Clinical Trial Agreements Toolkit

Term and Termination

Subject	Results/Comments
Explanation of General Importance from a Business Perspective	A CTA should clearly state its basic term and the Sponsor's and the Site's respective termination rights.[1] The CTA also should clearly state the procedures to be undertaken in the event of termination. In particular, when termination occurs prior to completion of the Study, special attention should be paid to the safety and health of any Study Subjects. The CTA also should confirm the steps to be taken to close out the Study (including provision of any reports and return or destruction of Study Drug.) The CTA also should clearly identify those provisions that survive termination.
Contract Language—Sample from Industry Sponsor's Perspective	**SECTION [15][2] TERM AND TERMINATION** **15.1 Term.** This Agreement shall commence on the Effective Date and, unless earlier terminated as expressly provided herein, shall remain in full force and effect until the later of: (1) one [1] year from the Effective Date[3]; or (2) the completion of all Study activities required under the Study Protocol (Term). **15.2 Termination.** **15.2.1** Sponsor may terminate this Agreement, in its sole discretion, upon giving thirty [30] days prior written notice to Site. **15.2.2** Sponsor may terminate this Agreement upon immediate written notice to Site upon the occurrence of any of the following events: (1) if Site and Sponsor are unable to secure a substitute Principal Investigator in accordance with Section [xx] hereof; (2) if Sponsor determines that there is insufficient enrollment for the Study; (3) if any person performing activities under this Agreement is debarred, excluded, or disqualified from participation in any federal health care program; (4) if Sponsor determines that termination is prudent to protect the safety of Study Subjects; (5) if Sponsor determines that

[1] We note that some industry sponsors elect to have a contract research organization (CRO) enter into CTAs on the sponsor's behalf. In such cases, it should be clear whether the CRO has the authority to exercise termination rights on the sponsor's behalf.

[2] The Section number (15) was selected at random, simply to provide a reference for the organization of the various sub-sections.

[3] The one-year term is suggested to provide potential protection under the federal Anti-Kickback Statute's (AKS') personal services safe harbor. See further reference in the federal laws section of this chart.

	the Study Drug may lack efficacy; (6) if approval for the Study is not granted[4] or is revoked or suspended, or if the Study is placed on clinical hold, by, as applicable, FDA, HHS, or the IRB; or (7) upon the occurrence of an event qualifying as a termination event under the Study Protocol. **15.2.3** Either Sponsor or Site may terminate this Agreement immediately upon written notice to the other party if the other party has committed a breach of a material term of this Agreement and has failed to cure such breach within thirty [30] days after receipt of written notice thereof. **15.3 Procedures Upon Termination** **15.3.1 Care of Study Subjects.** If this Agreement is terminated before completion of the Study, Site shall immediately cease enrolling Study Subjects and shall cease conducting the procedures set out in the Protocol to the extent that doing so is medically permissible and appropriate for the safety and well-being of the Study Subjects. Sponsor and Site shall promptly establish a plan for, as applicable, the withdrawal or transfer[5] of any Study Subjects who are still enrolled in the Study as of the effective date of termination. **15.3.2 Return to Sponsor.** Within thirty [30] days following the effective date of termination, Site shall: (1) provide to Sponsor all materials and Confidential Information provided by Sponsor or that have been obtained by Site or Principal Investigator pursuant to the Study; (2) return or dispose of any unused Study Drug, as directed by Sponsor and in accordance with applicable law; (3) deliver clinical study report or such other reports as may be required hereunder or reasonably requested by Sponsor; and (4) return to Sponsor any advance payments for services not yet performed. **15.3.3 Assignment of Site Contracts.** Upon Sponsor's written request, Site shall use reasonable efforts to assign to Sponsor (or Sponsor's designee) any subcontract or other agreement that the Site may have entered into in connection with the Site's performance of services under this Agreement.[6] **15.4 Payments Upon Termination.** If Sponsor terminates this Agreement

[4] The "is not granted" language may not be needed if the Effective Date is defined as being a date occurring after which the applicable regulatory/ethical approvals have been obtained or if the CTA is not executed by the parties until such approvals have been obtained.

[5] Transfer of a Study Subject to another site may be appropriate if, for example, the Study is terminated at the Site only due to the unavailability of the Principal Investigator and inability to identify a substitute Principal Investigator.

