CF Therapeutics Development Network Sponsor Packet

Welcome to the Therapeutics Development Network (TDN), a nationwide clinical trials network funded by the Cystic Fibrosis Foundation (CFF). Through efficient study design, optimized clinical trial execution, and high-quality data, the TDN helps speed the delivery of new and better therapies to people with CF.

The TDN is a collaborative organization composed of specialists in CF clinical research from a variety of disciplines and institutions:

- A central Coordinating Center at Seattle Children's Research Institute supports clinical trial development, management and analysis, and provides training, tools and templates to encourage and facilitate quality, efficiency and consistency within the network.
- CF Foundation-accredited care centers with demonstrated expertise in clinical research, called CF Therapeutics Development Centers, which recruit study participants and conduct clinical trials.
- A group of laboratories and interpretive centers, called National Resource Centers, which specialize in advancing new biomarkers and developing and measuring CF clinical trial outcomes.

We look forward to working with you and below are a few tips for maximizing an effective collaboration with the TDN:

- Submit your protocol and any significant amendments to study design or subject eligibility to the TDN Protocol Review Committee.
- Engage with the Cystic Fibrosis Foundation Data Safety Monitoring Board for appropriate safety monitoring of your study.
- Remember that our patient population is limited, and most studies rely on participants willing to enroll in multiple studies at different times. Be sure to treat your participants like the valuable resource that they are by ensuring that it doesn't cost them to participate in your study (See *TDN Guidelines for Payment to Study Subjects*).
- Maximize efficiency and improve the quality of your data by ensuring that sponsor generated central source document templates can be customized by sites to use for your study. The TDNCC can provide a template to customize as needed.
- As site selection decisions are made, communicate site selection decisions not only to selected sites but also those that aren't selected so that they can participate in other studies. And if site selection is delayed, communicate to all sites what your timeline will be.
- To maintain the financial health of our study centers we encourage sites to stipulate in their contracts that sponsor payments will be made over the course of the conduct of the study as specific milestones are met.

This welcome packet provides you with tools and information to help you understand how we work as a network and facilitate the execution of your clinical studies within the TDN. This information is divided into the following categories:

Consulting and Scientific Review

Study Conduct

Patient Recruitment

CF 101 Overview Training

If you have any questions or comments please don't hesitate to contact us:

TDNCC
tdncc@seattlechildrens.org

Consulting and Scientific Review

TDN Sponsor Engagement

With extensive experience in planning and conducting cystic fibrosis clinical research, the Therapeutics Development Network Coordinating Center (TDNCC) engages with industry sponsors to provide protocol development expertise. This early collaboration and advisement provides support for sponsors prior to the submission of their study protocols to the TDN Scientific Review process.

CF Foundation Community Voice provides sponsors access to the expertise of people with CF and those affected by CF. Whether you are looking for a larger group of CF Community members to survey or a small group of trained individuals to review your protocol or other study materials, this offering provides the opportunity to improve the feasibility and interest in your clinical studies. More information on this resource can be found on the Sponsor Engagement webpage.

Scientific Review: Compound and Protocol Review

Before a multi-center interventional or observational study can be designated as "TDN sanctioned" and called a "TDN Study," the study protocol must undergo scientific review by the TDN Protocol Review Committee (PRC) and Clinical Research Executive Committee (CREC). This scientific review is composed of two parts: compound review and protocol review. Compound review is done at the time of the first submitted protocol for a new agent. It includes an independent evaluation of the preclinical biological characteristics of the compound and an assessment of the likelihood it may have a strong, positive clinical impact. Once compound review is complete, the protocol is the evaluated in the areas of feasibility of study visits and procedures, feasibility of enrollment, and overall strategic fit (compound, scientific merit, study design, fit in network) within the current TDN clinical trial pipeline.

We offer US TDN-only scientific review as well as joint US and European Cystic Fibrosis Society Clinical Trial Network (ECFS CTN) and/or Canada Clinical Trial Network (CanACT) review. For global studies, utilizing joint review provides efficient and streamlined protocol review and ultimately results in simultaneous sanctioning of the protocol for multiple clinical trial networks. A fee is charged for protocol review services and a contract with the CF Foundation must be executed to initiate the review.

