National Dental PBRN Roadmap for Principal Investigators

Table of Contents

Abbreviations

ARC	Administrative and Resource Center
CIRB	Central Institutional Review Board
CRF	Case Report Form
DM	Data Manager
DMP	Data Management Plan
DQMP	Data Quality Management Plan
DSMB	Data Safety Monitoring Board
EQ	Enrollment Questionnaire
GCP	Good Clinical Practice
HSP	Human Subjects Protection
IIA	Individual Investigator Agreement
IRB	Institutional Review Board
LCR	Local Context Review
MOP	Manual of Procedures
MSA	Master Service Agreement
NC	Node Coordinator
NCC	Network Coordinating Center
ND	Node Director
NIDCR	National Institute of Dental and Craniofacial Research
NND	National Network Director
NOP	Network Operating Procedures
NPM	National Program Manager
PBRN	Practice-Based Research Network
PEC	Practitioner Executive Committee
PID	Practitioner Identification Number
PNC	Principal Node Coordinator
PND	Principal Node Director
QC	Quality Control
RCT	Randomized Clinical Trial
SAE	Serious Adverse Event
SM	Study Manager
SOW	Scope of Work
SPI	Study Principal Investigator
TD	Technical Director
TDL	Task Distribution List
UAB	University of Alabama at Birmingham
UAT	User Acceptance Testing
UIA	Unaffiliated Investigator Agreement
UP	Unanticipated Problem

Overview

The National Dental PBRN Roadmap is intended to serve as a guide to PIs carrying out studies in the National Dental PBRN. It describes, in general terms, the roles of the Administrative and Resource Center (ARC), the Network Coordinating Center (NCC) and the Study Team in support of PBRN studies, as well as activities that occur during various phases of a research project. For a given project, roles and responsibilities may vary, but should always be clearly spelled out. For purposes of this document, study activities have been broken out into the following phases: 1) **Start-up** (e.g., protocol and study materials development and review, IRB submission, data systems development, practitioner and research readiness tasks and training); 2) **Implementation and Analysis** (study launch, recruitment, data collection, monitoring and construction and analysis of analytics dataset); and 3) **Closeout** (for X01 and UH3 studies) or **Transition** (for UG3 grants/UH3 studies). Again, steps within each phase may vary, depending on the type of study, specific Node requirements or evolving regulations or network policies.

Study types: Several types of research projects are carried out through the network, including questionnaires, small developmental/exploratory, feasibility (pilot) studies, qualitative studies and large-scale clinical observational or experimental (trial) studies. Study length may range from a year (e.g., a questionnaire supported through the X01 mechanism) to several years under a UG3/UH3 mechanism. For the latter, the UG3 phase may include one or more small studies to assess feasibility and refine the final study design and documents prior to transitioning to the UH3 phase. (See **Figure 1**).

This document provides information about **roles and responsibilities** of the Study Team, ARC and NCC (**Table 1**), a high-level "**Study-At-A-Glance**" summary of common activities that take place during each of the study phases (**Table 2),** as well as subsequent figures and text describing general overall and study phase timelines and activities (**Figures, 2-5, pages 9-16**).

Links to key network resources are provided at the end of this document (**page 18**). In addition, the network **HUB** will serve as a key resource for all projects, for example, for storing key documents or sharing study reports. The NCs and SMs/DMs are the primary users of the HUB for a given project. PIs (along with other study team members) will gain access to the HUB via a username and password initialized by the NCC. An orientation/training video for the HUB can be found on the HUB under "Training."

Table 1. Roles and responsibilities for PBRN Studies

Study PI(s) (with Study Team)*	**PI** ▪ Scientific leadership, decision-making ▪ Lead/collaborate with Study Team: ND, PNC, SM, DM, Biostatistician. ▪ Register and update clinicaltrials.gov, if needed ▪ Oversee development of key study documents: protocol, consents, HIPAA, CRFs content, MOP, etc. ▪ Completion/ submission of deliverables ▪ Review data quality ▪ Dissemination
Administrative and Resource Center (ARC)**	**National Network Director** ▪ Assign and oversee ND and PNC to Study Team ▪ Work with PI to finalize budget for ARC resources ▪ Review protocol and key documents **Study Team Node Director** ▪ Contribute to protocol development. Advise on feasibility, design/flow, network processes/logistics **Regional Node Directors** ▪ Oversee practitioner recruitment and study readiness, local IRB submission processes and regional NCs **National Program Manager** ▪ Submit IRB docs to CIRB/share approved docs with individual regions ▪ Receive CIRB approval ▪ Send notification to NIDCR of IRB approval ▪ Oversee practitioner and patient remuneration **Principal Node Coordinator/NC** ▪ Support development of protocol and other study materials ▪ Submit and receive local context review/local IRB submission after CIRB approval ▪ Collaborate with PI and NCC, SM, and DM to develop and deliver training/implementation materials ▪ Guide practitioners through study-readiness activities (iSupplier, HSP training, IIA/UIA, MSA) ▪ Practitioner recruitment and retention ▪ Support practitioner implementation of protocol ▪ Review data quality
Network Coordinating Center (NCC)***	**NCC PI** ▪ Assign and oversee SM, DM, Biostatistician to Study Team ▪ Review protocol and key documents **SM** ▪ Establish communication, timeline, roles/responsibilities, meeting schedule/meeting minutes ▪ HUB support ▪ Support development of protocol and other study materials ▪ Perform NC protocol/study procedure training ▪ Collaborate with PI, PNC, DM, to develop and deliver training/implementation materials **DM** ▪ Facilitate development of data collection instruments ▪ Develop Data Capture (EDC) system, DQMP, tracking, payment, and other data systems as needed ▪ Test/retest procedures, if needed ▪ Review data quality ▪ Collaborate with PI, PNC, DM, to develop and deliver training/implementation materials **Biostatistician, Psychometrician** ▪ Advise on study design, power/sample size ▪ Develop Statistical Analysis Plan (SAP) ▪ Review psychometrics (questionnaires) ▪ Review data quality ▪ Oversee analyses
NIDCR	▪ Schedule, facilitate Introductory Call ▪ Approve Scope, Timeline and Task Distribution List ▪ Appoint DSMB or Medical Monitor, if needed ▪ Participate on Study Team ▪ Review/approve protocol, and other key study documents prior to IRB review ▪ (UG3s): Review Transition Package

