) does currently handle non-domestic SUSAR reporting for applicable NIAID clinical trials.

Question 42: On pg 12 of Attachment 2, under Safety Reporting, part C1, the RFP states “Paper case report forms for the submission of AE and SAE Reports shall be used strictly as a ‘back-up system’ for the main paperless remote data entry system”. Since all SAE reports require an investigator signature at the time of submission is it expected that the remote data entry system being used to report AEs and SAEs utilize a 21 CFR Part 11 compliant “electronic signature”?

Response to Question 42: Yes, the AE / SAE reporting system held by the SDCC will require electronic signature capability.

Question 43: On pg. 13 of Attachment 2, 3) establish, staff and operate a telephone help line, it states that SDCC staff should be available “to respond to inquiries about clinical events from study site personnel and to obtain AE and SAE Report information during the hours of 8am to 6pm EST, Monday through Friday.” Is this help line specific to SAE reporting or are SDCC staff expected to provide medical management and/or clinical support as well (e.g. a more general telephone help line)?

Response to Question 43: NIAID does require a “more general telephone help line” for general clinical operations support of these trials. In DAIT’s current SDCC system, the hotline forwards calls to a safety specialist or a designated back-up. The safety specialist takes the information from the site and answers any questions with feedback to the NIAID PM as needed. Each study has a NIAID medical monitor as a reference for review of safety issues. If an SDCC safety specialist needs to discuss the case in more detail, then he/she would have a NIAID medical monitor as a point of contact.

Question 44: On pg. 13 of Attachment 2, 6) prepare and electronically distribute to the DAIT Regulatory Management Center SAE reports or information reports. Is the expectation that reports will be sent via email as scanned MedWatch forms or will there be an electronic data transfer?

Response to Question 44: DAIT has implemented a fully electronic SAE distribution system with its current incumbent SDCC for biostatistics, data management, and pharmacovigilance. DAIT receives scanned MedWatch forms, as part of the delivery and plans to continue this system with the awardee of this RFP.

Question 45: We are having some difficulty reconciling one of the elements of the technical evaluation criteria with the RFP Statement of Work. Specifically, the Technical Evaluation language related to Other Technical Staff (Criterion 2 on pg. 64) indicates that personnel evaluation will be based on “appropriateness and adequacy of the education, training, experience, expertise and effort of other proposed scientific and technical personnel of the offeror and all proposed subcontractors, including the adequacy of the proposed mix of staff, expertise, experience, and training, to carry out contract requirements with respect to *preparation and/or evaluation of manufacturing procedures and methods for generating investigational products.*” This statement seems to suggest that relatively broad capability relative to evaluating and designing the actual procedures for generating investigational products is desired. However, the actual statement of work only addresses the manufacturing component of the protocol itself, which is a relatively narrow scope. Can you please provide further insight into the scope of services in the area of manufacturing that is likely to be required under the proposed contract?

Response to Question 45: The ITN may choose to develop new investigational agents (usually drugs or biological products) for human clinical trials to accomplish its research mission. The SDCC will provide one or more scientific personnel to assist NIAID in the critical review of the chemistry, manufacturing, and controls (CM&C) summaries and manufacturing procedures and methods used to create these new agents in preparation of IND submissions to health authorities. (See SOW Part C.1.B.3) [Other Scientific and Technical Personnel – Chemistry, Manufacturing, and Control Personnel]. Qualifications for these scientific personnel may include scientific expertise in basic chemistry, biochemistry, current Good Manufacturing Practices (cGMP) and/or current Good Tissue Practices (cGTP) requirements for the manufacture of investigational agents for use in human clinical trials.



Attachment #1: Draft ITN POLICY NO. XXX “Transfer of Clinical Data”.

POLICY NO. XXX Transfer of Clinical Data

Purpose: To provide a procedure for the routine transfer of ITN clinical data from Pharmaceutical Products Development, Inc. (PPD) to the ITN data repository.

Scope: Establishes procedures for the following:

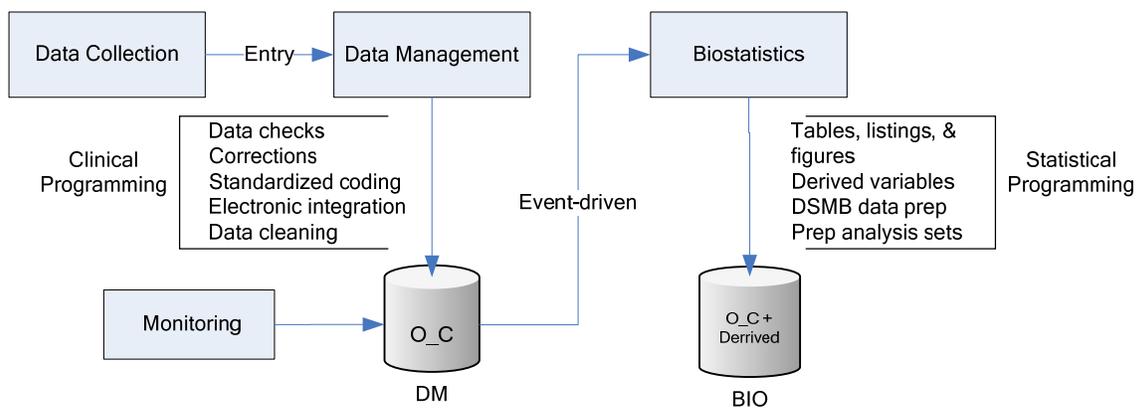
1. Scheduled transfer of clinical data sets.
2. Transfer of analysis data sets on an event-driven basis.
3. Transfer of clinical or analysis data sets upon request and approval.