Type of Review	Fee
TDN	$5,000
TDN + ECFS CTN	$10,000
TDN + CanACT	$7,000
TDN + ECFS CTN + CanACT	$16,000

Additionally, the TDN requests that any protocol amendments that result in a significant impact on eligibility, safety or study design, be submitted for administrative CREC review.

For more information on scientific review, please visit our webpages and flowchart.

CF Therapeutics Development Network Statement on Tobacco Entity Involvement

The mission of the Cystic Fibrosis (CF) Therapeutics Development Network (TDN) is to facilitate the clinical study of new and existing therapies to cure and control cystic fibrosis.

The Centers for Disease Control (CDC) notes the many significant, harmful effects of tobacco use, including disease, disability, and damage to nearly every organ of the body. The European Respiratory Society (ERS) and the American Thoracic Society (ATS) have publicly condemned the involvement of tobacco or nicotine delivery systems industries in developing pulmonary therapies, and therefore will not include clinical trials results from companies with such ties in their publications nor will accept any research for oral presentations at its conferences.

Because involvement with tobacco entities contradicts our mission, the CF TDN and its members are aligned with the position of the ERS and ATS. **The TDN cannot sanction a clinical trial for conduct within the Network that, in the TDN's view, has tobacco industry associations.**

CF Foundation Data Safety Monitoring Committee

The CF Foundation has established an independent Data Safety Monitoring Board (DSMB) that includes experts in CF clinical care, clinical and basic science research, bioethics, biostatistics, and CF community representatives. The DSMB is charged with the oversight of all clinical trials sanctioned by the TDN CREC and conducted in the network. Therefore, it is a requirement that every trial conducted in the network utilizes the DSMB in some capacity. The DSMB Chair will work with each sponsor to determine the appropriate level of oversight for the trial based on factors such as the trial phase, type of compound and number of patients to be enrolled. Initiating contact and completing preliminary work with the DSMB can start and be done in parallel with TDN scientific review; however, the DSMB will not execute the DMC charter until after the PRC completes its scientific review.

For more information on the CF Foundation DSMB, please visit our webpage.

Study Conduct

Solicitation of Study Interest

We encourage sponsors to utilize the TDNCC to perform site solicitation on their behalf to determine the interest of network sites for participating in the study. The TDNCC database of site contact information is maintained in real-time and ensures that the solicitation is going to the right people at each TDN site. To take advantage of this, sponsors complete a template solicitation that includes a non-confidential study summary. The TDNCC will collect and compile site responses and prepare a list of interested sites, the site's estimate of the number of subjects they can enroll and appropriate site contact information. This is complimentary for sponsors who submit protocols to the TDN for scientific review. Site solicitation is most often done in parallel with protocol review, but in some situations can be conducted before initiating protocol review. The timing is at the discretion of the TDNCC.

TDN centers are most responsive to study solicitation e-mails sent from the TDNCC because it confirms that the protocol is undergoing TDN scientific review. Given the number of CF studies in start-up at any one time, most TDN investigators will ignore requests for feasibility information from sponsors or CROs not previously identified by the TDNCC. Sponsors that choose to conduct their own feasibility and site solicitation, and not go through the TDN, should notify the TDNCC of their intention to contact sites directly. This notification helps the TDNCC field questions from sites accurately. Finally, the TDN asks that sponsors share a final list of selected sites with the TDNCC once site selection has been completed and also notify sites that aren't selected in a timely manner. This information will be used to populate our network database (more information provided below).

If you are interested and have not already requested this service in your TDN Protocol Review Application, please contact us to get started.