*Generally, the Study Team includes ARC Principal Node Director (PND), ARC Principal Node Coordinator (PNC), NCC Study manager (SM), NCC Data manager (DM), NCC Biostatistician, NIDCR Representative
**ARC includes National Network Director (NND), Principal Node Director (PND), National Program Manager (NPM), Principal Node Coordinator (PNC), Node Coordinator (NC)
***NCC includes NCC PI, Study Manager (SM), Data Manager (DM), Biostatistician

STUDY-AT-A-GLANCE				
Study Phase/Activity	**Timeframe**			**Comments/Notes**
	Practitioner Questionnaire	**Small-scale Clinical Study**	**Large-scale Clinical Study (multi-site)**	
Start-up				
1. Scope, Timeline and Task Distribution List (TDL)	30 days	30 days	30 days	- Introductory and Orientation calls scheduled; HUB access provided; Scope, Timeline and TDL Submitted to NIDCR
2. Document Development and Review (protocol, consents, data collection forms, training materials, etc.)	3-5 months	3-5 months	3-5 months	-Plan 2-3 months for development and 1-2 months for review process. -Request for data from the EQ, if needed -Study materials reviewed by: ▪ NCC Biostat group and Data Committee ▪ Practitioner Executive Committee (PEC) ▪ Cascading Review (Multi-region clinical studies only) ▪ Final review by NND, NCC PI, NIDCR
3. IRB approval(s) ***Obtain reliance agreements*** ***IRB submission and approval*** CIRB review Local context review (LCR), where needed CIRB amendment for LCR	1-4 months	3-8 months	3-8 months	-CIRB initially determines whether a study is exempt, expedited or requires full review. If determined exempt, participating node IRB/research institution submission required. -After CIRB approval and LCR, Nodes must also be approved by the CIRB
4. Pre-Implementation: Practitioner Recruitment Readiness and Study Readiness **4a.** Practitioner HSP training and GCP training (which is applicable for clinical trials) **4b.** iSupplier accounts set up with the UAB system **4c**. Individual Investigator Agreement (IIA) approval **4d.** Add practitioners to IRBs **4e.** Execute Master Service Agreement (MSA)/addendum.	NA	1-4 months	1-4 months	-HSP and GCP trainings can be begin at any time. iSupplier account setup may begin at any time. -HSP training must be completed and IIAs/UIAs executed locally before Practitioners can be added to IRB rosters. -MSA (or addendum) is executed after all of the above are completed.
5. Data systems and reports development **5a.** Requirements gathering (e.g., questionnaire/CRF development, monitoring/QC reports and payment)	2-3 months	2-6 months	2-6 months	-Programming starts after IRB approval. Timeline depends on system complexity.

5b. Definition of population pull **5c.** Systems development and testing				- Study Team defines a parsimonious set of variables that address the objectives of the project and do not include extraneous data elements -Study Team participates in systems testing. - Note: For UG3/UH3 studies, systems development generally begins after the transition to UH3 is approved by NIDCR - it is not typically supported during the UG3 period.
6. Training NCC trains the NCs on data systems PNC trains the NCs on the protocol NCs train Practitioners to prepare for subject recruitment	1 month	1-3 months	3-6 months	-NCC and PNC training can be carried out together. Practitioner training may continue as needed during the implementation phase for clinical studies.
Implementation				
7. Recruitment ***8.*** Data collection, Monitoring and QC ***9.*** Remuneration, if applicable	1-2 months	1-6 months	18-36 months	These timeframes are dependent on the type and complexity of the study.
Analysis				
10. Data cleaning/data lock ***11.*** Data analysis requests to NCC, creation of analytic dataset ***12.*** Manuscript development ***13.*** Public use data set created	3-4 months	3-4 months	6-12 months	-Note: For X01 studies NCC supports analyses for the primary manuscript only. -Publications & Presentations Subcommittee review of study manuscripts is encouraged - Public use dataset will be created from the analytic dataset.
Close-out/UH3 Transition				
14. Node/Practice close-out activities ***15.*** Database Close-out ***16.*** NIDCR Close-out activities ***17.*** Publish Public Use Dataset ***18.*** UG3/UH3 Studies: Pre-Transition Review Submit Transition Package	2 months	2-4 months	6 months	UG3/UH3 Studies: Pre-transition review should occur 2-3 months prior to submission of transition package.