Appendices: Appendix A: Data Validation Levels

References: ITN Policy XXX Data Analysis Request and Approval Process
ITN Informatics SOP Bio 001 (Managing the Secure FTP Upload Area for ITN Data Center)
ITN Informatics SOP Bio 002 (Setting up Secure FTP application for upload of data to ITN Data Center)

Overview Generation and Transfer of Data Sets

Within the data processing streams established by PPD, two operational phases have been established during which potential data sets could be generated and transferred to the ITN data repository: As illustrated below, the two sources of data for transfer are the operational Oracle Clinical (O_C) database (DM) and the extended biostatistics (O_C + derived) database (BIO) of the analysis group.



Processing of the data progresses in a linear manner, from data collection through data management and into statistical analysis, with data quality increasing as each process is performed. Each source has key advantages and limitations; in general data coming from the DM database is a direct reflection of data captured on the case report form (CRF), and will be used for report generation and status monitoring. The BIO database has derived variables and internal calculations defined and will be the data source for all analytical processing and integrating with mechanistic data.

Data Transfer Documentation

All transferred data will be accompanied by a Readme file describing the appropriate version of the following reference documents:

- data validation manual describing the data processing,
- data standards and tools (DST) describing the Oracle Clinical database structure, and
- created variable specifications for data sets from the BIO database.

Data Cleaning

Data cleaning comprises the following procedures:

Coding. Data received by PPD will be coded to a dictionary standardized and consistent within that study. These coding standards are defined during CRF design and enforced through the data entry process.

Query resolution. Data elements that are incomplete or noncompliant with the coding standards will generate queries for correction or clarification by the site.

Quality control checks. Electronic data checks.

Monitoring. Each protocol will have a data-monitoring plan that defines the level of monitoring for each element and percentage of patients.

Third-party vendor data. Any data coming from a third party vendor and not directly reported on the CRF will be validated and reconciled with the original source documentation before being deemed cleaned (level IV).

Process:

General Procedures

1. Data will be extracted and converted to SAS data files before it is transferred.
2. Transferred data will be accompanied by the applicable data validation manual and data specifications tables.
3. The level of validation for the transferred data elements will be specified, according to the table in Appendix 1.
4. For each clinical trial, the study management team (SMT) leader will maintain a schedule for transfer of clinical and analysis data sets as part of the Integrated Data Management Plan (iDMP).
5. The ITN clinical team will maintain a master schedule for transfer of clinical and analysis data sets. This schedule will be published in the clinical team trials tracking document and will be reviewed at each clinical team teleconference.
6. All transfers of clinical and analysis data sets will be coordinated by the trial SMT leader.

Scheduled Transfer of Clinical Data Sets

1. Scheduled transfers of clinical data sets will be performed for unblinded studies only.
2. Unless otherwise specified, it will be understood that clinical data in a scheduled transfer is of level 1 validation.
3. Scheduled transfers of clinical data sets may occur as often as quarterly.
4. For each clinical trial, the SMT will identify the appropriate transfer frequency

Event-Driven Transfer of Analysis Data Sets

1. Before study implementation the SMT and the clinical team will determine when data analyses will be required.
2. Applicable events include annual IND update reports, Data Safety and Monitoring Board reviews, protocol-specified interim analyses, and anticipated presentations at scientific conferences.

Unscheduled Transfer of Clinical or Analysis Data Sets

1. On rare occasions it may be necessary to request an unscheduled transfer of a clinical or analysis data set.
2. Requests for unscheduled transfers will be made on the Data Transfer Request and Approval Form. The form will be forwarded to the SMT leader.
3. Requests for unscheduled data transfers will require approval by the Director of the Immune Tolerance Network.

Appendix A

Data Validation Levels

| Level | Coding | Outstanding Queries | Quality Control | Site Data Monitoring | TPV Verification | SAE Integration |
|--------------|---------------|----------------------------|------------------------|-----------------------------|-------------------------|------------------------|
| I | Complete | Yes | Not performed | Incomplete | No | No |
| II | Complete | No | Not performed | Incomplete | No | No |
| III | Complete | No | Performed | Incomplete | No | No |
| IV | Complete | No | Performed | Complete | Yes | Yes |

Publications Policy and Procedures

Version: 2.2

Revised: 20 May 2005



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DEFINITIONS

i) Terms used in this document

Principal Investigator (PI) - refers to the individual responsible for the initial application submitted to the ITN.

