A Clinical Trial Site's Resource to Understanding Common Invoiceable Items & Services

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Section 1: Introduction

About This Resource

There are essentially three categories of billable items and/or services for protocol budgets. The first category is the "Per Subject/Per Visit" line-item which is the reimbursement tied to subject visits and/or visit procedures.

The second category is "Overhead" (a.k.a. Facilities & Administrative Costs or sometimes Indirect Costs) which are costs not directly attributable to a single protocol but allocable to a particular protocol, such as rent and utilities.

The third category, and the subject of this resource, is "Invoiceable Items & Services" which is for items and/or services that are either not directly tied to subject visits (e.g. Start-Up Costs) or tied to a subject visit but not routine to the visit (e.g. translation services).

SCRS developed this resource to assist sites in their understanding of key components to protocol budgets. Understanding these components and ensuring sites consider them for each trial budget is essential to the financial foundation of the site to ensure sustainability throughout the lifecycle of each protocol they undertake. Although it may seem as though sites and sponsors/CROs are sometimes at odds when at the negotiating table, sites and their sponsor/CRO customers do share this common goal.

It does none of these parties any good (and sometimes even causes harm to the relationships) when the parties begin a protocol only to realize they failed to appropriately budget for all of the site's costs associated with that trial, leading to a lack of resources to optimally complete the protocol. The failure to receive compensation for many trial activities is often, in part, due to a sites' lack of knowledge to properly budget for trial activities or to ask for them.

Arguably, many sites that have exited the business would be active sites today if they were compensated for all of their clinical trial activity, including what are often considered the "hidden costs". To ensure a sustainable industry to conduct protocols and to set sites up for the successful conduct of these protocols, sites and sponsors/CROs share responsibility in adequately addressing invoiceables in the budgeting process.

Section 2 of this resource provides a quick reference table of common Invoiceable Items & Services and the usual billable unit and/or frequency. Section 3 provides detailed information on each of these Invoiceable Items & Services beginning with a justification for each expense as an activity directly related to the conduct of the trial.

Following each description are helpful hints for calculating individual site costs associated with that Invoiceable Item and/or Service. Finally, Section 3 discusses alternatives to charging individually for

the Invoiceable Item or Service and other important notes are included for consideration. Section 4 provides a conclusive summary.

Overall, this resource has a two-fold purpose:

1) In the short term, we hope to (i) enhance a site's ability to identify and demonstrate protocol costs in a manner that justifies budget requests, and (ii) improve protocol success through transparent dialogue with sponsors and CROs regarding the true of conducting their protocols.

2) In the long term, we hope to provide a foundation for the normalization of very real "hidden costs" such that these become standard line-items in initial budget templates throughout the research industry.

Using This Resource

This resource is not all-inclusive but highlights most common Invoiceable Items & Services. It is important to note that costs will vary by site, by protocol, by other variables and can change over time. Nevertheless, adequate site budgeting is dependent upon a thorough analysis of operational and financial impact and securing an adequate budget with the initial Clinical Trial Agreement (CTA). Securing additional funding following CTA execution can be difficult and creates additional work for the site and the sponsor/CRO. Thus, a best practice is to secure a budget that can sustain the lifecycle of the protocol at the time of initial CTA execution.

As sites negotiate trial budgets, it is important they be aware that sponsors and CROs are often challenged to be able to defend added budget requests to their compliance departments or others, necessitating a sound justification for each expense. Providing a robust justification for each line-item at the time of budget submission will allow the sponsor/CRO to advocate on the sites' behalf in defense of their requests.

Not every line-item within this document will be relevant to every protocol nor to every site. This document means to serve as a guide. Sites must consider each trial individually and determine which line-items are applicable to the protocol. Blindly adding line-items to budgets that are not relevant to the protocol nor to the site will only serve to discredit the site. As many previous budgets do not account for these Invoiceable Items & Services, it may take effort from both the site and the sponsor/CRO to gain a clear understanding of each Invoiceable Items & Services and determine how and where to capture them within each budget.

Related Concepts Out of Scope of This Document

Protocol Feasibility Activity: Sites incur significant cost associated with each trial prior to their signing the CTA/budget. These costs include items and/or services such as business development, completion of qualification questionnaires, protocol feasibility review, CDA/CTA review, budget development, site qualification visits, investigator's brochure review and many others.

Usually the site is reimbursed for this from the sponsor/CRO if the protocol begins (e.g., reimbursed via the Non-Refundable Startup Fee) and possibly if the protocol was cancelled (e.g., reimbursed by the Protocol Cancellation Fee described herein).

What is out of scope of this document are activities that may not be invoiceable such as the cost to review and complete qualification questionnaires for protocols that do not proceed to CTA (e.g. a CRO that is querying sites for an unawarded protocol). Although not attributable to the cost of a different awarded protocol, it is a cost to the site thus usually included in their Overhead instead of an invoiceable to an unrelated protocol.

Costs Spread Over Multiple Protocols: There are certain costs that are germane to site operations that are technically not items and/or services allocable to a particular protocol budget but are allocable to the costs of running protocols in general. This includes a general non-protocol specific CTMS set-up, accounting systems, and contract development/review for sub-contracted services. An example of the latter would be the cost of creating a contract with an outside cardiologist to read EKGs across multiple protocols versus the direct cost of reading the EKGs particular to a protocol.

While technically not an item and/or service provided to the sponsor/CRO exclusively for a protocol, they remain a legitimate cost of the business and should be allocated to the protocols in some other manner (usually in Overhead) and not as an Invoiceable Item & Service unless done solely for the single protocol.

Screen Failures: While a site does invoice for screen failures, the concept and calculation of this expense relates more to the "Per Subject/Per Visit" budget category than to that of "Invoiceable Items & Services". Therefore, guidance on budgeting for screen failure costs is out of scope for this document.

Section 2: Quick Reference Tables

Invoiceable Items & Services Related to Protocol Start-Up	Typical Billable Unit
Non-Refundable Start-Up Fee	One Time
IRB/REB/EC Initial Submission Preparation Fee	One Time (Or Bundled in Start-Up Fee)
Insurance (i.e. Medicare/Medicaid) Coverage Analysis Fee	One Time (Or Bundled in Start-Up Fee)
Third Party Vendor Integration	Per Vendor (Or Bundled in Start-Up Fee)
Mock Subject Quality Assurance Run-Through Fee	Per Mock Run
Protocol-Required Test Scan Fee	Per Test Scan
Source Document Development Fee	One Time (Or Bundled in Start-Up Fee)
Pharmacy Set-Up Fee	One Time (Or Bundled in Start-Up Fee)
Lab Set-Up Fee	One Time (Or Bundled in Start-Up Fee)
Duplicative GCP Training of GCP Trained Staff Fee	Per Person (Or Bundled in Start-Up Fee)
Non-IRB/REB/EC Committee Interface (For Protocol Start-Up Issues) Fee	One Time (Or Bundled in Start-Up Fee)
Transcribe Provided Information To Sponsor/CRO Custom Form Fee	Per Form or Per Page (Or Bundled in Start-Up Fee)

Invoiceable Items & Services Related to Inter-Protocol Events	Typical Billable Unit
Recruitment Activity (Site Staff Time) Fee	Per Hour
Recruitment Activity (Third Party Vendor) Fee	Per Invoice
Diagnosis & Treatment for Protocol-Related Injury Fee	Per Service
Safety Report Review Fee	Per Report
Scheduled Monitoring Visit Fee	Per Time Unit (e.g., Per Half-Day)
Regulatory or Sponsor/CRO Audit Visit Fee	Per Time Unit (e.g., Per Half-Day)
Unscheduled Monitoring Inquiry Response Fee	Per Time Unit (e.g., Per Hour)
Certified Copy of Electronic Health Record Fee	Per Record or Per Page
Protocol Amendment Review & Set-Up Fee	Per Amendment
Subject Reconsenting Due to ICF Change Fee	Per Subject
Translation/Interpreter Services Fee	Per Unit of Service
Third Party Transportation Fee	Per Invoice
Interim/Continuing IRB/REB/EC Filing Fee	Per Filing
Unscheduled Subject Visit Fee	Per Visit

Non-IRB/REB/EC Committee Interface (For Post Protocol Start-Up Issues) Fee	Per Report/Fee
Change of Monitor Fee	Per Change
Subject Transfer Fee	Per Transfer
Non-Site Vendor Issue Resolution Fee	Per Hour
Subject Helpdesk Fee for Non-Site Provided Technology	Per Hour
Special Requested Added Staff Fee	Per Hour or Per Month
Post-Startup Meeting/Training Fee	Per Staff / Per Meeting
Periodic Protocol Maintenance Fee	Annually, although can be more or less frequently)

Invoiceable Items & Services Related to Protocol Close-Out	Typical Billable Unit
Protocol Close-Out Fee	One Time
IRB/REB/EC Close-Out Submission Preparation Fee	One Time (Or Bundled in Close-Out Fee)
Pharmacy Close-Out Fee	One Time (Or Bundled in Close-Out Fee)
Investigational (and/or Control) Product Return/Destruction Fee	One Time (Or Bundled in Close-Out Fee)
Record Packaging Fee	One Time (Or Bundled in Close-Out Fee)
Protocol Record Storage Fee	One Time (Or Bundled in Close-Out Fee)
Records Destruction and Electronics Recycling Fee	One Time (Or Bundled in Close-Out Fee)

Miscellaneous Invoiceable Items & Services	Frequency
Unexpected Cost Allotment Fund	Per Event
Post-Close-Out Record Retrieval Fee	Per Event
Subject Stipend IRS-1099 Determination & Filing (U.S. Sites) Fee	Per Subject
Cancelled Protocol Fee	Per Cancelled Protocol

Section 3: Activities with Annotations

Key Concepts

Billable Hourly Rate: This is the fully loaded hourly rate of an employee that is billed to a customer, not solely the hourly/salary rate of the employee. This is generally equivalent to Salary + Benefits + Overhead + Reasonable Margin. Often this is equal to twice the hourly/salary rate but may vary by site.

Inflation Adjustments: While everyone generally understands that $100 in the future is not worth as much as $100 is worth today, many fail to quantify that amount and negotiate this into multi-year budgets. This decrease in value in reimbursement of a site's costs is not difficult or time consuming to calculate. There are websites that can do this but recommendations are that budget professionals learn the Present Value (PV) and Future Value (FV) functions in finance calculators or software like Excel for better analysis and budget planning.

Note that cost-of-living rates vary over time (the U.S. average 2010-2019 was 1.7%, however 2022 inflation has been over 8%) and we do not know what they will be in the future, so predictive estimates must be made. In the examples below, it is important to note that these are not budget increases but the same budget numbers across three years with a cost-of-living adjustment based on the current expected inflation rate.

- Example 1: Have defined step increases in the budget based on an agreed inflation estimate: If the parties agree on a 5% annual rate increase, the budget would list Y1 at $1,000, Y2 at $1,050 and Y3 at $1,102.50 to make the payments a constant value in present day money.
- Example 2: Have defined step increases in the budget based on a publicly available statistic: Instead of agreeing on a rate, the parties would agree on a relevant published statistic. The budget would list Y1 at $1,000 and then indicate that each year there will be an increase based off of a mutually agreed upon independent statistic (e.g. the Consolidated U.S. Consumer Price Index or the published healthcare components of that index which may more accurately reflect a site's expense).
- Example 3: Maintain a constant rate, accounting for inflation. If the expected inflation would be 5% then the parties could agree to set Y1, Y2 and Y3 at ~$1050.83 to average out the inflation over the three years (i.e. ($1,000 + $1,050 + $1,102.5)/3).

