CCS Associates: An Introduction and Overview to DCP's Regulatory and Scientific/Technical Contractor

Beverly Smolich[1], Donya Bagheri[1], Snigdha Bezawada[1], Linda Doody[1], Reggie Kelly[1], Meena Navidi[1], Lynn Thomas[1], Carol F. Topp[2], Danielle Zaragoza[1], Caroline Sigman[1,2]
[1]San Jose, CA, [2]McLean, VA

To learn more about CCSA services:
http://www.ccsainc.com
regulatory@ccsainc.com
safety@ccsainc.com
protocols@ccsainc.com
nciprevent@ccsainc.com

Introduction

CCS Associates, Inc. (CCSA) is a woman-owned small business with 30 years' experience providing integrated technical, scientific, regulatory, bioinformatics, and overall research and development (R&D) support, as well as clinical project management. We have worked with the FDA, Foundation for the National Institutes of Health (FNIH) and NIH—including National Cancer Institute (NCI), National Institute of Child Health & Human Development (NICHD), National Heart, Lung and Blood Institute (NHLBI), National Institute on Drug Abuse (NIDA), and the 15 institutes and centers of the Blueprint for Neuroscience (BPN) Research—as well as established and emerging private sector pharmaceutical, biotechnology, and device companies. Our team of experts provides a range of R&D services including drug discovery and preclinical support, regulatory affairs, technical writing, editing and publication, project and site management, safety and pharmacovigilance, bioinformatics, data management and monitoring, quality assurance, statistical design and analysis, training, and meeting planning and execution. CCSA has offices in San Jose, CA and McLean, VA.

CCSA has been DCP's regulatory and scientific/technical services contractor for over 25 years, supporting their cancer prevention agent development program and clinical research program. In support of CP-CTNet, CCSA provides regulatory strategy/advice for novel agents; reviews protocols/Informed Consent Forms (ICFs)/system variable attribute reports (SVARs); submits and maintains regulatory dossiers in the US and Canada; processes Minimum Dataset (MDS) reports including AE coding and data query management; collects site essential regulatory documents; and provides pharmacovigilance services including processing of serious adverse event (SAE) reports.

CCSA Support for CP-CTNet Program: Preclinical/Clinical Development, Regulatory Dossier Preparation/Submissions

PREVENT Program Support	Regulatory Strategy	Clinical Study Concept	Clinical Study Development	Regulatory Support	Clinical Study Support
Agent, Target, Clinical Study Concept	IND-Enabling Study Plan	Agent/Indication Background	Protocol/ICF/SVAR Review	Regulatory Dossier Submission	Essential Regulatory Documents for DSA
	CMC Activities	Protocol Pharmaceutical Section	PSRC Meeting	IND Maintenance	Drug Safety
	Pre-IND Meeting	Informed Consent Risk Tables	Investigator's Brochures		Data Management
					Protocol/ICF/SVAR Review

CMC = Chemistry, Manufacturing, and Controls
DSA = Drug Shipment Authorization

Regulatory Strategy & Pre-IND/IND Process

When DCP IND support provided:

- Assess need for pre-IND meeting to obtain FDA input on clinical development plan, CMC, nonclinical program (toxicology, PK, pharmacology) and/or clinical study design
- Pre-IND meeting—prepare and submit request and briefing book; participate in meeting; interact with FDA
- Prepare gap analysis for PSRC meeting (nonclinical, drug, regulatory issues)
- Assess criteria for IND exemption of clinical study (marketed drugs only), prepare exemption request with IND "lite" (protocol, ICF, 1572s/CVs)
- Plan electronic Common Technical Document (eCTD) hierarchy and content of IND; write, publish, and prepare IND for submission

Initial Regulatory Submissions

- For studies for which DCP holds the IND, CIRB approval of the protocol triggers the initial regulatory submission
- New IND
  - Full IND submission for novel agent, first-in-human study
  - Cross-referenced IND if company or investigator has an open IND for the agent
- IND exemption requests and IND "lite" for studies with marketed drugs not intended to support change in label or advertising; no change in route of administration, dose, patient population or other factor that would increase risk
- Health Canada Clinical Trial application—Submitted when Canadian site is an AO

CP-CTNet Concept to Protocol Approval

CCSA Support:

- Scientific background information for concept solicitations—Review of agent and clinical indication, rationale for clinical trial, prior clinical experience, safety overview of agent
- Pharmaceutical section for protocol—Pharmaceutical properties of agent, safety overview, drug distribution information
- ICF risk tables—Possible side effects, organized by prevalence, based on Investigator's Brochure or package insert (for marketed drugs)
- Initial protocol review, participation in Protocol Safety Review Committee meeting—Regulatory and safety review
- Review drafts of protocol, ICFs, SVAR/CRFs

Regulatory Submissions for IND Maintenance

When DCP IND support provided:

- FDA specifies the general responsibilities of the sponsor of an active IND
- Submissions required for IND maintenance include:
  - Protocol amendments including revised ICF
  - CMC amendments including stability updates and formulation changes
  - Annual reports —Includes trial progress: accrual, CMC, and safety update
  - Other submissions include new investigator documentation, revisions to the Investigator's Brochure or Package Insert, new nonclinical results, and IND Safety Reports
- Information is provided by clinical sites, data management, and/or the agent manufacturer

Data Management

- Data preparation/review for regulatory submissions
- Monthly MDS review
- SVAR review
- Database development and maintenance—*CCSAe*, DSA Dashboard
- PREVENT support

Technical Solutions Development

- Data Management Solutions:
  - Preclinical
  - Clinical
  - Regulatory
  - Safety
  - Report and Manuscript Review
  - Custom Analysis
- Specialized Document Preparation:
  - Fillable Forms
  - Dashboard Interfaces
  - Data Reporting
- eCTD submissions

Site Essential Regulatory Document Management

Study Start-up Process with RCR for CP-CTNet Studies

Protocol receives initial approval by CIRB

CCSA Responsibilities

Sends protocol-specific DTL template to the LAO

↓

Downloads study staff member documents from RCR; all other essential site documents are provided by the LAO

↓

Issues DSA after conducting full quality review of the regulatory documents

↓

Uploads documents to DCP SharePoint for monitor access and updates the DSA Dashboard

Affiliated Organization (AO) Responsibilities

- RCR Registration
- Delegation of Tasks Log (DTL)
- Investigator's Brochure/Package Insert acknowledgement form
- Laboratory certifications (CLIA, CAP, CLP)
- Laboratory normal values
- IRB-CIRB/IEC approvals (protocol/Informed Consent Form (ICF), recruitment materials)
- CIRB approval of study-specific worksheet for local context
- Local ICF, recruitment materials
- Certificates of Translation
- Documentation of active FWA

→

Lead Academic Organization (LAO)

Review and Track AO Documents

→

CCSA Responsibilities

RCR Document Retrieval

- FDA Form 1572
- NCI BioSketch
- Financial Disclosure Form (FDF)
- Professional license (as applicable)
- Good Clinical Practice (GCP)

QC of AO DOCUMENTS
All other essential site regulatory documents are provided by the LAO

Safety Activities

CCSA's Safety Department handles the intake, triage, medical review, query resolution, and regulatory reporting for DCP SAEs

Drug Safety Physicians and Drug Safety Operations personnel provide the following support to DCP:

- Maintain 24-hour/7-day notification system for SAEs
- Maintain database of AEs from MDS reports and legacy DCP data
- Prepare listings from SAE database, *CCSAe,* for IND annual reports, manuscript and clinicaltrials.gov results reviews, and Investigator's Brochure preparation
- Prepare MedWatch/CIOMS forms for IND safety reports—Serious, related, and unexpected events
- Monthly SAE report to DCP Safety Assessment Committee (SAC)
- Provide guidance on safety reporting regulations (to sites, Medical Monitors)
- Coordinate and contribute to the SAC documentation and processes—SAC acts for the sponsor to provide a systematic approach to safety surveillance

Serious Adverse Event Case Processing

Day 0
- Site notifies DCP & CCSA of SAE within 24 hrs via phone or email
- Starts the FDA 15-day reporting clock

Day 1
- Site submits a completed DCP SAE Report Form to both DCP & CCSA within 24 hrs

Day 2
- CCSA assigns case number, performs initial assessment, preliminary MedDRA coding/mapping, enters case into *CCSAe*
- CCSA emails DCP Medical Monitor (MM) the case file

Day 3
- CCSA drafts the Narrative and Query Spreadsheet

Day 4
- DCP MM drafts assessment and emails review and any questions back to CCSA within 24 hrs

Day 5
- Updates *CCSAe* and emails case file to site–resolution of queries
- Completion of the site's records (no queries outstanding)

CCSA processes/reports all SAEs/expedited SAEs per FDA regulations

Prepared under DCP Contracts 75N91018C00017 and 75N91018C00030