Study Leader - refers to the individual (often, but not necessarily the PI) who is responsible for the overall conduct and/or coordination of the clinical protocol

Lead Author - refers to the individual who will coordinate the development, revision and submission of a publication arising from a Network study (generally, either the PI or the Study Leader themselves).

Publication – any manuscript, abstract, for scientific audiences. Does not include communications with the media, such as press releases or interviews.

ii) Abbreviations used in this document

DoC – ITN Director of Communications

NEC – Network Executive Committee

NSC – Network Steering Committee

NCO – Network Central Office

CAC - Clinical Advisory Committee

ITN – Immune Tolerance Network

1. GUIDING PRINCIPLES

1.1 Goals of this policy

The ITN Publications Policy aims to:

- ❖ encourage and facilitate high quality publications and presentations from ITN-sponsored studies
- ❖ ensure that publication proceeds in a fashion consistent with academic norms, adhering to the practice of presenting complete data to the public only after it is published in a peer-reviewed journal or through abstracts presented at scientific meetings
- ❖ facilitate the rapid dissemination of research results from ITN studies
- ❖ ensure appropriate academic recognition to individuals involved in ITN activities

1.2 Ownership and Network Data

It is an overriding principle with respect to data generated by Network activity, using Network resources or associated with the ITN that this data is the property of ITN investigators unless otherwise agreed upon by prior agreement. To facilitate the publications process in the collaborative environment of the ITN, investigators must agree to abide by ITN guidelines for the publication or presentation of the data, in whole or in part.

1.3 Cooperation with Industry

The ITN is conscious of the need to protect proprietary interests of academic/industrial partners. Clinical Trial Agreements (CTAs) with collaborating companies/institutions that agree to supply their proprietary materials (such as drugs and biologics) to member institutions of the ITN will be negotiated by the awarding agency, NIAID, on behalf of the ITN and its investigators. The ability of participating investigators and their respective institutions to fully participate in the ITN will likely depend upon the investigator's and Subcontracting Institution's ability to offer these necessary rights or options that are attractive to commercial providers of proprietary materials.

It is the expectation of the ITN that negotiated CTAs may contain a publications clause that will, upon the request of the industrial partner, delay submission of manuscripts/abstracts to ensure that associated intellectual property rights can be protected. Consistent with current industrial operating standards and NIH policy, it is expected that such publications delays would not exceed 90 days: industrial partner and/or the inventor's institution has 30 days from time of submission of draft manuscript/publication by study leader to determine if a patent is going to be filed; after this first 30-day delay, if a patent will be filed, the industrial partner and/or the inventor's institution has an additional 60 days to file the patent. Although these timeframes are goals within the ITN, the negotiated terms of the Clinical Trials Agreement, as outlined in the Terms of Award of the Subcontract Agreement from the Prime Contractor of the ITN – the University of California, San Francisco - shall supersede the timeframes outlined in this policy and shall be the governing terms of award. A copy of the final executed agreement will be forwarded to the Investigator and NCO by the awarding agency.

It is standard practice that publications arising from ITN studies where industry participation is involved may not disclose any confidential or proprietary information unless prior authorization is granted by the owner of such information.

Note that supplemental agreements between a Study Leader and an industry partner that affect publication of results from ITN research studies may be entered into only upon the authorization of the Network Executive Committee (NEC) and NIAID.

All Site Investigators, including the Study Leader, are expected to look to the office of the Authorized Official of their respective institution or organization and the ITN NCO for guidance and instructions in the interpretation of terms reflected in all fully executed Clinical Trials Agreements and ITN Subcontracts.

1.4 Open Access Policy

The ITN subscribes to the principles of open access to scientific research, as documented in the Bethesda Statement on Open Access (<http://www.earlham.edu/~peters/fos/bethesda.htm>).

1.5 Publications Oversight

The Network Executive Committee (NEC) acts as the primary decision-making body overseeing the publication and presentation of results, data, analyses and other information describing ITN research activities. The NEC will act as mediator in any disputes arising over the publications/presentation of ITN research results and/or information and will interpret publications rules in accordance with the stated goals of the policy.

The ITN Publications Committee manages, reviews and monitors publications policy, and provides recommendations regarding proposed changes in ITN publications policy.

Changes or alterations to ITN publications policy are subject to ratification by the Network Steering Committee (NSC).

1.6 Roles and Responsibilities

1.6.1 Principal Investigator & Study Leader

It is expected that the Principal Investigator will ensure that publication of results from their ITN study will proceed in a timely fashion. In cases where long, unwarranted delays in the publication of ITN study results occur, as a last resort, the NEC reserves the right to appoint an alternate Lead Author.

The Principal Investigator and/or Study Leader of a study have first right of refusal as Lead Author or to present or publish the results of ITN-sponsored studies. If declined, the PI/Study Leader may designate another individual to do so.

It is the responsibility of the Principal Investigator and/or Study Leader to ensure that authorship of publications and presentations provides fair and equitable acknowledgement for individuals contributing to the study.

1.6.2 Lead Author

It is the responsibility of the Lead Author to coordinate the writing, revision and submission of the publication. The Lead author will ensure that all co-authors of a publication or presentation are provided the opportunity to review all publication drafts, revisions and review comments.