Mixing Costs Among Line-Items: When the parties are unable to negotiate the necessary amount for a certain line-item, one mitigation strategy is to negotiate higher reimbursement in other line-items in an effort to break even. While the net effect may be to successfully cover the site's overall trial expense, the artificially altering of the documented fair market value (FMV) for those line-items impacts future negotiations. This practice can lead to a negative impact, not only for the site, but

also for other sites across the globe as well when they attempt to negotiate based upon actual expense associated with the respective line-item.

While a short-term solution may be obtainable via this method, this practice is discouraged as it invalidates the integrity of the FMV defense. Rather, for the long-term benefit for the industry to achieve better consensus around each line-item and ensure fair market values based on valid and related costs, we encourage open dialogue to educate all parties regarding each expense and maintain the integrity of the line-items and their FMV.

Third Party Invoice Management Costs: The costs of many line-items may involve third party fees to which the site is paying the third party and promised reimbursement from the sponsor or CRO upon invoice. Two key factors come into play when this occurs:

(1) While the site may predict the initial cost of the invoice amount for budgeting purposes, the site is cautioned on the risks of hardwiring in a number into the CTA as opposed to leaving it open ended (e.g. "$2,500 USD" instead of "Paid Upon Invoice") as with the former, the site bears the cost of any increases in the third party pricing over time.

(2) While the site's full Overhead percentage amount is usually not applied to third party invoiced amounts, there is administrative cost borne by the site (that would not be borne by the site if the sponsor or CRO contracted with the third party directly instead of the asking the site to do it). This often includes but is not limited to

> (i) the generation/review/execution of the contract with the third party (which can be burdensome especially if between healthcare providers where Stark and Anti-Kickback laws apply),
>
> (ii) the set up the third party in the site's accounting systems,
>
> (iii) the processing of the third party's invoice(s), and (iv) the invoicing of and collecting or reimbursement from the sponsor/CRO.

There is also the time value of the money lost on the financial float, meaning the time between when the site pays the invoice and the time the site receives reimbursement for it. This cost should be either budgeted for in an "Administrative Processing Fee for Third Party Invoices" or elsewhere.

Invoiceable Items & Services Related to Protocol Start-Up

Not all of these line-items are relevant to every protocol and/or to every site. Use professional discretion when including a line-item in a budget.

Non-Refundable Start-Up Fee	
Description	• This fee covers protocol costs related to the site's completion of protocol start-up activities that are required prior to opening of enrollment at the site. This fee should include all costs not otherwise provided for by the sponsor/CRO or compensated as a pass-through reimbursement (e.g. paid in full upon third party invoice such as IRB/REB/EC fees).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost specific to the protocol. • This fee often includes numerous costs such as Confidentiality Agreement (CDA) completion, feasibility questionnaire (FQ) completion, investigator/site meeting attendance, IRB/REB/EC preparation and submission, budget and contract review and completion, vendor set-up, staff training, supply procurement, regulatory setup and many more. Depending on the site preference and/or sponsor requirements, the site may invoice these activities as separate line-items, or bundle them into this single Non-Refundable Start-Up Fee. • Also important for consideration when calculating start-up expense are the costs associated with the use of any and all third party vendors the site must purchase items and/or services from (e.g., commercial IRB fees, Medicare Coverage Analysis by an independent party, use of a third party hospital that invoices a protocol set-up fee). If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs within this Non-Refundable Start-Up Fee or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").

	Alternatively, the site can include each third party vendor fee as a separate line-item (which may also include some Third Party Invoice Management Costs), reimbursable to site upon copy of the invoice. See Third Party Invoice Management Costs in the Key Concepts section of this document for more information.
Alternatives to Charging This as A Line-Item	• Although this is often a single line-item, it is acceptable to charge individually for each item and/or service associated with start-up activities. • For start-up services directly provided by the sponsor/CRO, there should be a resultant decrease/removal of this expense from this Non-Refundable Start-Up Fee (e.g. the sponsor is providing the Medicare Coverage Analysis or paying the IRB/REB/EC fees directly). Direct sponsor/CRO payment for a third party service should be specified in the CTA as a sponsor/CRO obligation to avoid future dispute as to whose responsibility it is to pay the vendor. • There are few alternatives a site has to this charge other than to be underfunded for this item and/or service. Attempts to reallocate these costs into other areas of the budget are not optimal.
Important Notes	• It is important to ensure the Non-Refundable Start-Up Fee is in the CTA as unambiguously non-refundable reimbursement for the start-up costs and not in any way dependent upon future performance of the site (i.e., it is not an advance payment or other cash advance that the sponsor/CRO deducts from future payments). • It is intentional and important that the term "Non-Refundable" is included in the line-item title in the event the sponsor or CRO cancels or indefinitely delays the protocol prior to site initiation. • A site may develop tiered charging options based on protocol complexity such as a lower Non-Refundable Start-Up Fee (Post-Marketing Observational protocol) and a higher Non-Refundable Start-Up Fee (Phase 3 protocol). sites can delineate as many of these tiers as they like such as Non-Refundable Start-Up Fee (IDE protocol without Hospitalization) versus the higher Non-Refundable Start-Up Fee (IDE protocol with Hospitalization).

IRB/REB/EC Initial Submission Preparation Fee	
Description	• This fee covers the protocol costs related to the site's preparation and submission of required documents to the IRB/REB/EC prior to the engagement of subjects in the protocol. It is not the IRB/REB/EC fee itself (which the site invoices separately).

Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • This fee should include at a minimum, (i) regulatory professional time for preparation, processing and filing of all regulatory-affiliated documentation and (ii) investigator time for review and signature.
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • In the event a sponsor/CRO completes a portion of the document preparation on behalf of the site and/or contracts with a third party to do so, this would reduce but not eliminate the cost of the site to provide the items and/or services. In other words, the calculated costs would still reflect the time & expense incurred by the site to assist with their portion of the regulatory document preparation and submission (e.g. review of essential documents, routing documents for signature, etc.).

Insurance (i.e. Medicare/Medicaid) Coverage Analysis Fee	
Description	• This fee covers the protocol costs related to the site's need to prepare the justifications for and build the infrastructure to bill of one or more Subject's health insurance (instead of the sponsor/CRO) for routine care items and/or services affiliated with the protocol. It usually involves, at a minimum, review of protocol materials (including but not limited to the protocol, consent form and Clinical Trial Agreement), physician consultations regarding local and national standards of care and third party review/communications (e.g. Medicare Administrative Contractors).
Calculating the Costs	• If the site conducts their own Coverage Analyses, then this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the item and/or service multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • If the site contracts with a third party to conduct the Coverage Analysis, then this fee should include the vendor charges (can be estimated based upon vendor fee schedule) PLUS the estimated cost

	of the site to work with that vendor (e.g., prepare required documents, facilitate dialogue with stakeholders in the process etc.) to bring the process to completion. • Also consider the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • Instead of requesting that the site bill the subject for routine care items and/or services required by the protocol, the sponsor/CRO can pay for those items and/or services. The site does not need an insurance coverage analysis if they are not billing insurance. On a side note, this may also eliminate a barrier to recruitment and retention of subjects. • The sponsor/CRO can either directly pay this cost to a site-approved third party service provider or provide the coverage analysis to the site. Note that while providing for the written coverage analysis alone would decrease this cost to the site, the site still must calculate its costs to implement the protocol-specific parameters.
Important Notes	• Not all protocols require this or a review at a high level of complexity. For example, if the protocol is for the pediatric population, then there is no need to do the Medicare portion of the coverage analysis thus costs may be lower. • Note that while the sponsor/CRO providing the coverage analysis document would likely save time and cost, the site (and affiliated providers) who would bill for such services are the ones bearing the risk of submitting false claims thus the site must review and concur with the coverage analysis prior to implementing it.

Per Third Party Vendor Integration Fee	
Description	• This fee covers the protocol cost related to the site's need to set up and integrate sponsor/CRO-imposed vendors into the site operations. The fee is incurred once per vendor (e.g. if there is an electronic diary vendor and a recruitment company vendor, each vendor incurs the integration fee).

Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the item and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost.
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • If the use of one or more vendor(s) and/or their technology is optional, the site can refuse to use the sponsor/CRO provided vendor and/or explore alternative solutions to accomplish the intended task. • A site may develop tiered charging options based on certain classes of vendors such as Per Vendor Integration Fee (Mobile Health Company); Per Vendor Integration Fee (Non-Connected site Technology); Per Vendor Integration Fee (Connected site Technology); Per Vendor Integration Fee (Subject-Facing Technology); etc.

Mock Subject Quality Assurance Run-Through Fee	
Description	• This fee covers the protocol cost related to the site's quality assurance program to run a hypothetical or living person through the steps of each visit to (i) assure all protocol-related equipment and workflows are working; (ii) ascertain the risk of protocol deviations prior to them occurring with actual subjects; (iii) ascertain the subject experience; and/or (iv) identify issues that need addressed prior to the first enrollee.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • Alternatively, assuming the costs for the procedures within the "Per Subject/Per Visit" budget are valid, this amount is usable as the basis for this fee. It is important to recognize however, that since not all procedures may be performed (e.g. the site may perform mock phlebotomy to ascertain workflow quality but not actually run the required lab tests), this amount would not include the costs of tests and procedures not completed as part of the mock run-through.
Alternatives to Charging	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee.

This as A Line-Item	• One alternative to not charging this line-item is not performing the mock subject analysis if consistent with quality assurance and risk-based monitoring preparation. • Another alternative is to calculate the cost of this quality assurance activity into the site's protocol Overhead.
Important Notes	• Oftentimes an employee at the site can serve as the mock subject with no actual protocol procedures performed during the walk-through. • If the site is using a human volunteer for this, the site should do this with full transparency with the IRB/REB/EC to determine if and when this activity requires IRB oversight (e.g., protocol, informed consent etc.).

Protocol-Required Test Scans Fee	
Description	• This fee covers the protocol costs related to the calibration of radiology equipment (e.g., CT scanners) at the site specifically for the protocol. This is done according to the protocol and/or sponsor/CRO instructions prior to the first enrollee via scanning (i) specialized equipment (a.k.a. "phantom scans") or (ii) a human volunteer.
Calculating the Costs	• Institutions with radiology equipment usually have well defined costs in this area on a charge master that tie to the CPT code (or equivalent) to meet the needs of the phantom/human scan. • Test scans for calibration purposes done on human volunteers will have additional costs that the site needs to add to the above (e.g. additional IRB/REB/EC filings and informed consents) related to using a human volunteer for this research purpose. It may also require calculation of the Billable Hourly Rate of the human volunteer. • Be sure to inquire about both technical and professional fees when exploring expenses related to imaging or other testing for which a professional fee might apply. If the charge involves third party professional fees that are billed separately from the vendor institution's billing of the technical fees, these need to be added in to the protocol budget as well. Most professional fees have well-established charge masters that tie to the CPT codes (or equivalent) to meet the needs of the phantom/human scan.
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee or bundled in the Mock Subject Quality Assurance Run-Through Fee. • The alternative to not charging this line-item is to not do the test scan (assuming it is optional in the protocol and Clinical Trial Agreement)

Important Notes	• Oftentimes an employee at the site can serve as the mock subject with no actual protocol procedures performed during the walk-through. • If the site is using a human volunteer for this, the site should do this with full transparency with the IRB/REB/EC to determine if and when this activity requires IRB oversight (e.g., protocol, informed consent etc.).

Source Document Development Fee	
Description	• This fee covers the protocol costs related to the site's creation and setup of custom source documents necessary for the protocol. It may include but is not limited to (i) a gap assessment on what documentation is routinely gathered during routine care as compared to the data needs of the protocol; (ii) the actual design of the paper or electronic source; (iii) printing costs of any paper source documents; and (iv) expense related to onboarding a sponsor-supplied eSource system or site-supplied e-Source system fees (plus some Third Party Invoice Management Costs).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • If the sponsor is supplying the eSource system, there may be required additive training expense involved in this set-up that the site must calculate via the Billable Hourly Rate method. • For any paper source documents, there will be the cost of both developing them and printing them. • For site supplied e-Source systems, there may be protocol level fees and/or Per Subject/Per Visit Fees which for the site needs to consider in this cost. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").

Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • The sponsor or CRO can create the source documents and provide these to the site. If supplied by the sponsor/CRO, the site must still build in the cost (usually the Billable Hourly Rate of the staff involved) of their process to ensure these are reviewed for completeness & accuracy, are consistent with site workflow and any setup in electronic systems not done by the sponsor/CRO. Costs will also apply for printing, as applicable.
Important Notes	• If the sponsor/CRO modifies the protocol after creation and quality assurance of the initial set of source documents, there will be additional expense to compare the previously developed CRFs to the new requirements and redesign them. Resulting from that, there would be an invoiceable cost likely included in the Protocol Amendment Review & Setup Fee. • This fee is for the development of the source and does not cover the cost of the technology platform itself if eSource is being utilized.

Pharmacy Set-Up Fee	
Description	• This fee covers the protocol cost related to the site's set-up of the pharmacy environment to accommodate the Investigational (and/or control) Product. It includes, but is not limited to, activities surrounding the creation of custom documentation solely for the protocol (e.g. inventory monitoring, temperature logs etc.) and the accommodation for training of pharmacy staff. It may include set-up costs to build the Investigational (and/or control) Product into pharmacy management systems and/or electronic medical records. It may also include the cost to create and/or modify the physical environment necessary for Investigational (and/or control) Product inventory and management.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • For protocols that do not work within existing workflows and documentation practices, this charge may be higher. For example, a protocol that uses the site's existing temperature monitoring equipment and documentation would have less start-up costs than

	one that requires additional equipment and/or the need for protocol-custom information and/or documentation. • There may be costs for physical goods as well, such as if the need for certain equipment specifically for the protocol (e.g., a dedicated refrigerator). • Of note, in a protocol with multiple locations managing the Investigational (and/or control) Product there may be additional charges to capture. For example, an outpatient site conducting a protocol requiring hospital pharmacy services may generate their site costs via the Billable Hourly Rate whereas the hospital may charge a flat fee for its services. Each of these need to be included in the budget. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • For self-administered products, the sponsor/CRO can handle this activity on their own via direct shipment of Investigational (and/or control) Product to the Subject's home. • The sponsor/CRO can supply any special equipment needed rather than having the site purchase it. Note that while this may lower the site's invoiceable cost for the equipment, it would not reduce the site's cost to set-up, maintain and dispose of the equipment.

Lab Set-Up Fee	
Description	• This fee covers the protocol costs related to the site's set-up of the laboratory environment to accommodate the physical and procedural needs of the protocol. It includes but is not limited to the creation of workflows, inventory QA/management and the coordination of training for lab-related staff. It also may include the cost to create the physical space necessary for storage of lab-related equipment supplied by the sponsor/CRO. It does not include the costs of the actual lab services and tests which are invoiced separately in the Per Subject/Per Visit Budget.

Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • For protocols that do not work within existing workflows and documentation practices, this charge may be higher. There may be additional costs if equipment is needed specifically for the protocol that the site does not already have. This cost should be predictable as to the price of the equipment plus some Third Party Invoice Management Costs (if not included in the site's Overhead charges) involved with the sourcing of the equipment. • There may be additional costs for protocol dedicated storage space that can be calculated based on the space (e.g., the usual metric of cubic ft. or cubic meter) needed multiplied by a standard market rental rate for that metric. • Of note, in a protocol with multiple locations there may be additional charges for the site to capture. For example, an outpatient site using a hospital for lab services may generate site costs via the Billable Hourly Rate whereas the hospital may have a flat fee charged to the site that needs to be included in the budget. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • The sponsor/CRO can supply any special equipment needed rather than having the site purchase it.

Duplicative GCP Training of GCP Trained Staff Fee	
Description	• This fee covers the protocol expense related to the site's time required for their staff to complete sponsor/CRO specific training in ICH E6: Good Clinical Practices when they either (i) maintain current certification by a professional society such as ACRP or SOCRA; or (ii)

	have already completed an industry acceptable training course (e.g. a TransCelerate approved course) within the past two years.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • GCP courses vary widely so the site needs to derive an estimated time to complete the duplicative course required by the sponsor/CRO to calculate the cost impact.
Alternatives to Charging This as A Line-Item	• The alternative to billing this is to not do the duplicative training (assuring there is no contractual obligation to do so). • In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee; however, accommodating duplicative training, even if paid to do it, is a practice that should be discouraged in the industry.

Non-IRB/REB/EC Committee Interface (For Protocol Start-Up Issues) Fee	
Description	• This fee covers the protocol costs related to (i) the time required for the site staff to work with regulatory required committees other than the IRB/REB/EC required for protocol start-up (e.g., Institutional Biosafety Committee and Radioactive Drug Research Committee) and (ii) the cost of those committees themselves as a pass-through expense plus Third Party Invoice Management Costs.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • This would include, but not be limited to, investigator time, research coordinator time and regulatory professional time. • This cost also includes any direct committee fees charged to the site. Note that third party fees almost certainly do not include cost of the site staff time (and non-site staff that the site may be responsible for) to prepare for, attend and perform any follow-up duties for that committee. Thus, the total cost must include the cost of the Billable Hourly Rate of those staff.

	• If further assessments are required as a condition of committee approval, then those costs should be included as well. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • The sponsor/CRO can contract with and directly pay the third party committee(s), although this only covers the direct fee reimbursement and not the site time to prepare, interface with and/or be a part of those committees.

Transcribe Provided Information to Sponsor/CRO Custom Form Fee	
Description	• This fee covers the protocol expense related to the site time required for their staff to transcribe information provided in a generally accepted manner to sponsor/CRO provided custom forms. For example, when the sponsor/CRO requires that the investigator's CV be transcribed to the sponsor/CRO's custom CV form. Other examples include completing site profile sheets with information already shared with the sponsor/CRO on TransCelerate' s Shared Investigator Platform (SIP), financial disclosure information already provided for previous protocols with the same sponsor but on a new form, etc.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • This would include, but is not be limited to, research coordinator time and regulatory professional time.
Alternatives to Charging This as A Line-Item	• The alternative to billing this is to not do the transcribing (assuring there is no contractual obligation to do so). • In lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee; however, accommodating unnecessary work, even if paid to do it, is a practice that should be discouraged.

Invoiceable Items & Services Related to Inter-Protocol Events

Not all of these line-items are relevant to every protocol and/or to every site. Use professional discretion when including a line-item in a budget.

Recruitment Activity (Site Staff Time) Fee	
Description	• This fee covers the protocol cost related to site staff time spent focusing exclusively on recruitment of new subjects into the protocol.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services to which sponsors/CROs often impose a maximum limit on this effort (see Important Notes section in this table). Alternatively, the site can bundle this as a flat rate, based upon total estimated time to complete this Service multiplied by the Billable Hourly Rate. • Fee includes, but is not limited to, investigator, coordinator, and recruiter time spent on activities for the purpose of recruitment of new subjects into the trial. Examples of protocol-specific activities to be included in this fee are: o medical record searches, reviews and other pre-screening activities; o direct face-to-face recruitment time in new environments (e.g.,, presenting at a patient advocacy meeting, manning a tent at a community health fair, special community activities to help the diversity of protocol enrollment match the diversity of the disease population); and/or o time spent in support of in-house or third party advertisements (e.g. the time spent preparing content for a radio or print advertisement). • Since advertisements require IRB/REC/EC submission, site should decide whether to add the site staff fees for the preparation and submission of the documents for regulatory review to this fee or to the Interim/Continuing IRB/REB/EC Filing Fee. In either case, the site needs to ensure the fees associated with this activity are captured once and only once for each instance in which the expense is incurred.
Alternatives to Charging	• Portions of this fee, if known at protocol start-up may be bundled into the Non-Refundable Start-Up Fee.

This as A Line-Item	• If the site were distributing these efforts across multiple protocols, then in lieu of a separate line-item, the site would more appropriately include this in their Overhead charges across those protocols.
Important Notes	• Oftentimes it is seen that this line-item is capped at a certain amount (e.g., "Up To $____") unless permission is granted from the sponsor/CRO to exceed this amount. The site should be aware of this limit and be prepared to justify the reasons and expected returns if requesting additional funds for this line-item, especially if prior activity was not successful. • Recall that the offering/accepting of a bonus or other pay differential based on enrollment of a certain number of subjects or a certain number within a certain period of time (a.k.a. "Enrollment Bonuses") are generally considered unethical and can impose liability risk to the site so always be ensure that reimbursement is tied to the effort to enroll and not conditioned upon a certain rate or number of subject enrollment.

Recruitment Activity (Third Party Vendor) Fee	
Description	• This fee covers the protocol costs related to items and/or services invoiced to the site from third party vendors for the purpose of protocol recruitment efforts.
Calculating the Costs	• This is usually a predictable cost based on third party vendor contracts (with the addition of Third Party Invoice Management Costs. Note that unless sponsors/CROs reimburse this a 100% pass-through expense, the site will be at risk for price increases imposed by the third party vendor. Vendors include a wide variety of services necessary to accomplish the recruitment activity such as designing advertisements (e.g., graphic designers), media planning, direct placing of the advertisement and even personnel to assist the site with support such as call centers, medical record screening and community outreach. • Note that this line-item does not include any required IRB/REC/EC fees (e.g. for review of advertisements) as that is billed to the sponsor/CRO under a separate line-item. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-

	item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• If the site does this solely at protocol Start-up, then in lieu of a separate line-item, this cost may be bundled into the Non-Refundable Start-Up Fee. • If the site were distributing these efforts across multiple protocols, then in lieu of a separate line-item, the site would more appropriately include this in their Overhead charges across those protocols • The sponsor/CRO can contract directly with the third party vendor.
Important Notes	• Oftentimes this line-item is capped at a certain amount (e.g., "Up To $____") unless given permission from the sponsor/CRO to exceed this amount. The site should be aware of this limit and be prepared to justify the reasons and expected returns if requesting additional funds for this line-item, especially if prior activity was not successful.

Diagnosis & Treatment for Protocol-Related Injury Fee	
Description	• This fee covers the protocol costs related to the diagnosis and/or treatment of a protocol-related injury provided that the requirements for sponsor covering the cost has been met.
Calculating the Costs	• Unlike an Unscheduled Visit Fee for reasons not related to a protocol-related subject injury, this line-item is generally not amenable to being a flat fee. In most cases, since these items and/or services would generally tie to established CPT (or equivalent) codes with established reimbursement rates from health insurers and/or cash pay, the site will contract based on an agreed upon pricing, usually a multiple of published Medicare rates. • Note that if the CTA requires the site to take on the obligation to cover all providers' items and/or services, not just the site's, (i.e. the outpatient site, not the sponsor/CRO, is the party obligated to purchase the hospital services to hospitalize a protocol-injured patient), then if the rates are hardwired in the CTA (e.g., 150% Medicare) as opposed to a pure pass-through (with Third Party Invoice Management Costs) the site bears the risk if their negotiated rate is not consistent with what the third party provider(s) will charge the site. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice

	Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• There are few alternatives a site has to this expense other than be underfunded in this area and liable for the care, especially of the informed consent overpromises the actual commitment the sponsor makes in the CTA. Attempts to reallocate this expense to other areas of the budget are difficult and not optimal. • One alternative to charging this line-item, albeit not without a potential negative impact on Subject's willingness to participate in the sponsor's protocol, is to agree with the sponsor/CRO that payments for protocol-related injuries will not be paid by the sponsor. This requires that the ICF also disclose this financial risk to the subjects and that they will be responsible for the cost of their own care for protocol-related injuries. Under that circumstance if the Subject does experience a protocol-related injury and incurs costs on their own, they can independently discuss their options with the sponsor. While this does resolve the site budgeting issue, it is not without debate and additional challenges.
Important Notes	• If the site has agreed in the CTA to be responsible for all care related to the injury and such care requires items and/or services provided for by a third party (e.g., an Emergency Room or Urgent Care Clinic, hospital or physician not employed at the site), then the site should be cautioned that the rate amount they negotiated may not be enough to cover the charges of those third party providers and the CTA will have to be revisited. Alternatively, the site could assure they are only responsible for the items and/or services that they provide and let the sponsor/CRO negotiate independently with the third party providers.

