U.S. Department of Health & Human Services • National Institutes of Health

National Center for Complementary and Integrative Health

Overview of a HEAL Cooperative Agreement

Wendy Weber, ND, PhD, MPH
Clinical Branch Chief, NCCIH, NIH

What is a U Mechanism?

- U mechanisms – U01, **UG3/UH3**, and U24 – are cooperative agreement awards
  - Used for Investigator-Initiated applications
  - Used by the federal government when the funding agency anticipates federal staff will have involvement in the activities of the award
  - At the time of funding, NIH will assign two staff members to work with investigators:
    1. Program Director/Official who is responsible for the administration of the award, review of progress reports, etc.
    2. Project Scientist who works directly with the investigators as part of the team and participates in trial planning and oversight

Benefits of a Cooperative Agreement with a Shared Coordinating Center

- Allows active partnership between NIH and Investigator Team
- More frequent communication
  - Program Scientist is part of your team
  - Tell us what is really going on so we can help
  - Connect you with resources across NIH to resolve challenges and overcome barriers
- Coordinating Center for the PRISM/HCS Collaboratory
  - Have assisted 15 ePCTs successfully transition and implement
  - Working Groups/Cores set up to address the challenging areas
  - Additional scientific expertise to help your project

What Is a Phased Award?

- Used when the supported research has two distinct phases (e.g., UG3/UH3) with separate aims
- Transition to the second phase is dependent on whether the first phase achieves the negotiated milestones
  - Examples include: test and refine data extraction methods; Institute/Center and DSMB approval of study protocol; finalize all training manuals for sites; active participant in PRISM/HCS Collaboratory activities, etc.

- If milestones are met, transition to the second phase of funding occurs after administrative review by funding Institute/Center (may get input from trans-NIH PRISM/HCS Collaboratory Implementation Team)

Transition Process

- Pre-Award negotiation of milestones
  - Want them to be objective
  - Easy to evaluate if they have been met – Yes or No

- Letter from NIH will describe the process
  - Submit per instructions, 2-3 months prior to transition time (build into timelines)
  - Document how you have met milestones
  - Still need to submit progress report electronically on due date

NIH Review Considerations

- UG3 milestones met
- Potential for meeting UH3 milestones
- Participation in PRISM/HCS Collaboratory Activities
- Input from NIH Implementation Team (possible)
- Fit of UH3 milestones and NIH priorities
- Availability of funds

HEAL Initiative Additional Requirements (Terms in NOA)

- **Declaration of Exceptional Circumstances (DECs)**
  - This award is funded through the NIH HEAL Initiative (https://www.nih.gov/researchtraining/medical-research-initiatives/heal-initiative).
  - The requirements here include but not limited to **reporting requirements and data sharing** … due to the need to respond to the national opioid public health crisis
  - NIH intends to maximize the availability of publications and the sharing of underlying data for NIH HEAL Initiative supported research projects
  - Award recipients are expected to cooperate and comply with all NIH data sharing including … central data sharing platform requirements developed for this public health emergency during the project period

HEAL Initiative Additional Requirements (Terms in NOA)

- **Participation in Annual Investigator Meetings**
  - The NIH HEAL Initiative will require a high level of coordination and sharing between investigators.
  - It is expected that NIH HEAL Initiative awardees will cooperate and coordinate their activities after awards are made by participating in Program Director/Principal Investigator (PD/PI) meetings

  - First annual HEAL Investigators Meeting to be on **January 16-17, 2020**
    - 1-2 Investigators per project

HEAL Initiative Additional Requirements (Terms in NOA)

- **ANNOUNCEMENT/COORDINATION**:
  - NIH would like to coordinate the announcement of NIH HEAL Initiative awards with FY2019 awardees
  - Coordinate with NIH by providing the name and contact information for the Public Information Officer (PIO) at the awardee institution to renate.myles@nih.gov and emma.wojtowicz@nih.gov at the NIH Office of Communications and Public Liaison
  - Coordinate the timing of announcements

HEAL Initiative Additional Requirements (Terms in NOA)

- **HEAL Central Data Sharing Platform Requirements**
  - The award recipient and its collaborators must comply with all NIH HEAL Initiative Data Sharing policies established during the project period.
  - Compliance with the NIH HEAL Initiative central data platform requirements and timelines developed through the HEAL consortium.
  - Expected that all data collected by award recipients and their collaborators, as part of the NIH HEAL Initiative, will be shared with the NIH HEAL Initiative central data platform.
  - All data collected as part of the NIH HEAL Initiative are so collected under a Certificate of Confidentiality and entitled to the protections thereof.
  - Institutions who receive Data and/or Materials from this award for performance of activities under this award are required to use the Data and/or Materials only as outlined by the NIH HEAL Initiative…