It is the Lead Author's responsibility to submit all requested copies of manuscripts, abstracts, presentations, reprints, etc for ITN review and/or or tracking purposes as required according to ITN publications policy.

1.6.3 ITN Reviewers

Individuals requested to review publications or presentations arising from ITN research activities must endeavor to provide timely, thoughtful and objective feedback to authors. Conflicts that could prevent a reviewer from carrying out this responsibility must be reported immediately to the ITN so that alternate reviewers may be assigned.

1.6.4 Network Central Office

The Network Central Office (NCO) acts as a clearinghouse for all information related to the ITN that is released to the public domain, including both peer-reviewed and non-peer-reviewed scientific publications, abstracts and presentations. All such materials must be submitted to the NCO for inclusion in a central publications database. The NCO assist the NEC with the gathering and distribution of all materials and information necessary to carry out ITN publications policy matters. For tracking and historical purposes, the NCO must receive copies of internal reviews, drafts and revisions of manuscripts

and presentations at milestones defined in this policy. The NCO will file copies of all final manuscripts, abstracts and reprints with the NIAID in a timely fashion.

The ITN Director of Communications (DoC) is the ITN staff member responsible for coordinating NCO publications activities and will act as liaison between the ITN reviewers, staff and authors in publications matters. The DoC also provides authors with assistance in the preparation of publications and presentations, and in the interpretation of ITN publications policy.

1.7 ITN Reviewers

In general, the following individuals will act as reviewers for ITN abstract, manuscript, presentation or other reviews. However, alternate individuals may be asked to supply reviews depending on the expertise required:

- the CAC representative of the relevant disease or assay subgroup
- ITN Directors of the CTG and/or TAG
- an NIAID representative
- the Network Director and/or Deputy Directors
- area experts within the NSC

1.8 Confidentiality of ITN Reviews

Manuscripts submitted to the ITN for review and the subsequent review will be held in the strictest confidence and will not be shared with any individuals except for those directly involved in the manuscript review process and/or program staff of the awarding agency, NIAID.

1.9 Dispute Resolution

In all disagreements and disputes relating to the publication of Network related research materials, every effort should be made to resolve the issues amongst the relevant parties.

In those cases where consensus agreement cannot be reached through this process, a written request may be forwarded to the Director of Communications for immediate review by the ITN. Disputes will be mediated by the NEC, who will solicit information for all relevant parties to produce a recommendation that is binding upon all involved.

1.10 Exceptions

Under exceptional circumstances, those not specifically covered by this policy, the NEC shall have final decision-making authority and is bound to interpret these policies in the spirit of their stated goals.

Exceptions to this policy may only occur in order to allow rapid release of clinical trial results to disseminate information that is of public health importance. Such exceptions may be authorized only by the NEC.

2. MANUSCRIPTS

2.1 Overview of Manuscript Preparation, Review and Submission

Manuscripts are defined as writings that describe the results of ITN research activities that are submitted for publication to a professional journal, periodical, proceedings or other widely circulated publication, both peer-reviewed and non-peer-reviewed. These include papers detailing ITN study results, progress reports and reviews of ITN research activities, whether solicited or unsolicited. Manuscripts authored by ITN staff are subject to the same policy and procedures as those written by ITN members and investigators.

It is the responsibility of the Principal Investigator to initiate the publication process. Thereafter, the task of organizing the process of writing and editing the manuscript will fall upon a Lead Author (usually the PI, but otherwise appointed by consensus of the co-PIs and/or collaborators). Authorship of the manuscript should be assigned based upon the Authorship Guidelines contained in Section 5. It is expected that the Lead Author will maintain communication with other authors during development of the manuscript, soliciting their input and feedback wherever necessary, such that the content of the final manuscript is acceptable to all listed authors.

If the study from which the manuscript has arose had an associated CTA with industry, authors are strongly advised to update company personnel on the status and content of the manuscript throughout the process, as this will speed company approval of the final draft and minimize delays in the publication process.

It is the responsibility of the Lead Author and Principal Investigator to ensure that ITN requirements and forms are met in order to ensure timely ITN review and authorization.

An overview of the action items for the ITN manuscript publications process is shown in Table 1 for quick reference.

NOTE: Authors should note that many journals (including NEJM, JAMA, etc) that reporting of randomized clinical trials must conform to the standards detailed in the CONSORT Statement. The CONSORT statement provides evidence-based guidelines designed to improve the quality of reports of randomized trials. CONSORT comprises a checklist and flow diagram, offering a standard way for researchers to report trials. The CONSORT statement, checklist, and flow diagram are available at <http://www.consort-statement.org>.