Figure 1. UG3/UH3 Timeline Overview

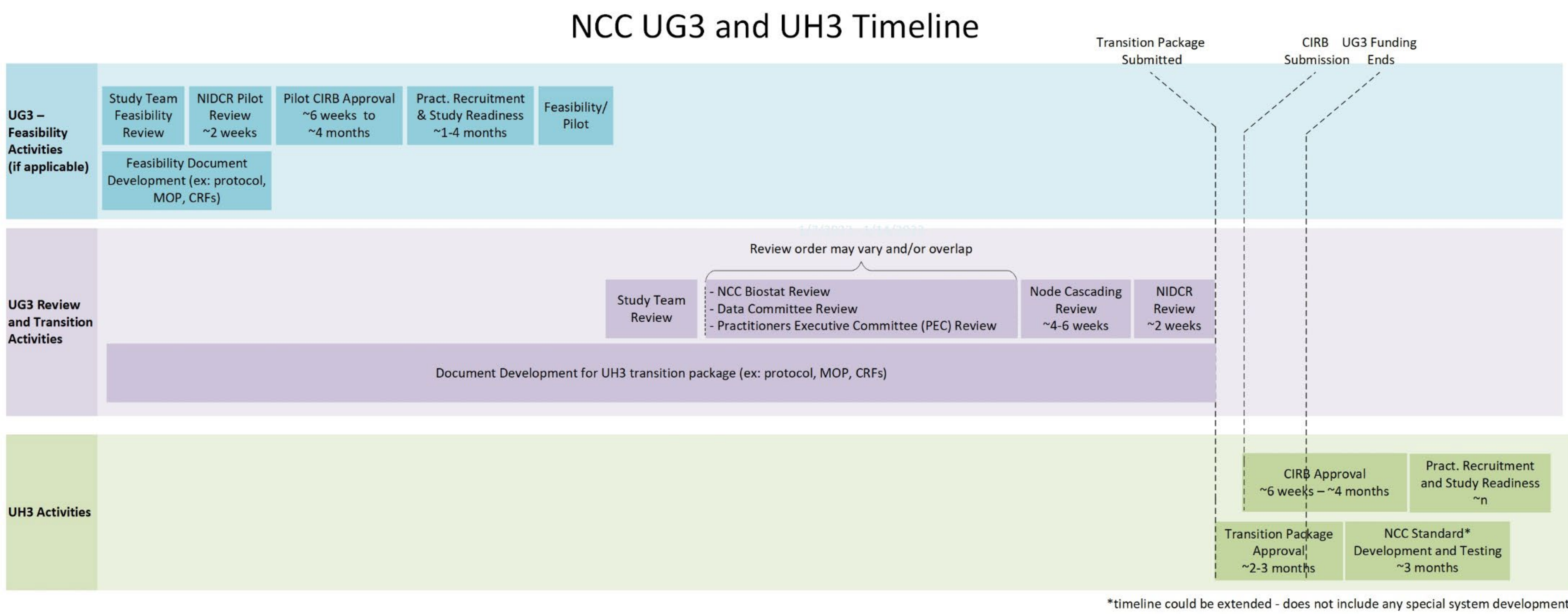
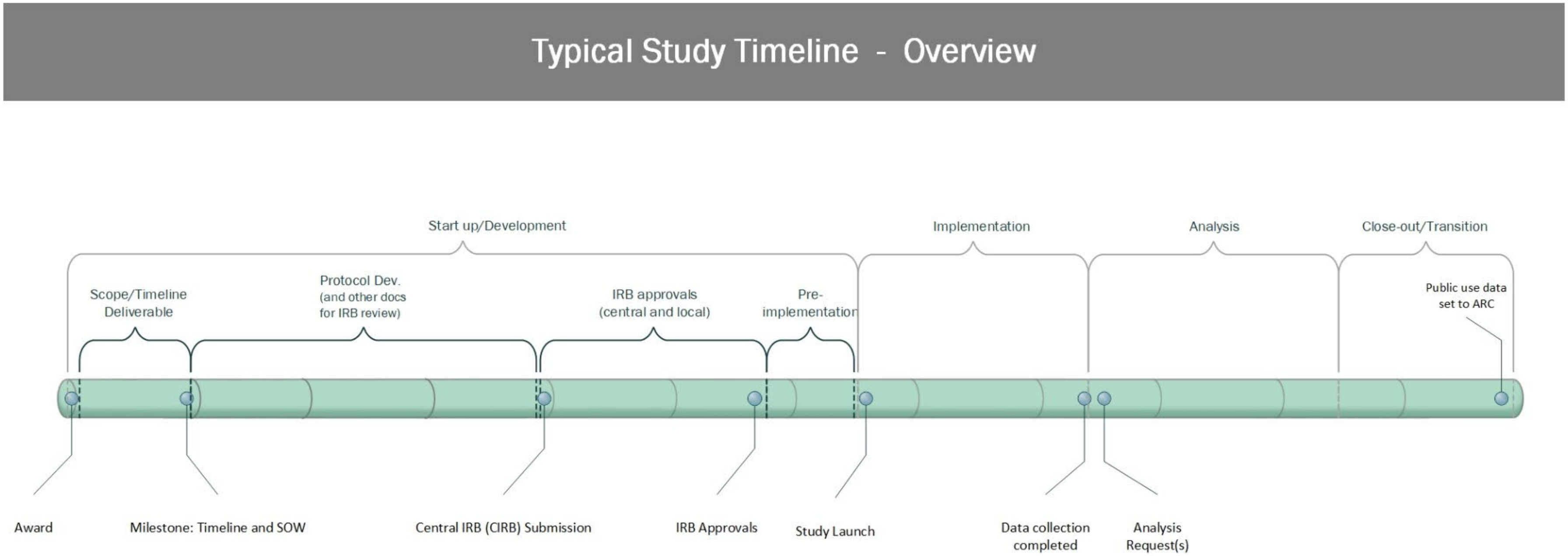


Figure 2. Study Timeline Overview



Overview of items for each phase

Startup/Development

- NIDCR introductory call
- NCC orientation
- Scope, Timeline, Task Distribution List
- ARC (IRB) orientation
- Reliance Agreements (UAB serves as Central IRB)
- Document Development and Review
- IRB Submission
- Pre-Implementation
  - Practitioner Study Readiness
  - Data and reporting systems development

Implementation

- Study Launch (Recruitment)
- Study specific trainings
- Monitoring and quality control reporting
- Remuneration, if applicable