CF Regional Cooperative Initiative

The goal of the CF Regional Cooperative initiative is to further cultivate trust and relationships amongst Therapeutic Development Center (TDC) programs as well as between CF care centers and TDC programs through opportunities to share best practices and foster collaboration around clinical research. All CF Care Centers are associated with a regional cooperative. We anticipate that these cooperatives will increase opportunities for all people with CF to access clinical trials by increasing awareness about the need for referrals for many studies and ensure that all CF care centers are familiar with the resources available to foster such referrals. We encourage sponsors to approach site selection with a regional mindset and minimally select at least one site within each region, when feasible, to facilitate referrals. A map of the Regional Cooperatives can be found in the attached *Regional Cooperative Map* For a full list of sites and regions, please contact us at TDNCC@seattlechildrens.org

TDN Central IRB: Advarra

The TDN has partnered with Advarra IRB to serve as the central IRB of choice for the TDN. Advarra has significant prior experience in supporting academic research networks and has incorporated both CF medical and CF community expertise onto their boards. We hope that you will join us in this endeavor and use Advarra as the central IRB for review of your CF clinical trials. Currently, the majority of TDN sites have agreements with Advarra and we continue to work with the remaining sites to gain universal acceptance of Advarra. We hope that the efficiencies of using the central IRB will allow you to focus earlier on issues around budget and contract negotiation in the early phases of study start-up, since these items are often the rate limiting steps. Please contact us if you have any questions about utilizing Advarra for studies conducted in the TDN.

TDN Research Database

The TDNCC has established a database of clinical studies to manage overall network activities; this database allows us to populate the Clinical Trial Finder (see below), project the total number of subjects to be enrolled and participate in CF studies, and track TDN site performance. The TDNCC will contact sponsors to collect key study information to maintain this database. The timeline and enrollment data noted below are kept strictly confidential and are only provided to senior leaders at the CF Foundation and the TDNCC. More information can be found in the attached *Fact Sheet for Sponsors*.

Protocol Review (collected from PRC application):

- Study Timeline:
  - Date of first patient enrolled
  - Date of last patient enrolled

    - Date of last patient completed
- Intended site regions (e.g. US, Canada, Europe, Australia)
- Best contact at sponsor to provide future updates to TDNCC

Start-up:

- Final site list
- Adjusted timelines (as applicable)

During Clinical Trial (quarterly):

- Total enrollment
- Adjusted timelines (as applicable)

It is essential that sponsors respond in a timely manner to these metrics requests, as this information is crucial to network function. We appreciate your partnership. For more information or questions, please contact us.

Payments to Study Subjects

In an effort to standardize study subject payments across the network at a level that is both appropriate and ethical, the TDN has developed *TDN Guidelines for Payments to Study Subjects*. The current guidelines are attached. Although individual IRBs have the ultimate say in how study subjects at each site are compensated, sponsors are encouraged to use the dollar figures in these guidelines as the basis for patient compensation costs in their initial budgets. Additionally, based on feedback from our TDN centers we encourage sponsors to use a clinical trial payment software for subject reimbursement to ensure that patients are paid in an easy and timely manner.

National Resource Centers

Specialized procedures are often needed to measure outcomes in CF clinical trials, including laboratory-based measurements, such as sweat chloride, microbiologic endpoints, and inflammatory markers; and interpretive outcomes, such as multiple breath washout/lung clearance index and nasal potential difference.

There are two types of National Resource Centers (NRC):

- NRC Outcome Measure Advancement Cores: These cores seek to develop and validate new outcome measures relevant to CF clinical research. Over time, outcome measures supported through this mechanism can mature into NRC Clinical Research Service awards.
- NRC Clinical Service Cores: These established core research services provide centralized and standardized assays/outcome measures relevant to CF clinical research.

The NRCs are available to provide consulting services to sponsors as well as provide support for specific studies. If you plan to use specialized procedures in your trial, it is recommended that you contact the corresponding NRC early in your development plans. More information including descriptions and contact information for each NRC can be found on our webpages.

Publication of TDN Study Results

We expect all TDN studies to be published and results shared on the clinicaltrials.gov website in a timely fashion. It is particularly important to the CF community that study results for ALL studies are published, regardless of outcome, for the following reasons:

- People with CF are repeatedly asked to participate in studies; thus, it is important that they believe their time and effort participating in a study contributed to the scientific knowledge about the disease, a product, or product type regardless of whether the study had a positive or negative result.
- Investigators within the TDN are largely from academic institutions. Their ability to continue engaging in studies is hampered when their time and effort as investigators is not recognized through publication or presentation of the data at a national meeting.