Safety Report Review Fee	
Description	• This fee covers the protocol costs related to the processing of Safety Reports (e.g., IND Safety Reports) sent by the sponsor or CRO to the site requiring review and/or action.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This fee would likely include at a minimum (i) investigator time for reviewing and signing off and (ii)

	regulatory professional time for receiving, processing for signature and filing the report and any affiliated documentation. • Unless the sponsor is paying the IRB/REB/EC directly, the billed cost of the IRB/REB/EC fees must be included in this calculation unless there is a separate line-item or other term in the Clinical Trial Agreement indicating that the sponsor/CRO will reimburse the site for the IRB/REB/EC fees upon receipt of a copy of the invoice. A site should be able to predict this cost from the agreement with the IRB/REB/EC; however, these fees may increase periodically and thus unless the site is reimbursed upon copy of the invoice, consideration for such increases should be built into the charges or budget language.
Alternatives to Charging This as A Line-Item	• There are almost no alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • A site may negotiate not having to process/sign a report whenever not required by local regulation.
Important Notes	• In many cases, these are not a regulatory requirement and thus an added cost to the site. This is specifically when the forms are not required to be submitted to the IRB/REB/EC because they are not meeting criteria for processing, specifically meeting all three criteria of being (i) serious, (ii) unexpected (meaning essentially not already in the investigator brochure or consent form) and (iii) related to the protocol. Seek regulatory guidance on what the national/local regulatory authorities require.

Scheduled Monitoring Visit Fee	
Description	• This fee covers the protocol costs related to the site staff to prepare for, be available to and accomplish follow-up tasks related to the scheduled monitoring visit.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include at a minimum (i) investigator time for dialogue with the monitor and (ii) regulatory professional and research coordinator time for any work preparatory to the visit, during the visit and post-visit follow-up requirements. • While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner for the amount of time preparing for and

	sitting with the monitor, most agreements settle on a fixed amount "per day" or "per half-day" (where the site invoices two half-day visits if they monitor a full day) unit. A site can define a "half-day" unit as something like "billable in 4 hour increments). The billable unit is the sum of the expected time of these Billable Hourly Rates.
Alternatives to Charging This as A Line-Item	• There are almost no alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • A site may consolidate this cost with the Regulatory or sponsor/CRO Audit Visit Fee and rename it Scheduled Monitoring/Audit Visit Fee, however nothing that an audit may be more costly to the site than a monitoring visit.
Important Notes	• In this document we do not differentiate between "On-site Monitoring" and "Remote Monitoring" because it is projected the costs are calculated similarly. It is worth noting however, that there are some fundamental differences such as the potential for increased costs for scanning/uploading documents for remote monitoring. • Note that some monitoring can occur without much need for staff time. For example, if the monitor can access necessary documents in their native environment via technology in a manner that does not require time with site staff, this would arguably not trigger a charge unless the sponsors/CROs are requiring resending or re-uploading into other viewing portals for the monitoring visit. The intent of this line-item is to capture the expense for site staff time related to the monitoring function.

Regulatory or Sponsor/CRO Audit Visit Fee	
Description	• This fee covers the protocol costs related to the time it takes the various research staff to prepare for the audit, be available to the auditors during the scheduled audit and accomplish follow-up tasks related exclusively to the audit (i.e. not the time it takes to address legitimate queries, quality and/or regulatory issues but time such as re-scanning/uploading documents, writing responses simply to re-document previously documented information, etc.).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a fixed amount "per day" or "per

	half-day" (where the site invoices two half-day visits for a full day monitoring visit) units. • This would likely include at a minimum (i) investigator time for dialogue with the monitor and (ii) regulatory professional and research coordinator time for work preparatory to the visit, during the visit and any post-visit follow-up requirements.
Alternatives to Charging This as A Line-Item	• There are almost no alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • The site may consolidate this cost with the Scheduled Monitoring Visit Fee and renamed Scheduled Monitoring/Audit Visit Fee, however nothing that an audit may be more costly to the site than a monitoring visit.
Important Notes	• In this document we do not differentiate between "On-site Audits" and "Remote Audits" because it is projected the costs are calculated similarly. • Note that although similar to the Scheduled Monitoring Visit Fee, this rate is usually higher due to the increased complexity and demands over a typical monitoring visit. Also, note that part of an audit is not only to assure the site did their work adequately but also to assure the sponsor/CRO did their work adequately as well so the cost impact to the site extends beyond the scope of purely checking site performance.

Unscheduled Monitoring Inquiry Response Fee	
Description	• This fee covers the protocol costs related to the time it takes the various site staff to be available to the protocol monitor (whether remotely or on-site) at unscheduled times.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner for the amount of time the monitoring inquiry takes to resolve, most agreements settle on a "per inquiry" estimate. The estimate for this Item can be a challenging number to derive as the impact of the unscheduled inquiry can vary widely thus the expense can have a wide margin. The site may need to revisit line-items such as this more often than other line-items. This would likely include at a minimum (i) investigator time for dialogue with the monitor and (ii)

	regulatory professional and research coordinator time for responding to the inquiry.
Alternatives to Charging This as A Line-Item	• One alternative to this line-item is to contractually or otherwise document an agreement that no (or limited, such as imminent safety related issues) monitoring communications will be responded to outside of scheduled monitoring visits. This protects the site from these hidden costs and business/workflow interruptions as well as the sponsor/CRO from receiving invoices due to sporadic monitoring inquiries that could be handled during scheduled monitoring visits.
Important Notes	• In this document we do not differentiate between "On-site Monitoring" and "Remote Monitoring" because it is projected the costs are calculated similarly. • Note that some monitoring can occur without much need for staff time. For example, if the monitor can access necessary documents in their native environment via technology in a manner that does not require time with site staff, this would arguably not trigger a charge unless the sponsors/CROs are requiring resending or re-uploading into other viewing portals for the monitoring inquiry. The intent of this line-item is to capture the expense for staff time when interrupted from other activities to support the monitoring function. This is a related but not a duplicative charge to the Expedited Issue/Query Resolution Fee; however, requests may invoke both charges.

Certified Copy of Electronic Health Record Fee	
Description	• This fee covers the protocol costs for the site to generate and/or obtain printed certified copy of a Subject's electronic health record when needed for source documentation purposes (e.g., under ICH E6 (R2) Good Clinical Practices).
Calculating the Costs	• Often this is a "per page" pass-through expense as the hospital or clinic that houses the electronic medical record has an established fee structure. Advance communication with the Health Information Management department of the healthcare provider is key, as there may be circumstances where charges do not apply. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-

	item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• One alternative to charging this as an invoiceable line-item is to, if reasonably predictable and with prior knowledge, apply it to the Per Subject/Per Visit budget. For example, if a Subject is requires neurological testing from an independent neurologist as part of a screening visit, the Per Subject/Per Visit budget would include the cost of obtaining the certified copies from the independent neurologist in that screening visit fee (along with Third Party Invoice Management Costs if the charges are from a third party)
Important Notes	• Caution is necessary when the certification must be labeled as "complete" as a complete medical record may contain hundreds or even thousands of pages of information not relevant to the needs of the protocol that can add to the site/protocol expense.

Protocol Amendment Review & Set-Up Fee	
Description	• This fee covers the protocol costs related to the operational and financial impact to the site for reviewing and training on the proposed revision to the protocol as well as updating all necessary documents, technologies and processes for the updated version.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a fixed "protocol Amendment Review & Set-Up Fee" based on the expected time of these Billable Hourly Rates. • One option may be to have a tier of charges such as a lower charge for a "Minor Change" and a higher charge for a "Major Change". For example, a Minor Change could be a protocol amendment that only does minor clarifications, changes the number of subjects to be enrolled and alters the statistical plan would arguably not require a re-review of informed consent forms and Medicare Coverage Analysis but does require updating CTMS, regulatory documents and IRB/REB/EC filings; whereas a Major Change would be one that does require a re-review of more quantity and complexity of documents and processes at high risk of needing alteration. This cost would likely include at a minimum (i) investigator time for reviewing protocol changes; (ii) research coordinator time for protocol review and for assessing the operational changes and their impact (e.g.,, impact on

	current and future visits added or removed, updating technology such as CTMS and source documents systems etc.); (iii) regulatory professional time for re-reviewing all affiliated materials to determine what changes need to be made (e.g., consent forms, Medicare Coverage Analysis, IRB/REB/EC filings); (iv) training of staff, subcontractors and vendors as needed. • Some of these may be very defined costs especially if outsourced to a third party, such as if the site outsources their Medicare Coverage Analysis to a third party that charges a flat fee or the site is paying the IRB/REB/EC fees directly to a central IRB/REB/EC and reimbursed by passing the invoice to the sponsor/CRO. A site should be able to predict this cost from the agreement with the vendor; however, these fees may increase periodically and thus unless the site is reimbursed upon copy of an invoice, consideration for such increases should be built into the charges or budget language.
Alternatives to Charging This as A Line-Item	• While not an alternative to charging, note that the more the sponsor/CRO provides, the less this charge should be. For example, if the sponsor is providing the updated Medicare Coverage Analysis or filing to the IRB/REB/EC directly on behalf of the site, the site can accordingly decrease the fee for the costs.
Important Notes	• Of note, this line-item is solely for the review and set-up of the revised protocol. It does not include the alteration of the protocol's original budget based on the changes. Specifically, after review, it may be determined that there should be a budget change in the Per Subject/Per Visit line-items (e.g.,, the revision added procedures and/or visits); Overhead (e.g.,, the revision changed a paper system to an electronic system); or to the Invoiceable Items & Services (e.g., the revision requires a new piece of equipment to be purchased and trained on). • Note that the CTA's language should support that the site (not just the IRB) must approve the proposed amendment to the protocol, as this is key to assuring continued protocol compliance. It is possible that the sponsor and IRB/REB/EC (especially if the sponsor/CRO is filing to the central IRB on behalf of the site) can approve a change in the protocol that is infeasible for the site to adopt. Regardless if this protocol Amendment Review & Set-Up Fee is in the budget as an invoiceable line-item, the CTA should allow either party to propose an amendment to the budget when a protocol amendment is proposed to assure that the site is operationally and financially able to adopt the revision.