HEAL Initiative Public Access

- Given the urgency of this crisis, as highlighted by the declared public health emergency, rapid availability of Publications and the primary data behind them promotes dissemination of new knowledge, enhances reproducibility and accelerates the ability of researchers to build upon NIH HEAL Initiative research to make new discoveries.
  - NIH HEAL Initiative Research Projects are required to submit a Public Access and Data Sharing Plan that
    1) Describes their proposed process for making resulting Publications and, to the extent possible, the Underlying Primary Data immediately and broadly available to the public or
    2) If applicable, provides a justification to NIH if such sharing is not possible. Underlying Primary Data should be made as widely and freely available as possible while safeguarding the privacy of participants and protecting confidential and proprietary data.

- https://heal.nih.gov/about/public-access-data

HEAL Initiative Public Access

- The Public Access and Data Sharing Plan should, at a minimum, address the following general elements:
  - Release of Publications
    - How publications will be made **immediately** available to the public
    - The methods through which the public, including other researchers, will locate and access the publication
    - Any anticipated limitations to the immediate and broad release of publications with an associated justification
  - Sharing of Underlying Primary Data
    - The type of data that is expected to be generated by the research
    - The data that will be shared
    - Who will have access to the data
    - The timing and the medium for immediate sharing of the data
    - The methods through which the public, including other researchers, will locate and access the data
    - Any anticipated limitations to the immediate and broad sharing of data with an associated justification

HEAL Initiative Data Sharing

- Must think about this now!
- Informed consent documents must describe the data sharing aspect of the HEAL Initiative
  - Per the public access policy:
    - “Before submitting Underlying Primary Data, Awardees through their institutional review boards (IRBs), privacy boards, or equivalent bodies will assess the informed consent materials to determine whether the Underlying Primary Data may be shared as contemplated in this Policy.”

- https://heal.nih.gov/about/public-access-data

HEAL Common Data Elements (CDE)

Laura Dover Wandner, Ph.D.
Program Officer
Office of Pain Policy and Planning
National Institute of Neurological Disorders and Stroke

Definitions

Data Element

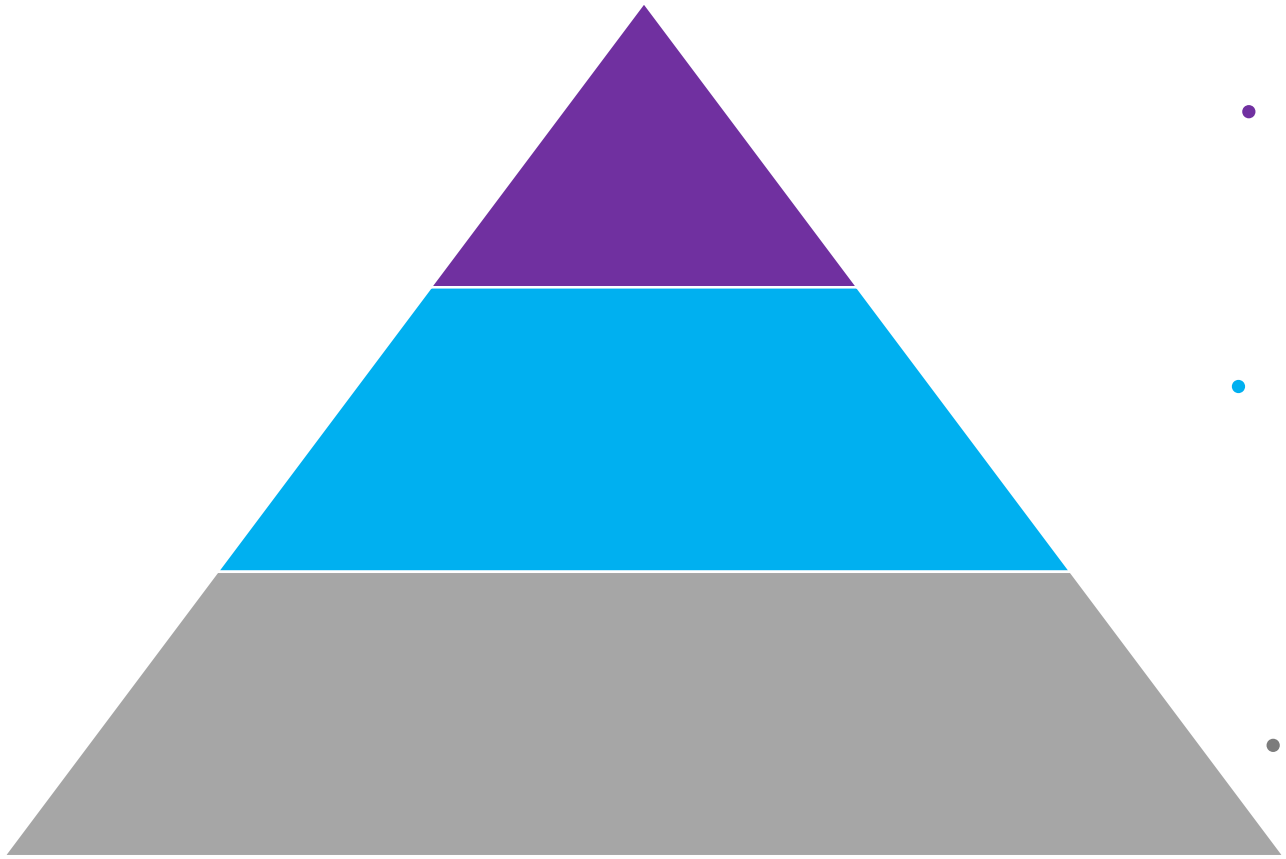
Information that describes a piece of data to be collected in a study*