Patient Recruitment

CFSmartReports Clinical Trial Query Tool

The CF Foundation has developed an online reporting tool, CFSmartReports, which uses CF Patient Registry data to populate key patient information for sites. This reporting tool, which is only available to staff at a CF care center, can run high level queries that provide an initial list of potentially eligible subjects for a study at an individual study site. These queries can improve the accuracy of a site's estimate of how many subjects they are likely to enroll, shorten the timeframe in which sites respond to Sponsors' feasibility surveys, and facilitate recruitment once enrollment begins. To build this query, the sponsor will need to provide a protocol synopsis or full protocol. These are usually provided at the time of PRC scientific review. Any changes in the inclusion and exclusion criteria from the original protocol initially provided should be communicated to us and request that the query be updated.

CF Clinical Trial Finder

The CF Foundation maintains a Clinical Trial Finder tool on their website to allow potential study participants to search for TDN-sanctioned studies. Each study page includes a brief description of the study design, basic eligibility criteria and a list of participating study sites. Users can narrow their search with filters such as age, location and therapeutic approach, and can contact research coordinators at specific sites if interested in a study. Users may also enroll in an e-mail alert system to be notified of new enrolling studies when they are posted on the finder tool.

In combination with the Trailblazer campaign (see below) and other resources, the Clinical Trial Finder tool helps facilitate the enrollment process by making study information accessible and easy to understand. It provides a direct avenue for patients and families to indicate interest in a study without waiting to be approached by their care provider.

For more information on the Clinical Trial Finder, please visit our webpages.

CFF Drug Development Pipeline

The CF Foundation maintains an interactive Drug Development Pipeline tool on their website to track the progress of cystic fibrosis drugs through the different phase of clinical research and, in some cases, approval by the Food and Drug Administration (FDA). For a drug or a program to appear on the Pipeline, it must meet certain conditions. The CF Foundation will facilitate adding and removing drugs in the Pipeline and the timing of when this occurs.

For more information on the Drug Development Pipeline, please visit our webpages.

Research Subject Referral

Historically, a CF patient's access to trials has been limited to those studies conducted at the nearest CF center. We have now entered an era of CF clinical trials in which we have a full clinical trial pipeline. Often these studies include restrictive eligibility requirements or procedures that can only be performed at a small subset of study sites. As a result, study sponsors are encouraged to plan for research subject referrals to study sites in order to successfully enroll their studies. To facilitate such referrals, the TDN has created a series of documents called *Successful Research Subject Referral for CF Clinical Trials* to provide tips for the referring site, the study site and the study sponsor.

CF 101 Overview Training Program

CF 101 Overview Training Program

The TDN has developed an online educational program that covers specific aspects of clinical research that are unique to cystic fibrosis. This program is designed to provide training for clinical research monitors and includes basic introductory information about CF, CF treatment strategies and medications, a brief overview of the TDN Network and the CF Foundation, and some specific aspects of monitoring CF clinical trials. We encourage all sponsors and CROs to offer this training program to their monitors, especially if they are new to CF. The cost of the course is negotiable. Please contact us to learn more about the training program and how to purchase.

CFF TDN Clinical Study Metrics Database
Fact Sheet for Sponsors

In an effort to improve the clinical trial performance of sites in the CFF Therapeutics Development Network (TDN) and assist sponsors with the identification of sites that have the appropriate training, resources, and patient base needed for a new study, the TDN has developed a database that tracks site performance metrics, overall study milestones, and enrollment. In order to keep this information up-to-date, Cystic Fibrosis Foundation (CFF) requires that sites that receive TDN research funding provide certain information about their study activities on an ongoing basis.

Note that all study milestone information and enrollment information is kept strictly confidential and is only provided to senior management at CFF and the TDN Coordinating Center (TDNCC). Both the CFF and TDNCC maintain confidentiality agreements with all corporate sponsors.

Specifically, the information collected from TDN sites about each study includes:

- Number of subjects site agreed to enroll
- Date the regulatory packet was received
- Date of IRB approval
- Date of contract execution
- Date of budget agreement
- Date site was approved to enroll (i.e. date all regulatory documents were received and site was approved to receive study drug)
- Date first subject screened
- Date first subject enrolled
- Date last subject enrolled
- Number of patients enrolled

These metrics are used to provide sites with regular quality improvement reports that can help them identify bottlenecks at their site and also to give them some idea of how they are performing relative to other sites in the network. The sites are only provided with detailed information from their own site; they do not see data from other participating sites.