2.2 Declaration of study participants

Principal Investigators must complete and submit a “Authorship Declaration” form prior to the initiation of any ITN study. The purpose of this form is to provide a reference list of the anticipated authorship for publications arising from each ITN study that may be referred to in case of disputes over authorship at a later time during the publications process. It is understood that any such list is likely to be subject to change as research progresses, and the supplied author list is not intended to translate directly into the

Table 1: Overview of the action items for the publication of manuscripts

| Milestone | Action |
|-------------------------------|---|
| Beginning of study | Submit “Authorship Declaration Form” |
| Begin Writing manuscript | Submit “Manuscript Notification Form” |
| Final Draft | Submit manuscript + “Request for Manuscript Review”, await review |
| Revised Final Draft | Submit Manuscript Agreement Form; All authors submit “Author Agreement Form”; Industry partners supply “Manuscript Approval Form” |
| First Submission to publisher | Notify ITN that publication has been submitted |
| Submit revision to publisher | Submit revised manuscript + journal reviews |
| Final Revision Accepted | Submit to PubMedCentral |
| Proofs | Notify ITN of receipt + intended publication date |
| Publication | Submit reprints to ITN |

final author list of any given publication arising from the study. This information will provide the ITN with some perspective should mediation be necessary.

In submitting the form, the PI will be asked to acknowledge that the supplied author list has been reached through a consensus among co-investigators and collaborators.

For clinical studies, a Declaration of Study Participants Form must be submitted prior to treatment of the first patient in the trial. For Tolerance Assays, the form must be submitted prior to the first application of the assay for the purposes of validation and/or accrual of data.

Should significant changes in individual contributions to the study occur during the course of the study, the Principal Investigator is expected to complete an amendment to the Declaration of Study Participants form in a timely manner.

2.3 Notification that writing of a manuscript has begun

A completed "Manuscript Notification Form" must be filed with the ITN when writing of a manuscript begins. This form requires: the working title, the list of authors as it shall appear on the published manuscript (or the first draft of the list of authors), a brief synopsis of the results and the conclusions of the proposed manuscript, a timeline for submission; the anticipated target journals and other simple information.

Submission of this form at the beginning of the writing process will allow the ITN to anticipate publications, provide writing and editing assistance and allow for timely review.

2.4 Review and approval of manuscripts by the ITN

Upon completion of the final draft of a manuscript and after all named authors have had the opportunity provide their input on its contents, the Lead Author must submit a completed "Request for Manuscript Review" form to the ITN. By completing this form, the Lead Author must provide confirmation that all authors named on the manuscript have had the opportunity to review and comment upon the manuscript and agree with its contents.

The ITN will then coordinate an internal review of the manuscript, the results of which will be forwarded to the Lead Author *within 5 business days*

ITN manuscript reviews will contain three sections: i) General comments; ii) Required changes; and iii) Recommendations. "General Comments" will contain the reviewers' broad observations on the manuscript, the results and their interpretation. "Required Changes" are those specific changes of high importance that must be included in the manuscript prior to submission to the journal in order for ITN approval to be received. "Recommendations" will detail specific suggested changes that the reviewers believe will strengthen the manuscript, although they are not strictly required for ITN approval. It is strongly recommended that lead authors share the results of ITN reviews with all authors of the manuscript.

Upon incorporation of required changes and/or ITN recommendations into the manuscript, the Lead Author must complete an "ITN Publications Agreement Form", which includes the revised manuscript and a response to the ITN review. The response to the ITN review should briefly summarize the changes to the manuscript and provide responses to ITN requirements and/or recommendations that were rejected by the author.

If there were Required Changes listed in the ITN review, the author must await ITN approval of the final draft. If the author was provided with no Required Changes, submission to the journal may proceed, as ITN approval of the final draft is implicit.

Note that if authors do not agree to incorporate the Required Changes of the ITN and intend to publish without ITN approval, the author remains bound by the confidentiality requirements of a fully executed Clinical Trial Agreement (CTA) and/or ITN subcontract. The ITN reserves the right to attach the following statement within the acknowledgement section of any manuscript submitted for publication without ITN approval:

"This research was performed as a project of the Immune Tolerance Network, a collaborative clinical research project headquartered at the University of California San Francisco and supported by the National Institute of Allergy and Infectious Diseases, the National Institute of Diabetes, and Digestive and Kidney Disease and the Juvenile Diabetes Research Foundation.

This manuscript was not prepared in collaboration with members and investigators of the Immune Tolerance Network. The content and/or conclusions of this manuscript do not necessarily reflect the opinions or views of the Immune Tolerance Network or its sponsors."

Once the final draft has been approved by the ITN, authorization to publish will be granted once all authors and industry partners have documented their approval of the final draft, as below. Note that the ITN will not authorize publication until Manuscript Agreement forms have been received by all authors.

Sign-off by all authors: Prior to final ITN authorization, all authors named on the manuscript must forward a completed "Author Agreement Form" to the ITN that confirms they have reviewed and approve of the manuscript and details individual authors responsibilities.

Sign-off by industry partners: If the study from which the manuscript was derived involved a CTA with one or more industrial partners, the ITN must receive a completed "Manuscript Approval Form" from the designated individuals from each company, as detailed in the original CTA. Authorization to publish will not be

Once sign-offs have been received by the ITN, the lead author will be notified of ITN authorization and may then proceed with submission of the manuscript to the journal.

2.5 Journal Editors' Reviews and Subsequent Revisions

Once a revision of the manuscript has been completed based upon the reviews received from the journal editor and prior to re-submission of the revised manuscript, the Lead Author will complete a "Revised Submission Form," which consists of a copy of the revised manuscript and copies of the journal's review comments/requirements for publication.