Common Data Element (CDE)

Combination of a precisely defined question (variable) paired with a specified set of responses to the question that is common to multiple datasets or used across different studies**

*National Library of Medicine, **Sheehan *et al. Clin Trials. 2016;13(6):671-676.*

CDE Classification



- General Core
- Supplemental
- Exploratory

Goals of CDE and Case Report Form (CRF)

1 Harmonization

- Common definitions
- Consistency
- Minimize variability

2 Collaboration

- Systematic data collection
- Data sharing
- Analysis

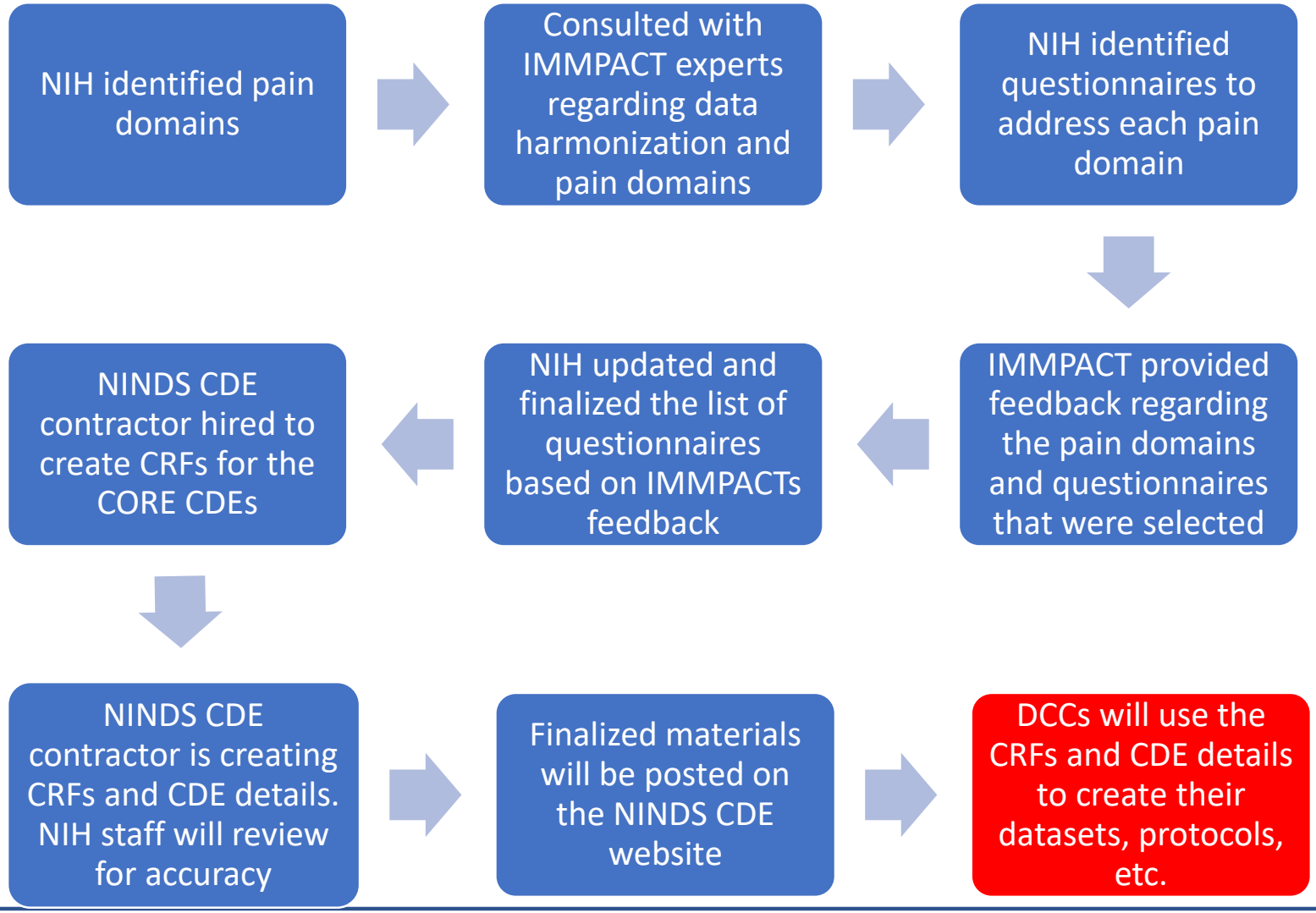
3 Efficiency

- Study start-up
- Clinical projects
- Data collection

4 Data

- Data quality
- Data integrity
- Promote interoperability

CDE Development Process: Core HEAL CDEs



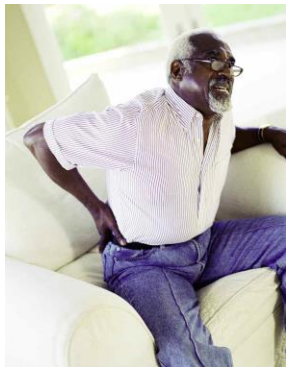
CORE HEAL CDE – Patient Reported Outcomes (PRO)

- Depression
  - PHQ-2
- Anxiety
  - GAD-2
- Global Satisfaction with Treatment
  - Patient Global Impression of Change (PGIC)
- Substance Use Screener
  - Tobacco, Alcohol, Prescription Medications, and Other Substances (TAPS)
- Pain Intensity
  - BPI Pain Severity
- Pain Interference
  - BPI Pain Interference
- Physical Functioning/Quality of Life
  - SF-8
- Sleep
  - Sleep Scale from the Medical Outcomes Study
- Pain Catastrophizing
  - Pain Catastrophizing Questionnaire

*Core CDEs; Total 53 questions
**Administer at baseline and 1x follow-up (except for 1)TAPS – only have to administer at baseline; 2)PGIC – only have to administer at follow-up)

Core HEAL Demographics

- Age
- Gender
- Marital Status
- Race
- Ethnicity



- Education
- Employment Status
- Family SES
- Disability
- Pain Duration

*Questions will be coded using CDISC

Examples of Supplemental/NIH Approved Questionnaires

- Body Maps/Pain Inventory