Subject Reconsenting Due to ICF Change Fee	
Description	• This fee covers the protocol costs related to the requirement of the site to re-consent active subjects when required by regulation and/or resulting from a circumstance outside of the site's control, (e.g. sponsor/CRO initiated protocol amendment).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. Typically for this line-item, the estimated average of the cost is done and charged on a "per Subject" basis. This would likely include at a minimum coordinator time for any scheduling work required (e.g., if subjects have to be contacted prior to their next scheduled visit) and time for the investigator and/or coordinator(s) to process the reconsenting.
Alternatives to Charging This as A Line-Item	• Note that many instances where a revised consent form is generated does not require the sitting down with the subjects/LARs to achieve a signed revised form. For example, a change of protocol that adds an EKG to visit #2 may not require the reconsenting of subjects that have passed that visit; however, if the EKG was added due to a newly identified safety concern, then that may warrant re-consenting. Similarly, if the change of consent was relatively innocuous (e.g.,, to simply change the contact information), then it may be permissible to send a communication to the subjects with that information, thus the costs to achieve the goal of informing the subjects of the protocol changes may be minimized but not eliminated.
Important Notes	• If the change in the consent form was initiated by the site solely due to site preference, this may not be a justifiable charge to the sponsor/CRO unless driven by an outside factor (e.g., the sponsor has not compensated for a research-related injury as originally agreed to, thus the site desires to update the current and future subjects to this change). • Note that the re-consenting fee must be tied to the effort to reconsent and not be contingent on the Subject actually reconsenting. In other words, the cost is the time it takes to inform the Subject of the new information and is an Invoiceable Item & Service regardless if the Subject desires to continue in the protocol.

Translation/Interpreter Services Fee	
Description	• This fee covers the protocol cost related to the additional resources needed at the site to aid in the verbal and/or written communication between subjects (or potential subjects) and the site when language barriers exist. This is important for diversity, equity and inclusion initiatives as well as important for data quality.
Calculating the Costs	• When in-house translators are used, this is most often an estimate of the Billable Hourly Rate of the staff. As the utilization may not be predictable, it is often not amenable to have a lump sum and thus would generally need to be reimbursed based on an hourly rate. • When a third party translation service is utilized, while the gross cost for the protocol may be unpredictable, the rates for paper and/or voice translation should be predictable based on the contract with the translation service provider (e.g., per hour or per page for written documents). • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• As communication between subjects and site staff is essential, one alternative is to not pursue enrollment of this diverse population and to decline screening for the trial if they present on their own. Sponsor/CRO and site should understand that this would decrease the potential for adequate diversity, equity and inclusion of the enrollment. • Sponsor or CRO can provide translation services through a centrally contracted vendor; however, assurances should be sought for any limitations and adequate turnaround time.

Third Party Transportation Fee	
Description	• This fee covers the protocol cost related to cover the third party transportation needs of the protocol subjects; specifically transportation companies (taxi, ride apps, etc.) that the sponsor/CRO asks the site to advance the payment to (and be reimbursed upon

	invoice) in lieu of the sponsor/CRO compensating the vendors directly. This is not to be confused with a patient stipend which is invoiced by the site separately.
Calculating the Costs	• Due to the unpredictability of the cost, the only pragmatic manner is to have this reimbursed upon invoice. Note that the sponsor/CRO may impose limitations on distance and/or amounts in their transportation program thus the site should be cognizant of any limitations in the CTA budget for this as well as be able to educate the subjects of any of the sponsor/CRO's limitations as applicable. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• As the subject's ability to be present at the visit is essential to protocol compliance and ethical conduct of research, one alternative is to not pursue enrollment of a population that cannot make the visits due to lack of available transportation resources. The site may also need to decline the trial if sufficient resources are not available for transportation related to recruitment and retention based on geography and the location of the Subject population. Both the sponsor/CRO and site should understand that this would decrease the numbers and potential for adequate diversity, equity and inclusion of the enrollment. • Sponsor or CRO can provide transportation services through a centrally contracted vendor; however, assurances should be sought for any limitations and adequate turnaround time.

Interim/Continuing IRB/REB/EC Filing Fee	
Description	• This fee covers the protocol cost for the preparation and processing of documents (not otherwise compensated for in the Non-Refundable Start-Up Fee and/or protocol Close-Out Fee) for submission to the IRB/REB/EC as required by regulation and/or sponsor/CRO. It is not the IRB/REB/EC fee itself (which the site invoices separately).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to

	charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include at a minimum (i) regulatory professional and/or research coordinator time to prepare the documents, submit the documents and document completion and (ii) principal investigator time to review and sign off on documents as required.
Alternatives to Charging This as A Line-Item	• To the extent that the sponsor/CRO completes a portion of the document preparation on behalf of the site or contracts with a third party to do so, this cost can be reduced but not eliminated due to the other efforts the site has in relation to this process. • There are few alternatives a site has to this expense other than be underfunded in this area. Attempts to reallocate this expense to other areas of the budget are difficult and not optimal.
Important Notes	• This fee reimburses for items and/or services such as continuing review, SAE/UPIRSO/UADE reports. It would not be for the initial review (unless excluded from the Non-Refundable Start-Up Fee), Protocol Close-Out report (unless excluded from the Close-Out Fee) or other affiliated line-items (i.e., a protocol amendment could be included in this line-item or bundled with the Protocol Amendment Review & Set-Up Fee). The intent of this fee is to ensure reimbursement of expense to the extent the cost is not covered by other invoiceables Items & Services.

Unscheduled Visit Fee	
Description	• This fee covers the protocol cost related to site staff and resources required to complete a subject visit (whether in-person or telephonically) in-between protocol-scheduled visits when not otherwise compensated under the Diagnosis & Treatment for Protocol-Related Injury Fee but for other reasons related to subject safety, data integrity and/or protocol compliance.
Calculating the Costs	• This expense can be charged as, (i) a flat rate, using an estimate of the Billable Hourly Rate of the staff required to complete the Visit multiplied by the respective hours necessary to complete the task(s); or (ii) based upon the Per Subject/Per Visit Fee Schedule (assuming individual procedure fees are itemized in the budget). Tiered charges may be applied based on the type of visit (e.g., in-person visit versus a remote visit).

Alternatives to Charging This as A Line-Item	• If not in conflict with the CTA or the Informed Consent, the site could charge the Subject and/or their medical insurance for the visit if related to routine medical care. • There are few other alternatives a site has to this expense other than be underfunded in this area. Attempts to reallocate this expense to other areas of the budget are difficult and not optimal.
Important Notes	• Note that if the visit relates to a subject injury that the sponsor/CRO committed to compensate for in accordance with the terms of the Clinical Trial Agreement, then this charge is more appropriately billed as the Diagnosis & Treatment for protocol-Related Injury Fee line-item. • Examples of this may be visits due to adverse events that are determined not to be a subject injury, need to address problems with sponsor/CRO supplied technology provided to the Subject, coordination with Subject caregiver(s), addressing subject non-compliance and retention efforts.

Non-IRB/REB/EC Committee Interface (For Post Protocol Start-Up Issues) Fee	
Description	• This fee covers the non-startup related protocol costs of the site's (i) time required for the site staff to work with regulatory required committees other than the IRB/REB/EC required for protocol start-up (e.g., Institutional Biosafety Committee and Radioactive Drug Research Committee) and (ii) expenses of those committees themselves as a pass-through expense plus Third Party Invoice Management Costs.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • This would include, but not be limited to, investigator time, research coordinator time and regulatory professional time. • This cost also includes any direct committee fees charged to the site. Note that third party fees almost certainly do not include cost of the site staff time (and non-site staff that the site may be responsible for) to prepare for, attend and perform any follow-up duties for that committee. Thus, the cost of the Billable Hourly Rate of those staff need to be added.

	• If further assessments are required as a condition of committee approval, then those costs should be included as well. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• The sponsor/CRO can contract with and directly pay the third party committee(s), although this only covers the direct fee reimbursement and not the site time to prepare, interface with and/or be part of those committees.
Important Notes	• Note that this does not include the cost for the site to staff its own committee and/or third party charges to manage these committees (e.g., companies that charge management fees to run local Institutional Biosafety Committees). The site should include these into the budget as separate invoices.

Change of Monitor Fee	
Description	• This fee covers the protocol costs related to the time required by the site to accommodate a sponsor/CRO initiated change of their protocol monitor (i.e. not a change requested by the site). Such costs include, but are not limited to, (i) updating site/protocol documents, systems and communication pathways; (ii) orientation of the new monitor to the site's SOPs; (iii) re-addressing historical issues; and (iv) other miscellaneous impact on the site's obligations to the protocol and its documentation impacted by this change.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This fee includes, but is not be limited to, investigator time, research coordinator time and regulatory professional time.
Alternatives to Charging	• There are little alternatives a site has to this charge other than be underfunded in this area.

This as A Line-Item	
Important Notes:	• Should the protocol monitoring plan call for specialized monitors instead of a single monitor assigned to the site (e.g., a specialist for different functions such as Start-Up monitor, a Close-Out Monitor, an SDV monitor and a Regulatory Document monitor) this may be more challenging to define the triggering event of what constitutes a change of monitor. • Note that many times a sponsor/CRO will counter this fee with a reciprocation request should the site change coordinators. While this could be entertained, it should exclude situations if the CRC was hired away by the same sponsor/CRO.

Subject Transfer Fee	
Description	• This fee covers the protocol costs related to a site's accepting a transfer of a subject from another site. The expenses are directly related to the transfer (as the Per Subject/Per Visit Budget will cover future visits at the receiving site). The costs include but are not limited to reconsent of Subject(s) and orienting them to the local site, quality review and assimilation of prior site's paperwork and data, updating technology/systems to include the new Subject (often requires coordination with vendors and their helpdesk personnel to override systems which were not designed to accommodate transfer of subjects mid-protocol.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost.
Alternatives to Charging This as A Line-Item	• There are no alternatives a site has to this charge other than be underfunded in this area. sites can choose to not accept transfers of currently enrolled subjects from other sites and thus they would not incur the unreimbursed expense.

Non-Site Vendor Issue Resolution Fee	
Description	• This fee covers the protocol costs related to the site's role in addressing issues arising from sponsor/CRO-selected vendors in an

	effort to minimize the negative impact to protocol data, assure Subject continuity and regulatory compliance and make any corrective actions caused by the fault of the vendor.
Calculating the Costs	• As the issues vary in complexity, skillsets and length of time to resolve, in general this would be charged as an hourly rate (e.g., the Billable Hourly Rate) of the most likely staff that would handle the issue (e.g., $XXX.XX/hour). A single charge on a per-incident basis as opposed to a per-hour basis may be considered with some risk of under-payment
Alternatives to Charging This as A Line-Item	• There are no alternatives a site has to this charge other than be underfunded in this area.

Subject Helpdesk Fee for Non-Site Provided Technology	
Description	• This fee covers the protocol costs to have the site provide helpdesk services to subjects for sponsor/CRO-provided technology in lieu of the sponsor/CRO and/or their technology vendor providing the service to the subjects.
Calculating the Costs	• As the issues vary in complexity, skillsets and length of time to resolve, in general this would mostly be charged as an hourly rate (e.g., the Billable Hourly Rate) of the most likely staff that would handle the issue (e.g., $XXX.XX/hour). The site may consider, with some risk, a simplified single charge on a per-incident basis as opposed to a per-hour basis.
Alternatives to Charging This as A Line-Item	• The alternative to charging this fee is to have the sponsor/CRO/Vendor commit to providing helpdesk support to subjects for all subject-facing technology provided. This should be provided to the site staff and subjects in the form of a multilingual 24-hour toll free phone number or other access path. • In the absence of a centrally sourced helpdesk, there are no alternatives the site has to recoup this expense other than charge for this line-item. • Alternatively, the site can include this as part of the Unscheduled Visit Fee.
Important Notes:	• Be aware that even if the sponsor/CRO/Vendor provides helpdesk services, the lack of 24-hour support for centrally sourced technology can have a significant impact on site staff resources, especially if a lack of adequate and timely support results in protocol deviations and/or data queries.