[6] Such agreements may include laboratory services agreement, agreement for genetic testing, or other outsourced services arrangements.

	because of a breach by Site, then, notwithstanding any other provision of this Agreement, Sponsor shall have no obligation to pay any fees or costs associated with such breach. If this Agreement is terminated by either party for any reason other than breach by Site or the Principal Investigator, then Sponsor shall be obliged to pay Site for those fees and cost items set forth in the Budget that have been earned or incurred prior to the effective date of termination. Site shall provide to Sponsor, within thirty [30] days following the effective date of termination, a complete and final accounting (including any back-up documentation as may be reasonably requested by Sponsor) of any pre-termination fees and costs claimed by Site to be owed hereunder. All undisputed fee items will be paid by Sponsor on the later to occur of: (1) sixty [60] days of receipt of such accounting; or (2) Site's completion of its obligations in Section 15.3. **Survival Following Termination**. The following Articles, as well as any other terms hereof which by their intent or meaning are intended to so survive, shall survive any termination or expiration of this Agreement: [Open Payments, Confidentiality, Privacy and Security, Data Ownership and Use, Publication, Record Retention, Intellectual Property, Indemnification/Limitation of Liability (if mutual), Monitoring and Audit Inspection, Governing Law].[7] No termination hereunder shall constitute a waiver of any rights or causes of action that either party may have based upon events occurring prior to the effective date of termination.
Contract Language – Sample from Site's Perspective	**SECTION [15] TERM AND TERMINATION** **15.1 Term.** This Agreement shall commence on the Effective Date, and, unless earlier terminated as expressly provided herein, shall remain in full force and effect until the later of: (1) one [1] year from the Effective Date[8]; or (2) the completion of all Study activities required under the Study Protocol (Term). **15.2 Early Termination.** Either Party may terminate this Agreement immediately upon written notice to the other Party upon the occurrence of any of the following events: (1) if Site and the Sponsor are unable to secure a substitute Principal Investigator in accordance with Section [xx] hereof; (2) if Site or Sponsor determines that termination is prudent to protect the safety of Study Subjects; (3) if approval for the Study is not granted[9] or is

[7] We have listed certain provisions that, by the title thereof, are typically identified as provisions that survive termination; however, parties should carefully review the CTA to confirm whether certain provisions should be deleted or added.

[8] The one-year term is suggested so as to provide potential protection under the federal Anti-Kickback Statute's personal services safe harbor. See further reference in the federal laws section of this chart.

[9] The "is not granted" language may not be needed if the Effective Date is defined as being a date occurring after which the applicable regulatory/ethical approvals have been obtained or if the CTA is not executed by the parties until such approvals have been obtained.

	revoked or suspended, or if the Study is placed on clinical hold, by, as applicable, FDA, HHS, or the IRB; or (4) upon the occurrence of an event qualifying as a termination event under the Study Protocol. **15.3 Termination for Material Breach.** Either Party may terminate this Agreement upon written notice to the other Party if the other Party materially breaches this Agreement and the breaching Party fails to cure the breach within thirty [30] days after receipt of written notice of the breach from the other Party. **15.4 Procedures Upon Termination** **15.4.1 Care of Study Subjects.** If this Agreement is terminated before completion of the Study, the Site shall immediately cease enrolling Study Subjects and shall cease conducting the procedures set out in the Protocol to the extent that doing so is medically permissible and appropriate for the safety and well-being of the Study Subjects. The Sponsor and the Site shall promptly establish a plan for, as applicable, the withdrawal or transfer[10] of any Study Subjects who are still enrolled in the Study as of the effective date of termination. **15.4.2 Return of Study Drug.** Promptly following the effective date of termination, Site shall return or dispose of any unused Study Drug, as directed by Sponsor in accordance with applicable law and at Sponsor's sole expense. **15.5 Payments Upon Termination.** If this Agreement is terminated before completion of the Study by either Party for any reason, then, within thirty [30] days following the effective date of termination, Sponsor shall pay Site: (1) those fees and cost items set forth in the Budget that have been earned or incurred prior to the effective date of termination; and (2) any expenses incurred by Site in winding down and terminating the Study, including the costs of the Study during the wind down period and all expenses and non-cancelable commitments made prior to Site's receipt of notice of termination. **15.6 Survival Following Termination**. The following Articles, as well as any other terms hereof which by their intent or meaning are intended to so survive, shall survive any termination or expiration of this Agreement: [Open Payments, Confidentiality, Privacy and Security, Data Ownership and Use, Publication, Record Retention, Intellectual Property,

[10] Transfer of a Study Subject to another site may be appropriate if, for example, the Study is terminated at the Site only due to the unavailability of the Principal Investigator and inability to identify a substitute Principal Investigator.