In those cases where substantial changes that affect the conclusions of the manuscript are requested/required by the journal. The lead author must await ITN approval prior to resubmission to the journal. Where only minor changes are requested by the journal editors, lead authors may submit the revised manuscript to the journal without additional ITN review.

If an article has been turned down for publication by the editors, lead authors must complete the "Revised Submission Form," attaching only a copy of the journal's review comments/requirements.

Note that all co-authors and industry representatives are entitled to review and comment upon journal editorial responses and subsequent revisions.

2.6 Proofs

Proofs of manuscripts sent to the corresponding author by the publisher are *not* required to be forwarded to the ITN. However, at this time, it is requested that authors notify the ITN of the impending publication date of the manuscript by emailing the [Director of Communications](#).

2.7 Reprints

Within 7 days of publication of the manuscript, the Lead Author will email an original reprint of the article, in electronic format to the [ITN Director of Communications](#). If an electronic version of the article is not available, the ITN will accept a hardcopy version via fax.

2.8 Acknowledgements

All manuscripts must contain the following sentence within the acknowledgements section:

“This research was performed as a project of the Immune Tolerance Network, a collaborative clinical research project headquartered at the University of California San Francisco and supported by the National Institute of Allergy and Infectious Diseases, the National Institute of Diabetes, and Digestive and Kidney Disease and the Juvenile Diabetes Research Foundation.”

2.9 Assistance Available

During manuscript preparation, ITN statisticians and ITN Communications staff are available to authors to assist in data analysis and copy editing. Authors may request assistance using the appropriate fields in the “Manuscript Notification Form.”

3. ABSTRACTS & MEETING PRESENTATIONS

3.1 Overview

The following policy and procedures pertain specifically to the preparation, submission and review of scientific abstracts and meeting presentations. Among the types of publications falling under these guidelines are:

- scientific abstracts for meeting presentations or posters
- invited or keynote presentations at scientific meetings
- symposium presentations
- general ITN overview presentations

For the purposes of this document, scientific abstracts are defined as those that contain descriptions and/or references to original research performed in ITN studies..

In general, it is the responsibility of the Principal Investigator to initiate the process of preparing a scientific abstract. Thereafter, the task of coordinating, writing and editing the abstract will fall upon a Lead Author (usually the PI, but otherwise appointed by consensus of the co-PIs

and/or collaborators). Authorship of the abstract should be assigned based upon the Authorship Guidelines contained in Section 5. It is expected that the Lead Author will maintain communication with other authors during development of the abstract, soliciting their input and feedback wherever necessary, such that the content of the final abstract is acceptable to all listed authors.

It is the responsibility of the Lead Author and Principal Investigator to ensure that ITN requirements and forms are met in order to ensure timely ITN review and authorization.

An overview of the action items for the ITN abstract and presentation publications process is shown in Table 2 for quick reference.

Table 2: Overview of the action items for scientific abstracts

| Milestone | Action |
|-----------------------|---|
| Prior to submission | Submit "Abstract Review Request Form" await ITN review |
| Abstract Acceptance | Send notification of acceptance with time, date, session information |
| Prior to Presentation | Submit "Presentation Review Request Form" with presentation, await ITN review |

3.2 Abstract Review

Abstract Notification & Submission: Authors planning to submit an abstract for consideration at scientific meetings must complete and submit an authorized "Presentation Review Request Form" to the ITN **no less than 3 business days prior to the submission deadline.**

The ITN will coordinate a short internal review of the abstract, the results of which will be forwarded to the Lead Author *within 2 business days.*

ITN abstract reviews will contain two sections: i) Required changes; and ii) Recommendations. "Required Changes" are those specific changes of high importance that must be included in the abstract prior to submission to the journal in order for ITN approval to be received. "Recommendations" will detail specific suggested changes that the reviewers believe will strengthen the abstract, although they are not strictly required for ITN approval.

The author must demonstrate to the ITN that "Required changes" have been instituted in the abstract prior to its submission.

Note that if authors do not agree to incorporate the Required Changes of the ITN and intend to submit without ITN approval, the author remains bound by the confidentiality requirements of a fully executed Clinical Trial Agreement or ITN subcontract. The ITN reserves the right to attach the following statement within the body of abstracts submitted for publication without ITN approval:

"This abstract was not prepared in collaboration with members and investigators of the Immune Tolerance Network. The content and/or conclusions of this abstract do not necessarily reflect the opinions or views of the Immune Tolerance Network or its sponsors."

The results of ITN reviews should be made available to all authors at their request.

3.3 Abstract Acceptance

When the Lead Author receives confirmation of abstract acceptance or denial from the meeting organizers, he/she must notify the ITN of the result together with date, time and session information (including whether poster, plenary talk, symposium talk, etc) for the abstract.