Special Requested Added Staff Fee	
Description	• This fee covers the protocol costs related to sponsor/CRO requested additional site staff to perform defined protocol functions.
Calculating the Costs	• In general, this would be charged as the Billable Hourly Rate of the most likely staff that would handle the task (e.g., $XXX.XX/hour) but alternative fee structures (e.g., a cap or flat rate) can apply.
Alternatives to Charging This as A Line-Item	• The alternative to charging this fee is to not provide the service requiring the special staff or to provide the service but include this expense as a separate Invoiceable Items & Services or add to the Per Subject/Per Visit budget as appropriate.
Important Notes:	• This line-item is used on the rare occasion that a sponsor/CRO requests esoteric staff to be added that are untraditional. For example, a sponsor/CRO may request that the site add a dedicated Project Manager to perform unique and/or non-traditional duties to the protocol.

Post-Startup Added Meeting/Training Fee	
Description	• This fee covers the protocol costs related to the time required for the site staff to attend sponsor/CRO required meetings and/or training (in person or virtual) that were not contemplated at the time of protocol startup and not driven by fault of the site (e.g. CRC turnover).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost.
Alternatives to Charging This as A Line-Item	• Alternatives to adding this as an Invoiceable Item & Service are to either (i) not participate in the meeting/training (assuring there is no contractual obligation to do so) or (ii) participate in the meeting/training if the site concurs that the meeting/training content criticality outweighs the offset of the loss of other protocol functions (e.g., recruitment, retention, data entry).
Important Notes:	• Note that the intent is to compensate for the cost of meetings that are not caused by the site's failure to meet its obligations. An example of meetings/trainings that likely do not meet the criteria for this Invoiceable Item & Service include retraining of site staff due to

	excessive protocol deviations at the site or assignment of a new CRC to the protocol that needs initial training. Examples of meetings/trainings that likely do meet the criteria of this Invoiceable Item & Service include training related to upgrades in protocol supplied technology/apps, recruitment/retention enhancement meetings, general protocol update/troubleshooting meetings etc.

Periodic Protocol Maintenance Fee	
Description	• This fee covers the protocol costs related to site's efforts to prospectively assure key controls that expire or otherwise are prone to suffer from "protocol drift" remain intact to protect the quality of the data and minimization of protocol deviations. There are numerous quality and system checks that fall under this invoiceable that include but are not limited to Investigational (and/or control) Product accountability, policy validation, order sets, calibrations and system checks. This may also include third party fees charged to the site (e.g., annual protocol fees charged by a local hospital to assure protocol-custom services and inventory) to which Third Party Invoice Management Costs would apply.
Calculating the Costs	• The site must use caution in calculating these costs in that to not double charge something that is already invoiced for via other invoiceables included in the budget or included in the Overhead calculation. For example, re-calibrating an investigational (and/or control) product thermometer used across all the site's protocols would likely be considered part of site Overhead but providing the paperwork needed to renew an expiring hospital pharmacy order set created specifically for the protocol would be a protocol related cost. In a similar vein, if the budget includes an Interim/Continuing IRB/REB/EC Filing Fee to prepare the IRB continuing review request, then this cost would not be included in calculating this line-item however if a separate line-item is refused for such purpose then those costs should be included in part of this bundled cost. • In general, this is mostly the Billable Hourly Rate of the varying staff used multiplied by the respective hours needed to complete the task. While it is theoretically possible to just charge Billable Hourly Rates for the various staff in an open-ended manner, agreements may settle on a single amount based on a good faith estimate of the total cost. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is

	not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• One alternative to charging this as a separate line-item is for the site to add all possible costs, no matter how small, to the budget as separate invoiceable line-items, albeit this may require a large list of line-items thus is not practical.
Important Notes:	• This line-item may be broken into site costs and third party costs. For example, an outpatient research site may have to pay the local hospital an annual pharmacy fee. • There are little alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal.

Invoiceable Items & Services Related to Protocol Close-Out

Not all of these line-items are relevant to every protocol and/or to every site. Use professional discretion when including a line-item in a budget.

Protocol Close-Out Fee	
Description	• This fee covers the protocol costs related to the site performing activities related to closing out and archiving the protocol. Such costs are those not otherwise compensated in the Per Subject/Per Visit budget or pass-through reimbursement (e.g., IRB/REB/EC fees).
Calculating the Costs	• While the true amount of close-out costs cannot be adequately determined until the site incurs them, sites generally offer a good faith estimate of these costs in its fee. In general, this is mostly an estimate of the Billable Hourly Rate of the staff used multiplied by the estimated number of hours needed to complete the task. Added to that is the estimate of contracted items and/or services that are paid by the site (e.g., if the site contracts out to a record storage vendor) plus Third Party Invoice Management Costs. • A site may develop tiered charging options based on varying protocol complexities such as a lower Protocol Close-Out Fee (post-marketing observational protocol) and a higher Protocol Close-Out Fee (Phase 3 protocol). • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• Although this is usually a single bundled line-item, it is feasible to charge for one or more of the items and/or services related to close-out activities as separate line-items. • Note that the more the sponsor/CRO provides for this, the less this charge can be. For example, a site would not include in this bundled

	charge for the return/destruction of the Investigational (and/or control) Product if the sponsor/CRO representative comes on-site and takes any remaining product with them. If the sponsor/CRO is performing these kinds of tasks, this should be specified in the CTA as a sponsor/CRO obligation to avoid future dispute as to whose responsibility it is to perform this task. • There are almost no alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal.
Important Notes	• Note this Protocol Close-Out Fee is NOT the same thing as a "holdback". A "holdback" (a.k.a. "withhold") is a contractual term that a diminishing amount of sponsors/CROs attempt to impose on sites surrounding the withholding of a percent of a site's already earned revenue until a defined time when the protocol is considered closed by the sponsor/CRO in their sole discretion. Holdbacks are often justified by the sponsor/CRO as being dependent on the site completing all its close-out activities. This is misaligned as it is the protocol Close-Out Fee that is ties to the completion of the site's close-out activity, not earned revenue from earlier subject visits. • Note that the CTA should define that this fee is conditioned solely upon completion of activities under the site's control and (i) not dependent on deliverables outside of the site's control (e.g. completion of all the site's closeout activities and not completion of the close-out activities of every site in the multicenter protocol) or (ii) not having to wait more than a defined period of time after the site's Last-Subject-Last-Visit for a site close-out visit with the sponsor/CRO (which may take months to years after Last-Patient-Last-Visit. • Note that certain protocol close-out costs should also be billable if the site has been initiated but the protocol was cancelled by the sponsor/CRO prior to first enrollment.

IRB/REB/EC Close-Out Submission Preparation Fee	
Description	• This fee covers the protocol cost related to the site's preparation of the Final Report (a.k.a. Close-Out Report) and other requirements the site must deliver to the IRB/REB/EC. This is a regulatory requirement of conducting the protocol. This is also not including the cost of the IRB/REB/EC fees that the site invoices separately.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the

	respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include research coordinator time, regulatory coordinator time and Principal Investigator time. Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices").
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, this can be included in a bundled "Protocol Close-Out Fee". • There is little a site can do other than be underfunded in this area unless the sponsor/CRO provides some of these services to the site.
Important Notes	• Unless the sponsor is paying the IRB/REB/EC directly, the billed cost of the IRB/REB/EC fees must be included somewhere in the site budget unless there is a separate line-item indicating that IRB/REB/EC fees will be reimbursed to site (with added Third Party Invoice Management Costs) upon copy of the invoice. If this is the case, a site should be able to predict this billed cost from the IRB/REB/EC charge master; however, these fees may increase periodically and thus unless the site is reimbursed upon copy of the invoice, consideration for such increases should be built into the charges or budget language.

Pharmacy Close-Out Fee	
Description	• This fee covers the protocol costs related to the site's pharmacy management costs affiliated with closing out their infrastructure surrounding the Investigational (and/or control) Product. This does not include the shipping/disposal of the Investigational (and/or control) Product itself which is billed separately. It allows for the preparation of the final product accountability report and the closing of any affiliated activities related to Investigational (and/or control) Product management (e.g., custom storage monitoring equipment, removal of order sets created for the protocol, updating pharmacy systems etc.).

Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. • If third party pharmacies are used (e.g., an outpatient site doing an inpatient protocol utilizing the hospital pharmacy) then this may invoke invoiceables that need to be paid along with Third Party Invoice Management Costs. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, this can be included in a bundled "Protocol Close-Out Fee". • There are little alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • This may possibly be bundled as a unified "Pharmacy Set-Up and Close-Out Fee" as both activities will need to occur.

Investigational (and/or Control) Product Return/Destruction Fee	
Description	• This fee covers the protocol costs related to the site's final disposal of any remaining Investigational (and/or control) Product itself. It does not include items and/or services that relate to inventorying and management of the product (which the site invoices separately).
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include research coordinator time and pharmacy staff time. • Added to that is the estimate of contracted items and/or services that are paid by the site (e.g., sites may contract with a professional service

	to destroy drugs removed from inventory or some inpatient pharmacies have additional costs of removing IP from inventory and protocol-related order sets).
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, the site can include this cost into the bundled "Close-Out Cost Fee". • There is little a site can do other than be underfunded in this area unless the sponsor/CRO provides some of these services to the site. For example, a site would not charge for the return/destruction of the investigational (and/or control) product if the sponsor/CRO comes on-site and does the final accountability and takes any remaining product with them. If this is to occur, this should be specified in the CTA as a sponsor/CRO obligation to avoid future dispute as to whose responsibility it is to perform the task.
Important Notes	• While ideally a line-item in a budget, this is often seen in a CTA where the "site will return or destroy the IP at the sponsor/CRO's sole expense". Regardless of the presence of such a statement, there should be line-item and a defined charge to assure that the necessary staff time is also covered.

Record Packaging Fee	
Description	• This fee covers the protocol cost related to the site's packaging of all the protocol files in an organized manner so that in the event the records are required by the sponsor, CRO or regulatory authority in the future, they can be readily retrieved in a complete and organized manner.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include at a minimum research coordinator and regulatory professional time to package and label the records. • As opposed to archiving "as-is with all faults", many sites choose to do a final quality check prior to archival which may include things like confirmation of all informed consents being present, assurance of all signatures, lining out and initial/dating of any empty comment fields in source documents, purging of unnecessary items (such as duplicates, outdated drafts and non-essential documents) etc. If this is

	part the site's standard practice, then the site should add the cost into the calculation. • If digitization is to occur of paper documents then there is the Billable Hourly Rate of the scanning process plus the equipment cost (e.g., rental or depreciation of the equipment) plus the cost of proper destruction of the physical copies. Some of this may be outsourced to a third party vendor for which the site may have established contracted rates for a predictable cost; however, note that by the time a protocol ends those rates could likely be higher than what was quoted at the beginning of the protocol, thus the site should budget accordingly.
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, this can be added to a bundled "Protocol Close-Out Fee" or, less optimally, added to Overhead costs if spread across multiple protocols. • There is little a site can do other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • It is possible to bundle this fee with the Protocol Record Storage Fee as a "Record Packaging and Storage Fee"

Protocol Record Storage Fee	
Description	• This fee covers the protocol cost related to the site's storage of the records (including physical storage and inventory management) for the duration of the required retention period in a manner that the site can retrieve them in a reasonable amount of time if needed by the sponsor, CRO or regulatory authority.
Calculating the Costs	• In general, this includes the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. This would likely include, at a minimum, staff time to periodically audit the inventory to assure all documents/boxes/folders/files/etc. are there (including verification of ability to restore electronic files), environmental protections checks (e.g., fire/water/humidity damage prevention systems), verification of authorized/controlled access only, estimated need for relocation management resources, and other services germane to storage. • The site may contract with a third party for components of this function and those costs should be predictable based on the contract;

	however, this does not alleviate the site from many obligations of its ultimate oversight such as inventory audits and relocation management (e.g., if the vendor goes out of business). In addition, the site will bear the costs of any rate increases from the third party vendor unless the sponsor is paying the vendor directly or reimbursing the site upon each (monthly or annual) invoice from the third party.
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, the site can include this cost into the bundled "Protocol Close-Out Fee". • There are little alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal.
Important Notes	• When considering this line-item, the site is cautioned to (i) be knowledgeable of their legal obligated retention period as a site and (ii) be cognizant of the proposed terms requested by the sponsor/CRO in the CTA. sponsors/CROs often desire, for their business needs, for the site to not destroy the protocol records upon expiration of the site's legal retention period. However, instead of having the site ship the records to the sponsor/CRO's long-term record storage vendor/facilities, they request to engage the site to also be a long-term records storage vendor. The extended period proposed in the CTA is often years, decades and often indefinitely (e.g., CTA language that says the site "upon expiration of this period the site cannot destroy records without permission from the sponsor"). If the site does not have CTA language limiting their retention period solely to their legal obligation (e.g., "site will give sponsor a thirty (30) days written notice to the correspondence address indicated in this Agreement prior to intent to destroy records to allow sponsor to either a) provide verification that the Investigator's regulatory retention obligation has not expired; and/or b) provide the shipping information necessary for Institution to transfer records into sponsor's custody at sponsor's sole expense; failure to respond within thirty (30) days of the notice shall constitute the sponsor's waiver of the sponsor's option to have records shipped to them in lieu of destruction" the site may be challenged in determining their true costs here over the extended number of years. Resources for a site that wants to enter into the long-term record storage business is beyond the scope of this document and thus the site should seek contract and budget guidance from professional and trade associations in that arena. • It is possible to bundle this fee with the Record Packaging Fee as a "Record Packaging and Storage Fee".