Data from the TDN database is also linked to the Clinical Trial Finder on cff.org. The Clinical Trial Finder is an interactive website designed to help people with CF find a study and to assist CF care centers in referring their patients to other centers to participate in clinical trials. It is important that data is kept up to date so that information on the Finder is the most accurate. To that end, sponsors can ensure that the TDNCC has the final site list for their trials as soon as possible so that the appropriate sites show up on the Finder.

In addition, the TDNCC will contact sponsors of TDN studies once per quarter to obtain information about total enrollment in their studies and any changes to the following estimated study milestone timelines:

- Enrollment start: Date First Patient First Visit
- Enrollment end: Date Last Patient First Visit
- Study Complete: Date Last Patient Last Visit

This information will be used to project the total number of subjects anticipated to enroll and be active in CF studies in future and to determine if the TDN needs to add additional resources to meet the demands of sponsors.

Finally, at the conclusion of each study, the TDNCC will contact the sponsor to solicit information about the quality of the research conducted at each site in order to identify issues at the site that may require additional training or assistance.

If you have any questions about the database and security associated with it, please don't hesitate to contact Kelsie Pearson, Scientific Program Manager, Kelsie.pearson@seattlechildrens.org. We sincerely hope that you will help us with our endeavor to provide the highest quality sites for cystic fibrosis research.

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS DEVELOPMENT NETWORK

TDN MANUAL OF OPERATIONS

TDN Guidelines for Payment to Study Subjects

Purpose and Scope

This document provides guidelines for a unified approach to the payment of study subjects for participation in studies conducted through the CFF Therapeutics Development Network (TDN). Although the Institutional Review Board (IRB) at each participating site will have final responsibility for careful review and approval of payments to study subjects, the TDN has created these guidelines to assist sites in collaborating with their IRBs. While consistency among sites participating in TDN trials is desirable, sponsors are encouraged to honor the site-specific IRB approval for each study.

Approvals

The *TDN Guidelines for Payment to Study Subjects*, including the recommended payment schedule, will be reviewed as needed by the TDN Steering Committee and revised as necessary. This review will examine payment information from studies that have been conducted or are currently ongoing, as well as feedback from the various IRBs involved with those studies. This level of review will assist the TDN in making recommendations about payments to subjects that are unbiased and non-coercive.

Responsibilities

Each site participating in a TDN trial should adhere to these guidelines and the payment schedule whenever possible. It is the responsibility of the Steering Committee to review these guidelines.

Additionally, all TDN members must adhere to the FDA *Payment to Research Subjects Information Sheet*, included in the Guidance for Institutional Review Boards and Clinical Investigators materials found on the FDA's website.

It is recommended that each site participating in a TDN trial (where payment is being provided to study subjects) notify both their IRB and the subjects being recruited for the trial of the potential loss of benefits from Supplemental Security Income (SSI) and Medicaid due to trial payments that exceed the current $2,000 per calendar year exclusion. Please see the Guidance for Study Sites on Implementation of the Ensuring Access to Clinical Trials Act (EACT) document for further information and instructions for how patients can claim this exclusion. A payment schedule that best fits your needs will be agreed upon at study enrollment.

Process

Budgeting

Study sites participating in TDN trials should use the payment schedule included in this document to estimate costs of payment to study subjects, which will be included in the budget for TDN sanctioned trials. Study sites should also ensure that during budget and contract negotiations, the additional costs of

reimbursing study subjects for expenses such as their costs for meals, childcare, mileage, or other transportation as appropriate, lodging and parking are addressed, and that provision is made to pass these costs through to sponsors.

IRB Approval

Study sites should use the TDN guidelines in collaborating with their IRBs and inform their IRBs that such guidelines have been developed for TDN sites. The IRB at each site will have final approval of the schedule for payment to study subjects.

Payment Schedule

Individuals (or families) volunteering to participate in research studies deserve to receive reasonable and timely payment for their time and expenses incurred during participation. Such payment should not be excessive and should not be perceived as an inducement to participate. Also, payment should be timely through the use of the Greenphire ClinCard® or similar participant payment system. Current recommendations of the CFF Therapeutics Development Network (TDN) for appropriate payment follow.