Analysis

- Data Analysis requests
  - Variable definitions
- Creation of analytic data set
- Statistical analysis
- Manuscript development

Close-Out/Transition

Study Close-Out

- Regional/practice close-out activities
- Final data set(s) to PI
- Public data set(s) sent to ARC
- Complete dissemination activities

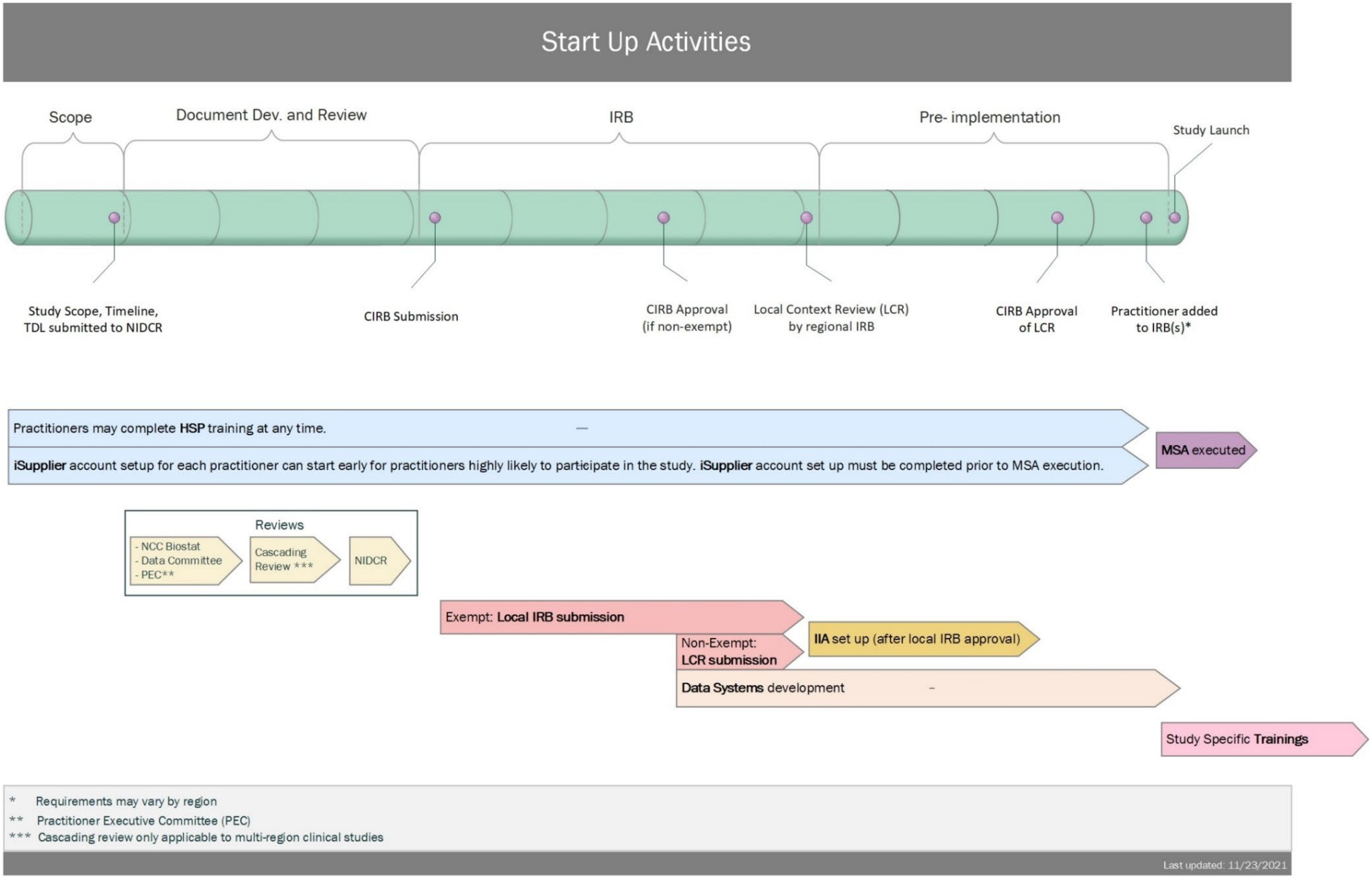
For UG3 transition phase, where applicable:

- Prepare transition packet
- Final document review
- Submit packet to NIDCR

Intended audience for this visual is a brand new study team, PI etc. Different groups (study team, NCC, ARC, NIDCR) have ownership of different tasks. This overview is not intended to show task ownership, please refer to other documentation (such as the task distribution list) for additional breakdown and ownership of the many steps and activities that need to be accomplished over the timeline of the project.

Last updated: 11/23/2021

Figure 3. Study Start-Up



Study Start-up

1. ***Scope, Timeline and Task Distribution List:*** The Study Manager will work with the Study PI to develop a Scope of Work (SOW), Timeline and Task Distribution List (TDL) to be submitted to NIDCR within 30 days of award. Templates are provided for the Timeline and TDL (links to these templates can be found in the NOP, Appendix A). The TDL lists study development and implementation activities and indicates who the responsible parties are.

2. ***Document Review:*** All Study Team members are responsible for finalizing the study protocol and other key documents as per the study design (e.g., Consent Forms, Remuneration Plan, Recruitment Materials, Case Reports Forms and/or Questionnaires, Interview Guides, Node Coordinator and Practitioner/Practice Training Materials). Prior to CIRB submission, the study protocol and supporting documents will generally undergo the following reviews: NCC Biostatistician(s) focus on study design and analysis. The Data Committee pays particular attention to the content and phrasing of data collection items as well as to practical implementation considerations. The Practitioner Executive Committee (PEC) focuses on operational work flow and practitioner-patient interactions. A cascading (or sequential) review by staff from three different regions is carried out for multi-site clinical studies to, among other things, identify any adaptations needed to implement the study across diverse practices. Final review of materials is carried out by the NND, NCC PI and NIDCR.