	Indemnification/Limitation of Liability, Monitoring and Audit Inspection, Governing Law].[11] No termination hereunder shall constitute a waiver of any rights or causes of action that either party may have based upon events occurring prior to the effective date of termination.
Arguments Supporting Sponsor's Position	The Sponsor typically wishes to have substantial flexibility to terminate the CTA, whether for regulatory reasons (e.g., in the case where a clinical hold is imposed by FDA or the IRB has withdrawn its approval) or for safety reasons (e.g., where there is concern about adverse events or a demonstrated lack of efficacy of the Study Drug). In general, Sites are open to termination on these grounds. Areas in which there is typically greater controversy are: (1) where a Sponsor requests the right to terminate if enrollment at the Site, or, more generally, at all sites in a multi-center study, are not meeting expected targets; and (2) where a Sponsor requests a "without cause" termination provision. Given the substantial costs and resources associated with a clinical study and the evolving safety and efficacy assessments for a Study Drug, it is important that the Sponsor maintains a broad right of termination. The practical reality is that Sponsors will not terminate CTAs unless there is very good reason for doing so, given the substantial investment Sponsors make in a clinical study. On the other hand, for those very same reasons, Sponsors are quite concerned when Sites propose a without cause termination provision, and Sponsors will typically reject such requests. Given the comparatively lower level of investment by a Site, Sponsors are concerned that a Site might propose to terminate a CTA based on a simple shift in institution/department priorities. Regardless of whether the Study is terminated early or at the completion of work under the Study Protocol, the Sponsor will want to ensure that it receives all relevant reports and materials from the Site and the Principal Investigator and that it receives a detailed accounting of final fees and costs, prior to making a final payment. The Sponsor will be concerned that if payment is made prior to completion of the above, there may be insufficient incentive for the Site and the Principal Investigator to deliver critical Study data and the clinical study report, which are needed for the Sponsor to prepare its reports to FDA. This is especially a concern in the case of Phase III pivotal studies.
Arguments Supporting Site's Position	The Site, like the Sponsor, typically wishes to have flexibility to terminate the CTA for regulatory and safety reasons—see examples mentioned above in the "Arguments Supporting Sponsor Position" section. Sometimes the Sponsor will express concern and request that such termination rights be subject to prior

[11] We have listed certain provisions that, by the title thereof, are typically identified as provisions that survive termination; however, parties should carefully review the CTA to confirm whether certain provisions should be deleted or added.

	consultation with the Sponsor. Although such consultation may in fact occur as a practical matter, a Site will wish to ensure that it has the ability to terminate a CTA and suspend treatment and other Study procedures where the Principal Investigator is concerned about safety. The Site will be concerned about liability issues if it feels that the Sponsor is not acting with appropriate diligence to address safety concerns raised by the Principal Investigator. A Site also will be concerned about a Sponsor request to terminate on the basis of insufficient enrollment at the Site. A Site may request that such right be subject to a prior consultation with the Site and/or that the Principal Investigator be given additional time and opportunity to conduct further, appropriate recruitment activities. A Site also will be concerned that, even if enrollment at the Site is sufficient, the Sponsor may request the right to terminate based on generally low enrollment across sites in a multi-center study. In such a case, a Site may request a termination payment in addition to any payments earned under the agreed Study Budget. Such payments must be carefully scrutinized for compliance with anti-kickback requirements. A Site may be similarly concerned about a Sponsor request for "without cause" termination rights. If a Sponsor is adamant about retaining such rights, one response for a Site may be to request a longer notice period (e.g., 90 days instead of 30 days) and to negotiate a termination payment (as discussed above) and a provision for payment of wind-up costs. Please see further discussion of "without cause" termination issues mentioned above in the "Arguments Supporting Sponsor Position" section.
Federal Laws and Directives	As referenced above, payments under CTAs are subject to analysis under the federal Anti-Kickback Statute (AKS) (42 U.S.C. § 1320a-7(b)(2)). The HHS Office of Inspector General (OIG) has issued regulations defining specific "safe harbors" for various payment and business practices between a health care provider and a referral source that, while potentially prohibited under the AKS, would not be prosecuted. One such "safe harbor" for "personal services and management contracts" relates to CTAs. For a CTA to fall within the personal services safe harbor, set forth at 42 C.F.R. § 1001.952(d), seven criteria must be met, including the requirement in Section 1001.952(d)(4) that the term of the Agreement be for "not less than one year."[12][13]

[12] 42 C.F.R. § 1001.952(d) states:

> *Personal services and management contracts.* As used in section 1128B of the Act, 'remuneration' does not include any payment made by a principal to an agent as compensation for the services of the agent, as long as all of the following seven standards are met—(1) The agency agreement is set out in writing and signed by the parties. (2) The agency agreement covers all of the services the agent provides to the principal