Compensation for Time Spent at Study Visits

Study Visits

Generally, study subjects should be paid a maximum of $30/hour for participating in a study up to maximum of $400 for a single visit. These amounts may be adjusted in areas where the cost of living is significantly higher compared to the rest of the country or the complexity of the study.

It is expected that all subjects will be compensated for the *anticipated average amount of time for each study visit*. The determination of the anticipated average amount of time each study visit will take is site specific and should be determined at the time that study budgets are being negotiated with the sponsor and before finalizing the informed consent document. Anticipated average visit time should be calculated to the nearest hour.

Special Considerations for Compensation When Study Subject is a Minor

When a study subject is a minor, additional considerations may be important regarding reimbursement for time and expenses incurred in study participation. Please review your institutional practices and guidelines or discuss this with your IRB chair if additional guidance is needed.

Reimbursement for Expenses

Subjects should be reimbursed for actual costs incurred for mileage or other transportation as applicable, childcare, parking, meals, lodging, etc. Transportation costs may be prepaid where appropriate. Reimbursement for actual costs incurred does NOT affect SSI benefits and Medicaid, and is important to keep it separate for these reasons.

Mileage

Reimbursement for mileage should be provided at the current federal business mileage rate

Other Expenses

Reimbursement for additional childcare costs related to study participation, parking fees and meals should be made at the rates applicable for the participating study site.

Guidelines for Long-Distance (>200 miles) Participation

In some instances, subjects traveling long distances (>200 miles) may require air transportation. If participation by subjects who travel long distance is required, the sponsor of the study should underwrite these costs. *Prior approval from the sponsor should be obtained by the site before subjects are recruited or payment is arranged*. It is expected that sponsors would cover theses expenses up front and that participants would not need to cover this cost and wait for reimbursement.

For minor children, travel expenses should be paid for the study subject and at least one parent/legal guardian. For adult study subjects, travel expenses should be paid for the subject. Consideration may be given to defraying travel costs (partial or complete) of a travel companion for adults.

Additional expenses related to study subjects traveling long distances (airfare, housing, meal expenses, and local transportation) should be negotiated and submitted as pass-through costs to the study sponsor. Since subject reimbursement for these expenses is for incurred costs, it will NOT affect SSI benefits and Medicaid. All arrangements should be made in the most cost-efficient manner possible. Participants' needs should be accommodated so that a minimal amount of expenses are covered by the participant for later compensation.

Guidelines for Filing Payment Records with Institution

Compensation for participation in a clinical study is ordinarily reported to the Internal Revenue Service (IRS) as *miscellaneous non-employee income* on an IRS Form 1099. The IRS requires such reporting if payment for services is made in the amount of $600/year or more. The institution should not include on the 1099 form any amount that was paid to the individual for reimbursement of expenses. Please determine with your institution accounting department what records they require to ensure that study visit payments are kept separate from receipts or other documentation required to obtain payment for reimbursable expenses.

Consent Form Considerations

For clarity to potential subjects and the IRB that will be reviewing your center's study material and for calculating budgets, it is important that the consent form include the specific amounts to be paid for each visit. The consent form should not include blanket statements like "you will be paid $30/hour for participating in this study" for two reasons: 1) if a visit exceeds the time that you estimated, the subject may expect to be paid for the additional time; and 2) it is difficult for an IRB to calculate the total compensation that is being offered and thus evaluate the proposed compensation appropriately. An example of consent language that is clear and provides complete information for both subjects and the IRB is found below:

Example Consent Language

Payments to Participants

All subjects will be paid up to $600.00 to cover the expenses and time for participating in the study. The following amounts will be paid for each completed visit:

Visit 1	$90	Visit 6	$90
Visit 2	$90	Visit 7	$60
Visit 3	$60	Visit 8	$60
Visit 4	$60	Visit 9	$60

Visit 5 $60	Visit 10 $60

If the study is not completed, subjects will be paid for those visits that are completed and will be prorated accordingly, plus $60 for an Early Termination Visit.

All subjects will receive reimbursement for parking and mileage (at the current federal business mileage rate).