3. ***IRB Approval***

   Reliance agreements (Smart IRB – forms only)

   A Reliance Agreement is a formal document that provides for an institution engaged in research to delegate IRB review to another IRB. The National Dental PBRN uses the SMART IRB only for reliance documents; the SMART IRB platform will not be used to request or track documents. The Study PI's IRB must be part of the SMART IRB:
   - Click the following link to see if your institution has already joined the SMART IRB platform; https://smartirb.org/participating-institutions/
   - Click the following link if your institution is not already participating to join the SMART IRB platform: https://smartirb.org/join/

   Central IRB: The UAB is the Central IRB (CIRB) of record for the National Dental PBRN for all studies. UAB personnel will complete the initial application for each study. All additional nodes and the study PI's IRB will use the SMART IRB to rely on the UAB IRB. The UAB NPM submits all documents to CIRB for review. The CIRB determines whether human subjects' research meets definitions of exempt, expedited, or if full review is needed. The NIH Single IRB policy does not apply to exempt research. If the team is confident that a study is exempt, all sites are encouraged to submit to their IRB at the same time for maximum efficiency.

   Local Context Review (LCR): Once the CIRB has approved a study, ceding and LCR documents will be sent to the participating NDs and NCs for submission to their IRBs and to the study PI to route to their IRB for approval. Regions and sites obtain partially executed LCRs and ceding agreements. These documents then go back to the CIRB for full execution/approval. LCR requirements can vary by region and type of study.

   The flow of IRB activities is depicted in **Figure 4**.

4. ***Pre-Implementation Practitioner Recruitment Readiness and Study Readiness***

   Practitioner recruitment may begin once the CIRB and LCR have been approved for the study. Practitioners must complete the following to be considered study ready:
   - Practitioner HSP training and, for RCTs, GCP training per node requirements. HSP can be completed once a practitioner has expressed interest in any clinical study.
   - IIA or UIA: These are agreements between the local institutions and practitioners for FWA/IRB coverage. IIAs are not related to a specific study, but overarching to the funding cycle and any clinical studies

practitioners will complete during that cycle. UIAs are for a specific study in which a practitioner will participate.

- iSupplier accounts are set up so that practitioners can receive remuneration through UAB. iSupplier accounts, set up with the UAB system, can be initiated once a practitioner has expressed interest in any clinical study: study:
  - Practitioners are considered Independent Contractors that provide a service to UAB
  - Setting up an account is a two-step process and is a requirement for the MSA
    - Step 1- Complete an initial survey with attestation button
    - Step 2- (1-4 days later)- complete registration and upload w9 and vendor disclosure form
    - NCs are heavily involved with the UAB team in this process to ensure a successful setup
- Practitioners must be added to the IRB(s) for approval, per regional requirements
  (Note: the CIRB is only responsible for practitioner training in SC region and NE region community practitioners)
- Master Service Agreements (MSAs) are financial contracts between UAB and practitioners. MSAs are executed by UAB so that practitioners can receive payment and be subject to U19 “flow-down” regulations. Practitioners may already have an MSA in place from participating in a previous (Cycle III) network study, in which case they will need an addendum to their existing MSA.

5. ***Data systems and reports development***
The NCC builds all data collection and reporting systems for X01 and UH3 network studies. The study team will include an NCC-assigned study manager and data manager to work on the development of the needed data systems. Timeline for development may vary depending on complexity of study and systems needed. Steps generally include:
   - Requirements gathering (i.e., for new systems not already developed, data collection instruments, study monitoring and QC reports, payment requirements, etc.)
   - Development of data collection and reporting systems
   - Population specifications
   - System testing (includes testing/review by study team)
   - Study launch (e.g., recruitment emails/reminders, data collection and reporting)

6. Training
Study-specific training begins after MSAs are executed and continues into the Implementation phase until the practitioner enrollment phase ends. Types of trainings may include:
   - The NCC SM and PNC training can be accomplished in collaboration during the same training session:
     - The NCC trains the NCs on the data systems
     - The PNC trains the NCs on the protocol
   - NCs train Practitioners to prepare for subject recruitment. The NCC SM and DM will provide troubleshooting support for technical issues as needed