3.4 Presentation/Poster Review

The Lead Author will submit copies of all materials to be presented (including slides, overheads, electronic presentations, handouts, and/or the content of poster presentations) and/or published (including abstracts, papers to be included in the scientific proceedings, or other materials) to the ITN together with a completed "Presentation Agreement Form". These materials are to be submitted no later than 7 business days prior to the presentation or meeting session to which the abstract was accepted.

The ITN will coordinate an internal review of the materials, the results of which will be forwarded to the Author *within 5 business days*.

ITN presentation reviews will contain three sections: i) General comments; ii) Required changes; and iii) Recommendations. "General Comments" will contain the reviewers' broad observations on the presentation, the results and their interpretation. "Required Changes" are those specific changes of high importance that must be included in the presentation prior to submission to the journal in order for ITN approval to be received. "Recommendations" will detail specific suggested changes that the reviewers believe will strengthen the presentation, although they are not strictly required for ITN approval.

The author must demonstrate to the ITN that "Required changes" have been instituted in the presentation prior to presentation at the meeting.

Note that if authors do not agree to incorporate the Required Changes of the ITN and intend to present without ITN approval, the author remains bound by the confidentiality requirements of a fully executed Clinical Trial Agreement or ITN subcontract. The ITN reserves the right to require the following statement be added to all materials that do not receive ITN approval:

"This presentation was not prepared in collaboration with members and investigators of the Immune Tolerance Network. The content and/or conclusions of this abstract do not necessarily reflect the opinions or views of the Immune Tolerance Network or its sponsors."

The results of ITN reviews should be made available to all authors at their request.

Note that if the abstract is to be included in a published book of abstracts, the author will notify the ITN of the complete bibliographical reference for the abstract (including page numbers).

3.4 Late Breaking Abstracts

Late breaking abstracts, those whose submission occurs after the official conference or meeting submission deadline, are covered by the same policies and procedures outlined in this Section. It is the author's responsibility to ensure the ITN has sufficient time for review. The ITN will work with investigators to meet deadlines whenever possible.

3.5 Other abstracts

In the cases where authors are preparing abstracts of a type not described in the previous sections, or where ITN policy is not specific, authors should contact the ITN DoC for guidance. Review of these abstracts will take place at the discretion of the DoC.

3.6 Invited Presentations

ITN members invited to present or discuss ITN study results or general activities at scientific meetings or other scientific forums should contact the ITN DoC with details of the request prior to acceptance. Invited speakers should note that the ITN maintains a number of materials that might assist in the preparation of presentations on ITN activities, as outlined in section 3.8.

3.7 Acknowledgement

Abstracts describing ITN research activities should include the following acknowledgement in the text:

“This research was performed as a study of the Immune Tolerance Network.”

All presentations detailing ITN research activities must include a short, appropriate acknowledgement of the ITN and its awarding agencies, NIAID, NIDDK and JDRF.

3.8 Presentation Resources Available

The ITN maintains a number of standard slide sets for use by ITN members. These include slides describing the ITN mission, research priorities, membership and structure, research activities, peer-review system, etc, as well as up-to-date progress reports on all ITN research studies. These are available for download on the members website. Investigators are free to use these slides and should contact the DoC with any questions or comments.

Standard slide templates, graphics and ITN logos are also available on the ITN members site for use in preparing presentations. In addition, ITN communications staff is available to assist members in preparing their presentation materials – authors who would like assistance should contact the DoC well before the presentation date.

4. OTHER TYPES OF PUBLICATIONS

4.1 Case Reports

From time to time, investigators may wish to publish a detailed report of the diagnosis, treatment, and/or follow-up of an individual patient that would be instructive to the medical community. Such case reports are covered under the same policy and procedures outlined for manuscripts in Section 2.

Investigators publishing case reports must ensure that the text of the manuscript complies with all HIPAA regulations regarding the disclosure of patient information. In general, all patient identifiers should be removed from the manuscript. However, if this is not possible (ie. this information is essential to the conclusions of the paper), investigators must provide the ITN with written proof that informed consent has been satisfied under HIPAA regulations and that the patient(s) have seen and approved the manuscript for publication.

Case reports must contain the standard ITN acknowledgement described in Section 2.10.

4.2 Invited Articles

In some cases, ITN members may be asked by editors of scientific journals or books to submit review articles dealing with ITN research activities. In general, such papers are governed according to the policies and procedures described in Section 2 of the ITN publications policy.

Authors approached to write such articles are asked to contact the DoC prior to accepting these commissions.

4.3 Other ITN-related articles

Other publications not specifically disclosing novel scientific results or interpretations of results from ITN research studies are also subject to ITN publications policy. Examples include general descriptions of ITN research activities, research priorities, operating procedures, etc. or other publications where the author is acting as a representative of the ITN. These could be published in various peer-reviewed journals or proceedings or non-peer-reviewed publications such as magazines, books, electronic publications (including e-zines and websites), etc.

Such publications may or may not be subject to standard ITN publications policy for submitted manuscripts. Authors of such publications must submit a Manuscript Notification Form to the ITN when writing begins – subsequent review of the proposed publication will take place at the discretion of the Director of Communications.

In the case of editorial content, the ITN reserves the right to request a disclaimer be added to the effect that the opinions contained do not necessarily reflect the opinions of the ITN or its sponsors, NIAID, NIDDK or JDRF.