Note: Because CF is a rare disease, if a study participant is currently receiving SSI, Medicaid, or Medicare low-income subsidies, they can receive up to $2,000 in a calendar year as payment for study participation without it affecting their continued eligibility for these benefits. A payment schedule that best fits your needs will be agreed upon at study enrollment.

CYSTIC FIBROSIS FOUNDATION
THERAPEUTICS
DEVELOPMENT NETWORK

Successful Research Subject Referral for CF Studies:
Tips for the Study Sponsor

A. Introduction & Overview

Many new studies are currently being initiated in the CF population and often these studies include restrictive eligibility requirements or esoteric procedures that may only be available at a smaller sub-set of study sites. As a result, study sponsors are encouraged to plan for the need for research subject referrals to successfully enroll their studies. This document provides tips for sponsors to successfully facilitate the referral process to meet enrollment goals.

B. Definitions

Study site: The site conducting the study.

Referring site: The site or physician that is not conducting the study but that provides care to CF patients who may be eligible to participate in the study.

C. Tips for the Sponsor for Successful Partnership

Site Selection Process

Notify study sites during the site selection process that you will support the referral of subjects from other sites, and provide a summary of the support that you will provide. This enables study sites to consider how they will be able to support referrals and to include referral recruitment numbers in their enrollment estimates.

Study Information Packet

Provide the study site with a packet of non-confidential information that can be shared with potential referring sites. This packet ideally will include:

- A synopsis of the protocol, including eligibility criteria
- Study-specific subject recruitment materials (e.g. scripts, recruitment letter)
- Travel and Other Expenses for Referred Subjects. If airfare or overnight hotel stays are required these should be paid directly by the company rather than expecting patients to pay for these expenses out-of-pocket and wait for reimbursement. It is strongly advised that the sponsor contract with a travel agent for the highest level concierge service to assist potential subjects with their travel arrangements as study site research staff generally do not have time for this activity. If study site staff are required to make the arrangements, expect to pay them for any additional time required to perform these services.
- For other types of out of pocket expenses (e.g.; mileage, food, taxi, parking) it is imperative that subjects are reimbursed in a timely manner.
- Please utilize the Greenphire ClinCard System, or similar type of clinical trial subject payment system, to ensure out-of-pocket expenses are paid for in real-time making payments simpler, faster and easier for study participants and study sites.

IRB Materials for the Study Site

- Provide study sites with written instructions regarding travel arrangements that can be included in their initial IRB applications. These instructions should include how arrangements for travel for referred subjects are to be made, how reimbursement of subject expenses will be made, what items will be reimbursed, what reimbursement rates are and requirements for documentation. Include details explaining which expenses will be paid directly by the sponsor and which will require that the subject retain receipts to receive reimbursement.
- Additionally, the informed consent template provided to the study sites should include template language to accommodate referral subjects.

Study Site Budget and Contract

The following costs should be included in the study site budget if referral subjects are anticipated:

- Compensation for the extra coordinator time involved in obtaining and reviewing medical records for referred subjects (eligibility criteria, AEs, SAEs and concomitant medications throughout the study).
- Any pass-through expenses not directly paid by the sponsor.

Finder Fees

It is **NEVER** acceptable to offer a finder fee for referral.