Records Destruction and Electronics Recycling Fee	
Description	• This fee covers the protocol costs related to the site's destruction of the physical records, electronic storage medium and/or other electronic equipment containing protocol records after the site's legal and contractual retention obligation is over. This prevents risk to the loss of confidentiality of the data as well as decreases the need for unnecessary retention costs.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. It also includes the equipment cost (e.g., rental or depreciation of the equipment such as shredders). • The site may contract with a third party for components of this function (e.g., a document shredding company or a certified e-waste recycler that can remove all remnants of confidential information prior to recycling electronic components) and those costs should be predictable based on the contract (with the addition of Third Party Invoice Management Costs; however, this does not alleviate the site from many obligations of its ultimate oversight. Also, be aware that the site will bear the costs of any rate increases from the third party vendor unless the sponsor is paying the vendor directly or reimbursing the site upon each invoice from the third party. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Alternatives to Charging This as A Line-Item	• In lieu of charging this as a separate line-item, the site can include this cost into the bundled "Protocol Close-Out Fee". • The sponsor/CRO can have these items shipped to them at their expense for destruction and/or recycling of e-waste.

Other Invoiceable Items & Services

Not all of these line-items are relevant to every protocol and/or to every site. Use professional discretion when including a line-item in a budget.

Unexpected Cost Allotment Fund	
Description	• This line-item covers the protocol costs for the site's miscellaneous items and/or services provided that, with prior written permission of the sponsor/CRO, can occur without the need for contract and budget renegotiation.
Calculating the Costs	• The costs of this can widely vary depending on the activity. It may be an item and/or service already contemplated herein but not originally in the budget, or it may be something completely new. Costs may include but not be limited to Billable Hourly Rates, third party vendor costs, purchasing/leasing costs etc. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Alternatives to Charging This as A Line-Item	• The alternatives are (i) to either have contemplated the line-item as a possibility in the current budget or (ii) to renegotiate the budget for the newly identified items and/or services necessary for protocol conduct.
Important Notes	• Note that this may be an effective strategy for both site and sponsor/CRO to include in budgets • Note that CTAs often put a maximum number to this line-item that would trigger the need to renegotiate the budget/CTA if the site's costs would exceed that maximum.

Post-Close-Out Record Retrieval Fee	
Description	• This fee covers the protocol costs related to the site's staff time and any third party fees necessary for retrieving documents requested by the sponsor/CRO after the close-out visit has occurred.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. In the event there are third party storage vendors that charge a retrieval fee, those costs should be added to the charge (plus an Administrative Processing Fee for Third Party Invoices). • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Alternatives to Charging This as A Line-Item	• To the extent that this is a function of a regulatory audit or a sponsor audit, then the site may include these costs into those invoiceable line-items as opposed to charging it in this line-item, reserving this line-item for items and/or services attributable to non-audit related inquiries. • One alternative to charging for this is to not complete the task assuming there is no contractual obligation to provide this information. The site should assess this on each case based on the nature of the demands and the relationship with the sponsor/CRO. • Another alternative, provided the site's legal retention obligation has expired, is for the site to counteroffer that the entire set of protocol records be shipped to the sponsor (or their storage vendor) for their long-term storage.
Important Notes	• Note that unless otherwise specified in the Clinical Trial Agreement, the Records Packing Fee and the Protocol Record Storage Fee is for the storage of the records and generally does not include retrieval costs.

Subject Stipend IRS-1099 Determination & Filing (U.S. Sites) Fee	
Description	• This fee covers the protocol costs related to assessing the need for and preparing and filing IRS Form 1099 to the IRS and the subjects.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. Usually this is a cooperation of a site manager and a finance/tax person. • For sites that outsource this function to a third party (e.g. a tax accounting firm), the costs can be predicted in the agreement with the tax accounting firm. This is likely to be a per form charge multiplied by the number of enrollees receiving payments or other transfers of value. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Alternatives to Charging This as A Line-Item	• This charge results from the payments or transfers of value to the subjects so the sponsor/CRO can minimize or eliminate this cost from the site budget if the sponsor/CRO (or their contracted vendor) issues and manages the subject payments themselves instead of contracting this work out to the site.
Important Notes	• This is for the cost related to tax filing only. The costs related to the gathering of the pre-tax documents (e.g., IRS Form W9), actual issuing of payments or other transfers of value to subjects (e.g., debit card fees, accounting staff and research coordinator costs) and the tracking of such transfers of value are direct costs related to Subject enrollment and would be in the Per Subject/ Per Visit Budget as a Stipend Administration Cost or Overhead. This also does not include the value of the stipend/reimbursement itself which is also to be delineated in the Per Subject/ Per Visit Budget.

Cancelled Protocol Fee	
Description	• This fee is part of the sponsor/CRO's costs to cover the expenses incurred by the site for a protocol that the sponsor/CRO cancels or indefinitely delays.
Calculating the Costs	• In general, this includes, at a minimum, the Billable Hourly Rate of the staff required to complete the items and/or services multiplied by the respective hours necessary to complete the task. While it is possible to charge Billable Hourly Rates for the various staff in an open-ended manner, most agreements settle on a single amount based on a good faith estimate of the total cost. The site should add any and all third party provided non-refundable items and/or services to the charge.
Alternatives to Charging This as A Line-Item	• There are little alternatives a site has to this charge other than be underfunded in this area. Attempts to reallocate these costs into other areas of the budget are difficult and not optimal. • Also important for consideration when calculating this cost are the costs associated with the use of any and all third party vendors from whom the site must purchase items and/or services. If the sponsor is not agreeing in the contract to pay these third party fees directly to the third party provider, the site should include Third Party Invoice Management Costs into the calculation of the total costs of this line-item or as a separate invoiceable line-item (e.g. "Administrative Processing Fee for Third Party Invoices")
Important Notes	• As the occurrences for this fee is, by definition, timed prior to an executed CTA/budget, usually a custom agreement will need to be signed regarding this issue. • Note that if the sponsor/CRO cancels or indefinitely delays the protocol after the parties have signed the CTA/budget, then this should not be double billed as post-CTA it is more so the Non-Refundable Start-up Fee and protocol Close-Out Fee that the site invoices.

Section 4: Additional Resources, Conclusion & Acknowledgements

There are multiple avenues to learn about site costs and budgeting, many of which focus on the related topics of Overhead calculation and Per-Subject/Per-Visit budgets but many of which are also directly address these kinds of Invoiceable Items & Services (often referred to in session titles as "Hidden Costs"). The educational offerings of SCRS, professional associations and private conferences often contain sessions on site budgeting as do many other industry events and publications.

Sites also offer resources and dialogue online on various websites and forums. In general, there is no shortage of information sources on how sites can understand their costs sufficient to work with sponsors/CROs to assure the protocol is adequately budgeted for success. Hopefully, this resource and any extended resources will enhance the industry's knowledge of these commonly invoiced areas and make the site's requested charges defendable.

SCRS would like to acknowledge all the individuals who have contributed to this document whether directly in its drafting or indirectly through numerous conversations. Thank you to the sponsor/CRO colleagues who understand the impact these line-items have on the success of their protocols and have either supported them through the years or are just starting to do so.

Appendix 1: A Site's Cut and Paste Table

This appendix presents no new information but provides a cut/paste-friendly version of the same information to ease the inclusion of the Invoiceable Items & Services into study budgets. It also provides a placeholder for the site to input their charges.

Not all of these line-items are relevant to every protocol and/or to every site. Use professional discretion when including a line-item in a budget.

Invoiceable Items & Services Related to Protocol Start-Up

Non-Refundable Start-Up Fee: __[Insert Site Charges Here]_____

- This fee covers protocol costs related to the site's completion of protocol start-up activities that are required prior to opening of enrollment at the site. This fee should include all costs not otherwise provided for by the sponsor/CRO or compensated as a pass-through reimbursement (e.g. paid in full upon third party invoice such as IRB/REB/EC fees).

NOTE: The below line-items in this sub-section are charged separately if they are applicable to the protocol start-up and not bundled in the Non-Refundable Start-Up Fee.

IRB/REB/EC Initial Submission Preparation Fee: __[Insert Site Charges Here]___

- This fee covers the protocol costs related to the site's preparation and submission of required documents to the IRB/REB/EC prior to the engagement of subjects in the protocol. It is not the IRB/REB/EC fee itself (which the site invoices separately).

Insurance (i.e. Medicare/Medicaid) Coverage Analysis Fee:__[Insert Site Charges Here]

- This fee covers the protocol costs related to the site's need to prepare the justifications for and build the infrastructure to bill of one or more subject's health insurance (instead of the sponsor/CRO) for routine care items and/or services affiliated with the protocol. It usually involves, at a minimum, review of protocol materials including the protocol, consent form and Clinical Trial Agreement, physician consultations regarding local and national standards of care and third party review/communications (e.g. Medicare Administrative Contractors).

Per Third Party Vendor Integration Fee:__[Insert Site Charges Here]_____

- This fee covers the protocol cost related to the site's need to set up and integrate sponsor/CRO-imposed vendors into the site operations. The fee is incurred once per vendor (e.g. if there is an

electronic diary vendor and a recruitment company vendor, each vendor incurs the integration fee).

Mock Subject Quality Assurance Run-Through Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to the site's quality assurance program to run a hypothetical or living person through the steps of each visit to (i) assure all protocol-related equipment and workflows are working; (ii) ascertain the risk of protocol deviations prior to them occurring with actual subjects; (iii) ascertain the subject experience; and/or (iv) identify issues that need addressed prior to the first enrollee.

Protocol-Required Test Scans Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the calibration of radiology equipment such as CT scanners at the site specifically for the protocol. This is done according to the protocol and/or sponsor/CRO instructions prior to the first enrollee via scanning (i) specialized equipment (a.k.a. "phantom scans") or (ii) a human volunteer.

Source Document Development Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the site's creation and setup of custom source documents necessary for the protocol. It may include but is not limited to (i) a gap assessment on what documentation is routinely gathered during routine care as compared to the data needs of the protocol; (ii) the actual design of the paper or electronic source; (iii) printing costs of any paper source documents; and (iv) expense related to onboarding a sponsor-supplied eSource system or site-supplied e-Source system fees (plus some Third Party Invoice Management Costs).