Figure 4a. Typical IRB Flow for Practitioner Questionnaire/Exempt Studies

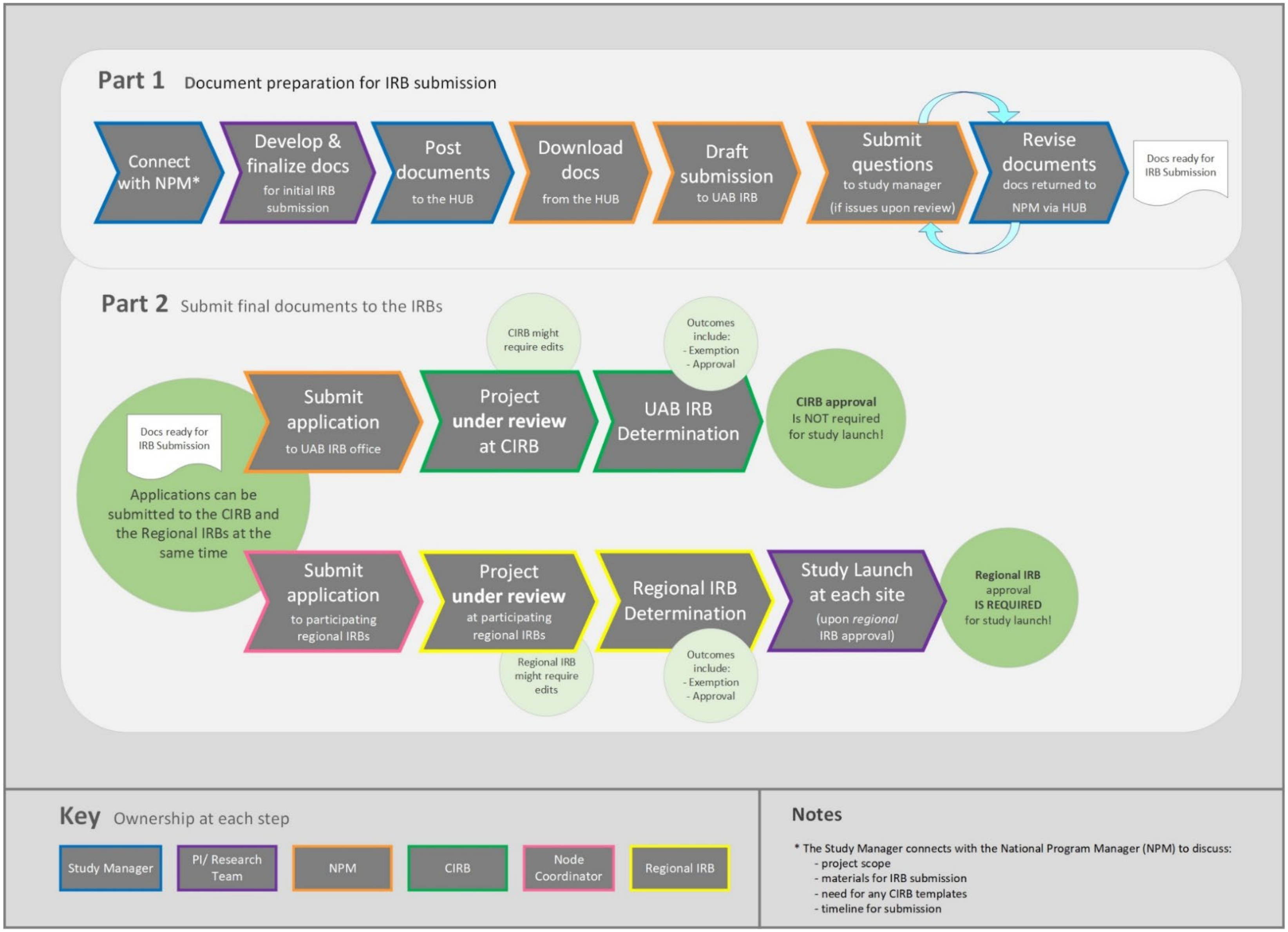


Figure 4b. Typical IRB Flow for Clinical/Non-Exempt Studies

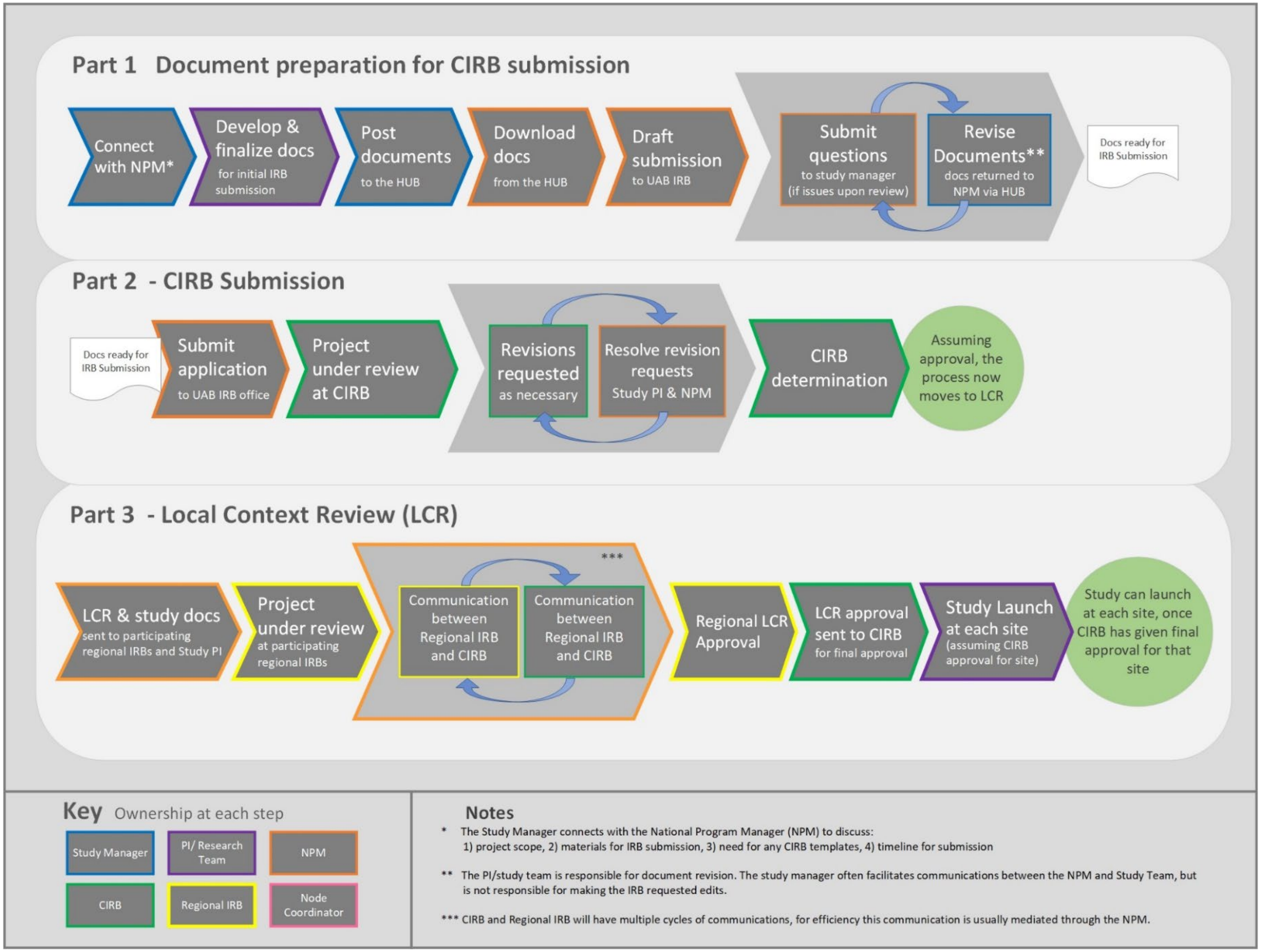
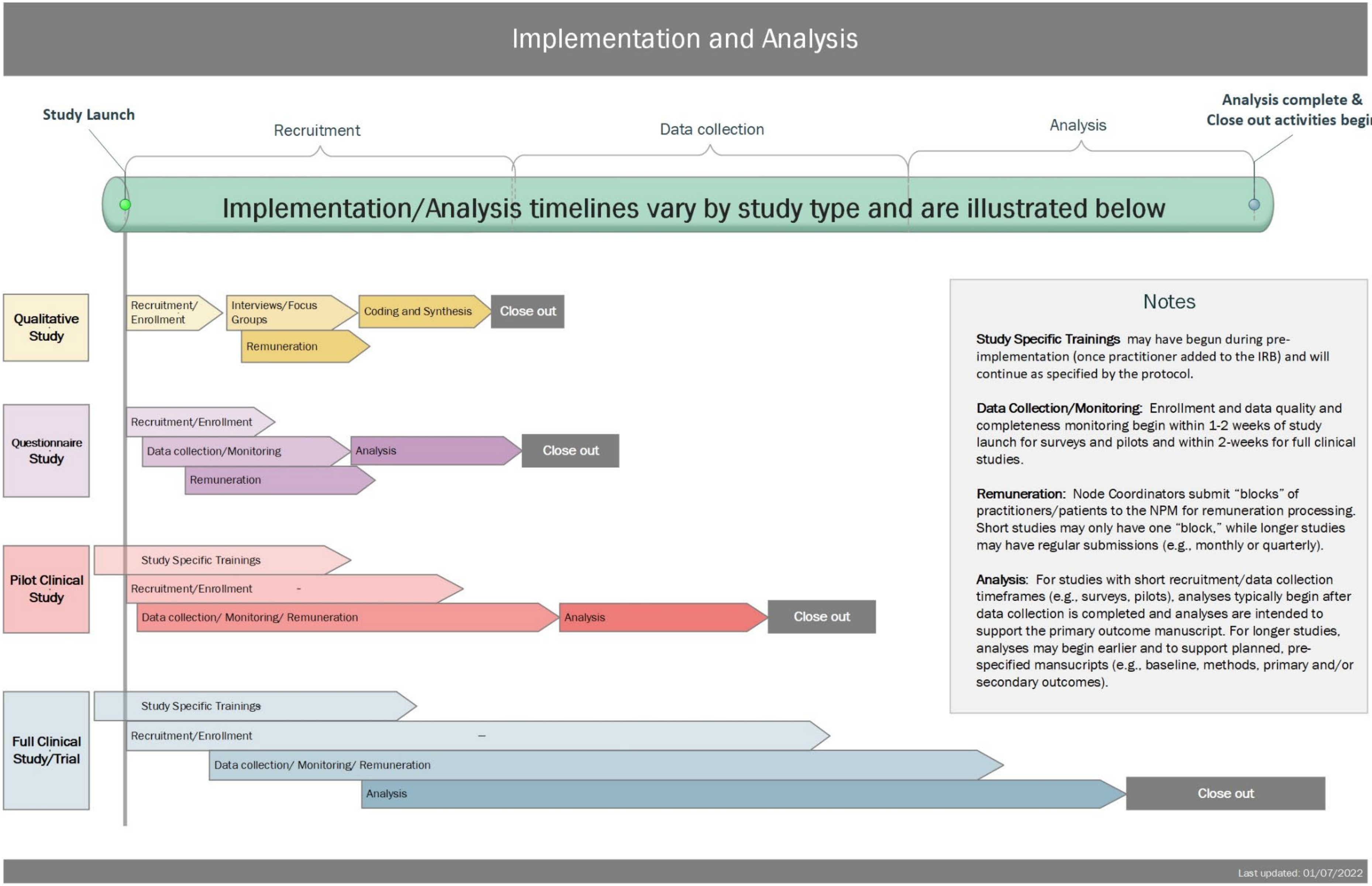


Figure 5. Study Implementation, Analysis and Closeout



Study Implementation, Analysis and Closeout

Study Implementation begins when the study is launched into the field. Implementation activities depend on the type of study. For example, for questionnaire studies the NCC generally delivers the initial recruitment and follow-up messages to practitioners via e-mail contact information in the HUB. NCs provide additional follow-up to meet recruitment goals, and the ARC manages remuneration. Qualitative studies are managed by the study team with help from the NCC and NCs to identify potential participants. Pilot/clinical studies are implemented into one or more National Dental PBRN Nodes and involve practitioner recruitment/enrollment and patient recruitment/enrollment in network offices/clinics. The PNC, NCs, SM and DM coordinate with the PI to carry out recruitment/enrollment, monitoring and remuneration activities.