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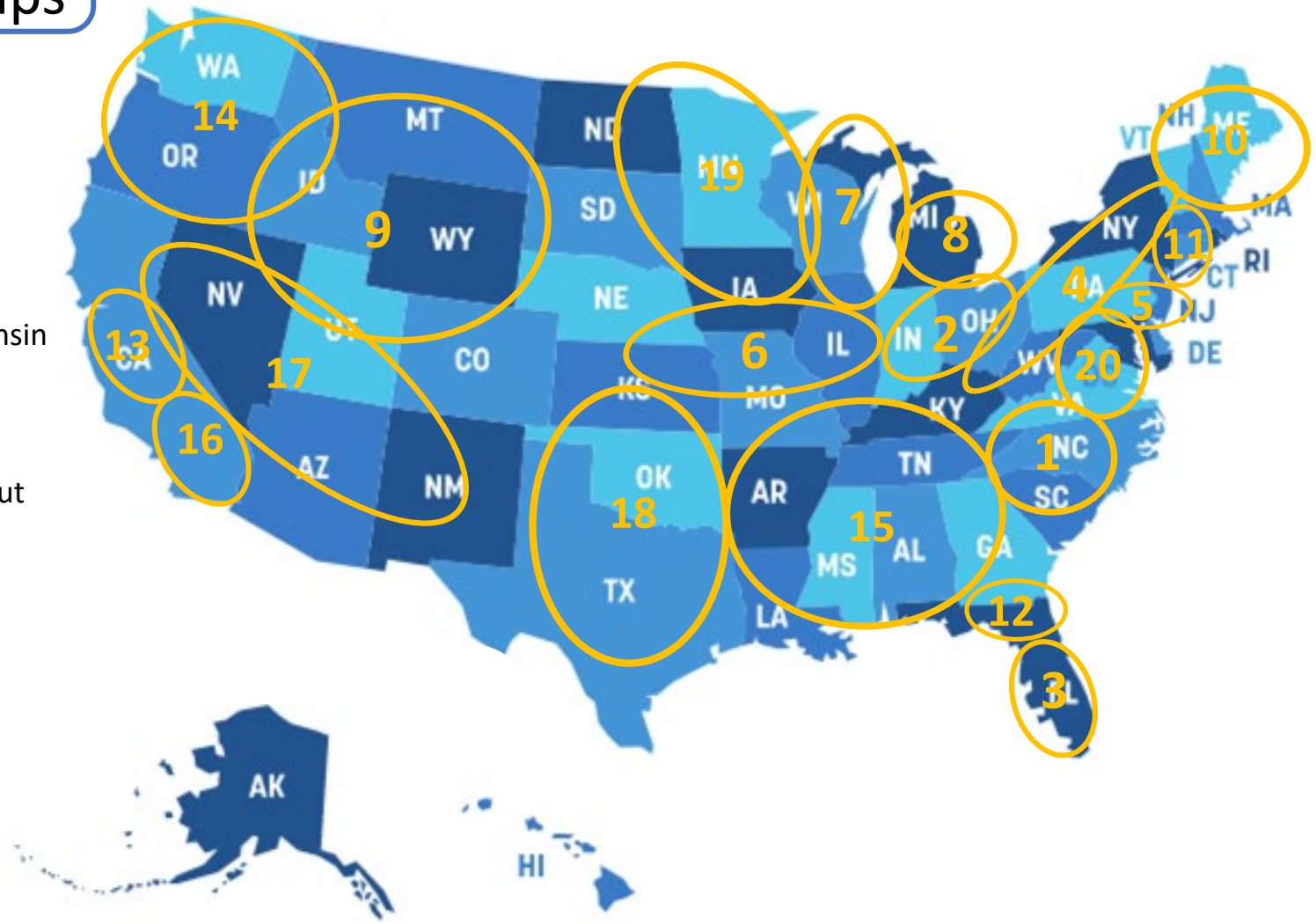
Regional Groups

1. Carolinas
2. Central Ohio/Kentucky
3. Central/South Florida
4. Eastern Great Lakes
5. Mid-Atlantic
6. Midwest Central
7. Midwest-Chicago/Wisconsin
8. Midwest-Northern Ohio
9. Mountain West
10. New England
11. New York City/Connecticut
12. North Florida
13. Northern California
14. Northwest
15. Southeast
16. Southern California
17. Southwest
18. Texas/Oklahoma
19. Upper Midwest
20. Virginia/Maryland/DC



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Site Facilitators

- Charleston, SC Adult
- Indianapolis, IN Peds
- Philadelphia, PA CHOP Peds
- Kansas City, MO
- Milwaukee, WI Peds
- Akron, OH Peds
- Denver, CO Adult
- Lebanon, NH Dartmouth-Hitchcock Adult
- Valhalla, NY Peds
- Gainesville, FL Adult
- Palo Alto, CA Peds
- Spokane, WA Providence Adult
- Hollywood, FL Joe DiMaggio Children's Hospital Peds
- Birmingham, AL Peds
- San Diego, CA Adult
- Tucson, AZ Peds
- Houston, TX Peds
- Minneapolis, MN Adult
- Pittsburgh, PA Adult
- Charlottesville, VA Adult