	Sponsors and Sites also should be familiar with FDA's regulations governing expanded access/compassionate use of a Study Drug, set forth in 21 C.F.R. § 312.300. In the event that a clinical study is terminated for safety, efficacy, or any other reason, FDA allows narrow access under the expanded access/compassionate use regulations to investigational new drugs to patients with serious or immediately life-threatening diseases who cannot otherwise obtain the drug under another Investigational New Drug or protocol. Notably, Sponsors (the company developing the drug) must approve an expanded access request. Sponsors and Sites also should have in mind an FDA policy regarding the reporting of clinical study data for subjects withdrawn early from a clinical study.[14]
State/Local Laws and Directives	There are generally no critical state laws that will affect term and termination provisions, though local anti-kickback statutes should be reviewed regarding any "safe harbor" time periods, such as exist in the federal AKS.
Case Law	Case law involving disputes between a Sponsor and a Site over term or termination rights in a clinical study agreement is sparse; however, it underscores

> for the term of the agreement and specifies the services to be provided by the agent. (3) If the agency agreement is intended to provide for the services of the agent on a periodic, sporadic or part-time basis, rather than on a full-time basis for the term of the agreement, the agreement specifies exactly the schedule of such intervals, their precise length, and the exact charge for such intervals**. (4) The term of the agreement is for not less than one year.** (5) The aggregate compensation paid to the agent over the term of the agreement is set in advance, is consistent with fair market value in arms-length transactions and is not determined in a manner that takes into account the volume or value of any referrals or business otherwise generated between the parties for which payment may be made in whole or in part under Medicare, Medicaid or other Federal health care programs. (6) The services performed under the agreement do not involve the counseling or promotion of a business arrangement or other activity that violates any State or Federal law. (7) The aggregate services contracted for do not exceed those which are reasonably necessary to accomplish the commercially reasonable business purpose of the services.
> For purposes of paragraph (d) of this section, an agent of a principal is any person, other than a bona fide employee of the principal, who has an agreement to perform services for, or on behalf of, the principal.

42 C.F.R. § 1001.952(d) (emphasis added).

[13] *See also* OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731 (May 5, 2003), *available at* http://oig.hhs.gov/authorities/docs/03/050503FRCPGPharmac.pdf.

[14] *See* Food And Drug Administration, Guidance For Sponsors, Clinical Investigators, And IRBs*: Data Retention When Subjects Withdraw From FDA-Regulated Clinical Trials* (Oct. 2008), *available at* www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf.

	the importance of clearly addressing this subject in a Clinical Study Agreement.[15] There also are cases in which Study Subjects have unsuccessfully brought suit – primarily on breach of contract and promissory estoppel grounds – against a Sponsor for failing to continue providing them with the Study Drug after early termination of a clinical study. However, in such cases, the courts have scrutinized the language of informed consents.[16]
International Laws and Directives	In general, for a Study being conducted at a U.S. Site, there should be no critical international laws or directives that bear on term or termination provisions. However, if the Study is being sponsored by a non-U.S. Sponsor entity or if the Study is being conducted in support of a marketing authorization to be obtained from a non-U.S. regulatory authority, it is possible that there will be terms requested by the Sponsor as a matter of local custom or regulatory directive.
Operational Considerations	From an administrative perspective, it will be important for both the Site and the Sponsor personnel to log into their records the key dates of termination and any required deadlines for providing final budgets or other deliverables. From the Site perspective, this will require close coordination with the Principal Investigator or his/her clinical study coordinator. In the event of early termination, both the Sponsor and the Site Personnel should have protocols in effect to ensure the safe management of Study Subjects who may be coming off treatment or may be transferred to another site. Both the Site and the Sponsor should have a point person already appointed to coordinate the development and implementation of a wind-up plan, including the preparation of any required reports to FDA, the IRB, and principal investigators at other sites (in case of termination for safety reasons).
Other Important Information	N/A

[15] *See, e.g., CTI Clinical Trial Servs. v. Gilead Scis., Inc.*, 2013 U.S. Dist. LEXIS 53844, 2013 WL 1641348 (S.D. Ohio Apr. 15, 2013) (involving a dispute over termination costs of a Site and repayment of fees and costs by a Sponsor to a Site).

[16] *See, e.g., Suthers v. Amgen, Inc.*, 441 F. Supp. 2d 478 (S.D.N.Y. 2006) (dismissing claims against drug manufacturer and study sponsor in suit by former subjects to continue supplying an investigational study drug after study concluded; court denied liability due to documentation of informed consent provided to and signed by subjects); *Abney v. Amgen, Inc.*, 443 F.3d 540 (6th Cir. 2006)(affirming the district court's denial of a motion for a preliminary injunction to force a sponsor to continue supplying an investigational drug to former subjects after a clinical trial study ended); *Vinion v. Amgen, Inc.*, 272 Fed. Appx. 582 (9th Cir. 2008) (granting defendant sponsor summary judgment and dismissing claims of an oral agreement to provide investigational study drug for free indefinitely to a study subject after the clinical study).