For questionnaires and clinical studies, data monitoring and reporting activities begin once data collection has started. For short-term studies (e.g., questionnaires, pilots), analyses usually begin after data collection is complete. For longer (multi-year) studies, analyses for dissemination activities may begin once sufficient data has accrued.

7. **Recruitment/Enrollment:** Practitioner recruitment may begin once CIRB IRB and local IRB have approved the study. NCs recruit practitioners from their Node based on interest and availability to complete the study. Once deemed study ready, the practitioners' names are submitted to the IRB for approval, per regional requirements.

    - Questionnaire Studies (non-CIRB)
        - NCC Sends out e-mail notifications and reminders
        - NCs follow-up with non-responders (populations may be prioritized for follow-up)
        - Questionnaire is closed when enough practitioners have responded or window is closed

    - Qualitative (if exempt- non CIRB)
        - Qualitative studies can be preliminary to planned Questionnaire or Clinical Pilot Studies.
        - NCs assist study team in identifying potential interviewees
        - Study team recruits and enrolls participants and conducts interviews or focus groups
        - Study team carries out qualitative analysis and synthesis

    - Pilot/Clinical Study
        - NCs recruit practitioners from their Node based on interest and availability to complete the study.
        - NCs enroll and train National Dental PBRN Practitioners and staff through a variety of methods (i.e., in-person, teleconference, Zoom, etc.)
        - NCs complete all communication and clinical follow-up with National Dental PBRN practitioners regarding:
            - The study process (i.e., training, overview, and design)
            - Data collection steps and processes (i.e., flow charts, study activities, procedures)
            - Important human subjects/HIPAA elements/consenting/eligibility criteria
            - The process for data collection and form management

8. **Quality management, adjudication, validation**

- The NCC SM/DM coordinate the generation, distribution and review of study quality management reports as defined during the start-up phase
    - Quality management reports are reviewed for recruitment progress and data quality and completeness
    - Any unanticipated problems, adverse events, and/or protocol violations will be documented on the Adverse Event Reporting System by the NC, followed up by the study team and node coordinators as needed. All events will be reported based on IRB and NIDCR reporting requirements

9. Remuneration process

- The remuneration process is completed through the UAB.
    - NCs verify subject recruitment and submit an invoice to UAB using the HUB payment system
    - UAB provides remuneration to practitioners and patient participants

10. Analysis

- The SM/DM coordinates data cleaning among the analyst(s), sites, PI and biostatistician(s)
- Once data cleaning is completed, the study database is locked
- The PI works with the Biostatistician and SM/DM to create comprehensive data requests to the NCC Analyst. Data requests must specify all variables needed and explicitly define any computed/derived variables.
- The Analyst creates an analytic dataset according to the data request. Data analyses are carried out by the Biostatistician or by the Analyst under the direction of the Biostatistician. Analyses are verified by independently by another analyst.
- Publications & Presentations Committee review is not required for manuscripts and presentations, but is highly recommended.

11. Close-out and Transition Package (UG3 studies)

- NIDCR provides a checklist for close-out activities: [https://www.nidcr.nih.gov/sites/default/files/2017-10/Study_Close_Out_Checklist_approved_v20.docx.](https://www.nidcr.nih.gov/sites/default/files/2017-10/Study_Close_Out_Checklist_approved_v20.docx)
  This checklist is a useful reference for determining what close-out activities are needed for your study.
- Node/Practice close-out activities, completed by NCs, include:
    - Verifying completion of data at practices
    - Clarifying any missing or unclear data
    - Returning all study documentation and study materials (e.g., practitioner or participant data collection forms or enrollment logs)
    - Study-specific supplies or equipment, if applicable
- Database Close-out
    - Analytic Datasets: The NCC will provide the final study analytic dataset(s) to the study PI
    - Public Use Dataset: The NCC will also prepare a de-identified public use dataset from the final analytic file, which will be provided to the PI. The PI will submit the Public Use Dataset, CRFs and other study materials to the ARC for posting on the public webpage.
- UG3 Awardees should submit their Transition Package to NIDCR for Pre-Transition Review 4-8 weeks prior the Transition Package due date.

Resources

NIDCR main page: nidcr.nih.gov

NIDCR Protocol Templates

- https://www.nidcr.nih.gov/sites/default/files/2019-04/nidcr-interventional-protocol-template.docx
- https://www.nidcr.nih.gov/sites/default/files/2019-10/nidcr-observational-protocol-template.docx).

NIDCR Single IRB: https://grants.nih.gov/policy/humansubjects/single-irb-policy-multi-site-research.htm

National Dental PBRN main page: nationaldentalpbrn.org

Handbook for Practitioners and Researchers

- https://www.nationaldentalpbrn.org/wp-content/uploads/2020/05/Handbook-for-Practitioners-and-Researchers_04-17-2020.pdf

National Dental PBRN HUB: https://www.kpchr.org/ndpbrn-hub/

HUB Resource locations

- **Orientation/training video for the HUB**: Network Hub / Training

- **Network Operating Procedures (NOP) on the HUB:**
  Network Hub / Documents / Network Documents / Policies and Procedures / Network Operating Procedures / _Network Operating Procedures V1 20210430.docx

- **Task Distribution List:**
  Network Hub / Documents / Network Documents / Policies and Procedures / Network Operating Procedures / Appendix A - National Dental PBRN Study Task Distribution and Timeline Template.xlsx

- **Orientation to the National Dental PBRN CIRB on the HUB:**
  Network Hub / Documents / Network Documents / Policies and Procedures / Network Operating Procedures/ Orientation.to.the.National.Dental.PBRN.Central.IRB.2021-11-15 V6.0.pptx