Pharmacy Set-Up Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to the site's set-up of the pharmacy environment to accommodate the Investigational (and/or control) Product. It includes, but is not limited to, activities surrounding the creation of custom documentation solely for the protocol (e.g. inventory monitoring, temperature logs etc.) and the accommodation for training of pharmacy staff. It may include set-up costs to build the investigational (and/or control) product into pharmacy management systems and/or electronic medical records. It may also include the cost to create and/or modify the physical environment necessary for investigational (and/or control) product inventory and management.

Lab Set-Up Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the site's set-up of the laboratory environment to accommodate the physical and procedural needs of the protocol. It includes but is not limited to the creation of workflows, inventory QA/management and the coordination of training for lab-related staff. It also may include the cost to create the physical space necessary for storage of lab-related equipment supplied by the sponsor/CRO. It does not include the costs of the actual lab services (e.g., phlebotomy) and tests which are invoiced separately in the Per Subject/Per Visit Budget.

Duplicative GCP Training of GCP Trained Staff Fee: [Insert Site Charges Here]

- This fee covers the protocol expense related to the site's time required for their staff to complete sponsor/CRO specific training in ICH E6: Good Clinical Practices when they either (i) maintain current certification by a professional society such as ACRP or SOCRA; or (ii) have already completed an industry acceptable training course (e.g. a TransCelerate approved course) within the past two years.

Non-IRB/REB/EC Committee Interface (For Protocol Start-Up Issues) Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to (i) the time required for the site staff to work with regulatory required committees other than the IRB/REB/EC required for protocol start-up, such as the Institutional Biosafety Committee and Radioactive Drug Research Committee, and (ii) the cost of those committees themselves as a pass-through expense plus Third Party Invoice Management Costs.

Transcribe Provided Information to Sponsor/CRO Custom Form Fee: [Insert Site Charges Here]

- This fee covers the protocol expense related to the site time required for their staff to transcribe information provided in a generally accepted manner to sponsor/CRO provided custom forms. For example, when the sponsor/CRO requires that the investigator's CV be transcribed to the sponsor/CRO's custom CV form. Other examples include completing site profile sheets with information already shared with the sponsor/CRO on TransCelerate' s Shared Investigator Platform (SIP) or financial disclosure information already provided for previous protocols with the same sponsor but on a new form.

Invoiceable Items & Services Related to Inter-Protocol Events

Recruitment Activity (Site Staff Time) Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to site staff time spent focusing exclusively on recruitment of new subjects into the protocol.

Recruitment Activity (Third Party Vendor) Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to items and/or services invoiced to the site from third party vendors for the purpose of protocol recruitment efforts.

Diagnosis & Treatment for Protocol-Related Injury Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the diagnosis and/or treatment of a protocol-related injury provided that the requirements for sponsor covering the cost has been met.

Safety Report Review Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the processing of safety reports (e.g., IND Safety Reports) sent by the sponsor or CRO to the site requiring review and/or action.

Scheduled Monitoring Visit Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the site staff to prepare for, be available to and accomplish follow-up tasks related to the scheduled monitoring visit.

Regulatory or Sponsor/CRO Audit Visit Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the time it takes the various research staff to prepare for the audit, be available to the auditors during the scheduled audit and accomplish follow-up tasks related exclusively to the audit. This does not include the time it takes to address legitimate queries, quality and/or regulatory issues but time such as re-scanning/uploading documents, writing responses simply to re-document previously documented information, etc.

Unscheduled Monitoring Inquiry Response Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the time it takes the various site staff to be available to the protocol monitor (whether remotely or on-site) at unscheduled times.

Certified Copy of Electronic Health Record Fee: [Insert Site Charges Here]

- This fee covers the protocol costs for the site to generate and/or obtain printed certified copy of a subject's electronic health record when needed for source documentation purposes (e.g., under ICH E6 (R2) Good Clinical Practices).

Protocol Amendment Review & Set-Up Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the operational and financial impact to the site for reviewing and training on the proposed revision to the protocol, as well as updating all necessary documents, technologies and processes for the updated version.

Subject Reconsenting Due to ICF Change Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the requirement of the site to re-consent active subjects when required by regulation and/or resulting from a circumstance outside of the site's control, (e.g. sponsor/CRO initiated protocol amendment).

Translation/Interpreter Services Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to the additional resources needed at the site to aid in the verbal and/or written communication between subjects (or potential subjects) and the site when language barriers exist. This is important for diversity, equity and inclusion initiatives as well as important for data quality.

Third Party Transportation Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to cover the third party transportation needs of the protocol subjects; specifically transportation companies such as taxi, ride apps, etc. that the

sponsor/CRO asks the site to advance the payment to (and be reimbursed upon invoice) in lieu of the sponsor/CRO compensating the vendors directly. This is not to be confused with a patient stipend which is invoiced by the site separately.

Interim/Continuing IRB/REB/EC Filing Fee: [Insert Site Charges Here]

- This fee covers the protocol cost for the preparation and processing of documents (not otherwise compensated for in the Non-Refundable Start-Up Fee and/or protocol Close-Out Fee) for submission to the IRB/REB/EC as required by regulation and/or sponsor/CRO. It is not the IRB/REB/EC fee itself (which the site invoices separately).

Unscheduled Visit Fee: [Insert Site Charges Here]

- This fee covers the protocol cost related to site staff and resources required to complete a Subject visit (whether in-person or telephonically) in-between protocol-scheduled visits when not otherwise compensated under the Diagnosis & Treatment for Protocol-Related Injury Fee but for other reasons related to subject safety, data integrity and/or protocol compliance.

Non-IRB/REB/EC Committee Interface (For Post Protocol Start-Up Issues) Fee: [Insert Site Charges Here]

- This fee covers the non-startup related protocol costs of the site's (i) time required for the site staff to work with regulatory required committees other than the IRB/REB/EC required for protocol start-up (e.g., Institutional Biosafety Committee and Radioactive Drug Research Committee) and (ii) expenses of those committees themselves as a pass-through expense plus Third Party Invoice Management Costs.

Change of Monitor Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the time required by the site to accommodate a sponsor/CRO initiated change of their protocol monitor (i.e. not a change requested by the site). Such costs include, but are not limited to, (i) updating site/protocol documents, systems and communication pathways; (ii) orientation of the new monitor to the site's SOPs; (iii) re-addressing historical issues; and (iv) other miscellaneous impact on the site's obligations to the protocol and its documentation impacted by this change.

Subject Transfer Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to a site's accepting a transfer of a subject from another site. The expenses are directly related to the transfer (as the Per Subject/Per Visit Budget will cover future visits at the receiving site). The costs include but are not limited to reconsent of subject(s) and orienting them to the local site, quality review and assimilation of prior site's paperwork and data, updating technology/systems to include the new subject, which often requires coordination with vendors and their helpdesk personnel to override systems which were not designed to accommodate transfer of subjects mid-protocol.

Non-Site Vendor Issue Resolution Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the site's role in addressing issues arising from sponsor/CRO-selected vendors in an effort to minimize the negative impact to protocol data, assure subject continuity and regulatory compliance and make any corrective actions caused by the fault of the vendor.

Subject Helpdesk Fee for Non-Site Provided Technology: [Insert Site Charges Here]

- This fee covers the protocol costs to have the site provide helpdesk services to subjects for sponsor/CRO-provided technology in lieu of the sponsor/CRO and/or their technology vendor providing the service to the subjects.

Special Requested Added Staff Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to sponsor/CRO requested additional site staff to perform defined protocol functions.

Post-Startup Added Meeting/Training Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the time required for the site staff to attend sponsor/CRO required meetings and/or training (in person or virtual) that were not contemplated at the time of protocol startup and not driven by fault of the site (e.g. CRC turnover).

Periodic Protocol Maintenance Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to site's efforts to prospectively assure key controls that expire or otherwise are prone to suffer from "protocol drift" remain intact to protect the quality of the data and minimization of protocol deviations. There are numerous quality and system checks that fall under this invoiceable that include but are not limited to investigational (and/or control) product accountability, policy validation, order sets, calibrations, and system checks. This may also include third party fees charged to the site (e.g., annual protocol fees charged by a local hospital to assure protocol-custom services and inventory) to which Third Party Invoice Management Costs would apply.

Invoiceable Items & Services Related to Protocol Close-Out

Protocol Close-Out Fee: [Insert Site Charges Here]

- This fee covers the protocol costs related to the site performing activities related to closing out and archiving the protocol. Such costs are those not otherwise compensated in the Per Subject/Per Visit budget or pass-through reimbursement (e.g., IRB/REB/EC fees).

NOTE: The below line-items in this sub-section are charged separately if they are applicable to the protocol start-up and not bundled in the Protocol Close-Out Fee.

IRB/REB/EC Close-Out Submission Preparation Fee: [Insert Site Charges Here]___

- This fee covers the protocol cost related to the site's preparation of the Final Report (a.k.a. Close-Out Report) and other requirements the site must deliver to the IRB/REB/EC. This is a regulatory requirement of conducting the protocol. This is also not including the cost of the IRB/REB/EC fees that the site invoices separately.

Pharmacy Close-Out Fee: [Insert Site Charges Here]___

- This fee covers the protocol costs related to the site's pharmacy management costs affiliated with closing out their infrastructure surrounding the Investigational (and/or control) Product. This does not include the shipping/disposal of the investigational (and/or control) product itself which is billed separately. It allows for the preparation of the final product accountability report and the closing of any affiliated activities related to investigational (and/or control) product management (e.g., custom storage monitoring equipment, removal of order sets created for the protocol, updating pharmacy systems etc.).

Investigational (and/or Control) Product Return/Destruction Fee:_[Insert Site Charges Here]___

- This fee covers the protocol costs related to the site's final disposal of any remaining Investigational (and/or Control) Product itself. It does not include items and/or services that relate to inventorying and management of the product (which the site invoices separately).

Record Packaging Fee:_[Insert Site Charges Here]___

- This fee covers the protocol cost related to the site's packaging of all the protocol files in an organized manner so that in the event the records are required by the sponsor, CRO or regulatory authority in the future, they can be readily retrieved in a complete and organized manner.

Protocol Record Storage Fee:_[Insert Site Charges Here]___

- This fee covers the protocol cost related to the site's storage of the records (including physical storage and inventory management) for the duration of the required retention period in a manner that the site can retrieve them in a reasonable amount of time if needed by the sponsor, CRO or regulatory authority.

Records Destruction and Electronics Recycling Fee:_[Insert Site Charges Here]___

- This fee covers the protocol costs related to the site's destruction of the physical records, electronic storage medium and/or other electronic equipment containing protocol records after the site's legal and contractual retention obligation is over. This prevents risk to the loss of confidentiality of the data as well as decreases the need for unnecessary retention costs.

Other Invoiceable Items & Services

Unexpected Cost Allotment Fund:_[Insert Site Charges Here]___

- This line-item covers the protocol costs for the site's miscellaneous items and/or services provided that, with prior written permission of the sponsor/CRO, can occur without the need for contract and budget renegotiation.

Post-Close-Out Record Retrieval Fee:_[Insert Site Charges Here]___

- This fee covers the protocol costs related to the site's staff time and any third party fees necessary for retrieving documents requested by the sponsor/CRO after the close-out visit has occurred.

Subject Stipend IRS-1099 Determination & Filing (U.S. Sites) Fee:_[Insert Site Charges Here]___

- This fee covers the protocol costs related to assessing the need for and preparing and filing IRS Form 1099 to the IRS and the subjects.

Cancelled Protocol Fee:_[Insert Site Charges Here]___

- This fee is part of the sponsor/CRO's costs to cover the expenses incurred by the site for a protocol that the sponsor/CRO cancels or indefinitely delays.

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