Some articles of this type may or may not require specific acknowledgements. Authors will be instructed on these requirements by the DoC.

4.4 Communications with the media

Communications with the media, such as interviews and press releases are covered in the ITN Public Relations policy.

5. AUTHORSHIP GUIDELINES

5.1 Overview

The goal of these guidelines is to provide a set of basic criteria for authorship to facilitate fair and equitable academic recognition of individuals contributing to ITN research studies.

It will be accepted by all participants, that the Study Leader and Principal Investigator, where different, will work to reach consensus on matters affecting publications such as assignment of lead authorship and general authorship, selection of appropriate journals/conferences for presentation, etc.

All disputes regarding publication authorship will be mediated by the NEC. Individuals wishing NEC mediation in authorship disputes should submit a written request containing relevant background information to the DoC prior to ITN internal reviews.

The Principal Investigator and/or Study Leader of a study have first right of refusal as Lead Author or to present the results of ITN-sponsored studies. If declined, the PI/Study Leader may designate another individual to do so.

5.1 Primary Publications

Primary publications are those manuscripts or abstracts that disclose data, analyses, opinions or other information central to the main objectives of the trial. This includes interim analyses of clinical or mechanistic data in ongoing trials.

The Principal Investigator (or Study Leader) will be the Lead author of the publication of the final study results and any interim analysis deemed appropriate by the CAC. The PI will assign authorship to individuals based on their contribution to the project. Authorship should be granted for individuals:

- participating in the accrual and/or treatment of patients
- participating in the design of the study
- participating in the analysis of results
- participating in mechanistic or tolerance assay studies or patient monitoring procedures that directly affect clinical procedures in the study or have specific relevance to the publication's hypothesis and/or conclusions
- generating/providing necessary reagents or compounds utilized in the trial

In addition, the ITN may require certain ITN or NIAID staff to be included as authors of publications for which their participation in the planning, execution or analysis of the study was central to its success. Authors and PIs are asked to bear this in mind when deciding authorship over given publications.

Order of authorship shall be based on the relative contributions of each individual participating in the conduct of the trial, as judged by the Study Leader and/or Principal Investigator, with input from the study participants where necessary.

5.2 Secondary Publications

Secondary publications are those manuscripts or abstracts that describe data, analyses, opinions or other information that is peripheral to the main objectives of a study, but have utilized resources or data generated in that study. Examples include comparison of assay techniques on a specific clinical samples set, methodological studies, etc. Secondary publications may also arise from the analysis of data generated from more than one clinical or tolerance assay study.

Unless otherwise agreed upon, the Lead author of secondary publications will be the principal investigator of the secondary or ancillary study. The Lead author will name additional authors based on their contribution to the project. The list of authors must be acceptable to the appropriate Subgroups. Authorship on the publication must be granted for:

- participation in the analysis of data for the publication

- participation in mechanistic or tolerance assay studies that have specific relevance to the publication's hypothesis and/or conclusions
- participation in the design of the study
- the study leader, PI and participants in the primary study(s)
- clinical site leaders of the primary study or study which provided clinical specimens that were analyzed

In addition, the ITN may require certain ITN or NIAID staff to be included as authors of publications for which their participation in the planning, execution or analysis of the study was central to its success.

Order of authorship shall be based on the relative contributions of each participant, as judged by the Principal Investigator, with input from the subgroup committee where necessary.

5.3 Ancillary Publications

Ancillary publications are those manuscripts or abstracts whose purpose is the general communication of ITN goals, methods, research activities, progress, etc.

Authorship of ancillary publications should be limited to those individuals directly contributing to the writing and preparation of the publication or those providing information pertinent to the conclusions or objectives of the publication. The ITN may request ITN staff members to be added to the authorship list in publications where descriptions of the results of ITN staff efforts/innovations are central to the objectives of the publication.

5.4 Invited Lectures

It is an overriding principle of the ITN publications policy that the Principal Investigator and/or Study Leader of a study have first right of refusal as Lead Author or to present the results of ITN-sponsored studies. Investigators who are invited to present ITN study results should discuss the invitation with the PI prior to acceptance.

5.5 Case Reports

Recommended authorship for case reports is limited to:

- contributing individuals at the primary clinical site presenting the case
- the principal investigator and co-principal investigators of the study
- individuals providing assay services relevant to the report ,and

In addition, the ITN may require certain ITN or NIAID staff to be included in the authorship of case reports where there was significant participation in regards to the subject of the case report.

5.6 Where the Number of Authors is Limited

In those cases where a limit on the number of authors is mandated by a publication, the authors of the publication must agree upon a suitable method of acknowledgement of all contributors that is acceptable to the specified journal. Options may include: i) the primary author listed as the appropriate Study Group (i.e. "Immune Tolerance Network Islet Transplantation Subgroup") with a complete list of contributing authors (as determined by the Study Leader, following the criteria listed above) placed in the acknowledgements section of the publication; ii) the group will agree upon a truncated listing of primary authors, with remaining contributors named in the acknowledgements.