  - McGill Questionnaire
  - Brief Pain Inventory
  - Michigan Body Map
  - Widespread Pain Index
- Physical Functioning
  - PROMIS-Mobility
  - PROMIS –Physical Function
  - BPI – Physical Functioning
  - Pain Outcomes Questionnaire
  - SF-36 physical functioning
- Disability
  - Pain Disability Index
  - Survey of Pain Attitudes
- Sleep
  - PROMIS – Sleep Disturbance
  - PROMIS – Sleep Related Impairment
  - Insomnia Severity Index
  - The Pittsburgh Sleep Quality Index
  - Sleep Need Questionnaire
  - Epworth Sleepiness Scale
- Depression
  - PROMIS –Depression
  - PROMIS- Emotional Distress – Depressed
  - PROMIS – Depression for Youth
  - PHQ-8
  - PHQ-9
  - Beck Depression Scale
  - Hospital Anxiety and Depression Scale - Depression

Examples of Supplemental/NIH Approved Questionnaires

- Low Back Pain
  - Owestry Low Back Pain Disability Questionnaire
  - Roland-Morris Disability Questionnaire
- Neuropathic Pain
  - Neuropathic Pain Scale
  - Neuropathic Pain Symptom Inventory
- Anxiety
  - PROMIS - Anxiety
  - PROMIS – Emotional Distress – Anxiety
  - PROMIS – Anxiety for Youth
  - GAD-7
  - Hospital Anxiety and Depression Scale – Anxiety
  - State-Trait Anxiety Inventory
  - Beck Anxiety Inventory
- Substance Use/Misuse
  - PROMIS – Alcohol Use
  - Brief Addiction Monitor
  - Brief Addiction Monitor Consumption
  - Opioid Risk Tool
  - Screening Instrument for Substance Use Potential
  - Screener and Opioid Assessment for Patients with Pain
  - Current Opioids Misuse Measure
  - Prescription Drug Use Questionnaire
  - Pain Medication Questionnaire
  - Pain Assessment and Documentation Tool
  - Addiction Behavior Checklist
  - AUDIT or AUDIT-C

Example of a Domain and Use of Core CDE

- Depression
  - Core CDE Questionnaire – PHQ-2
  - PHQ-8 or PHQ-9
    - The PHQ-2 is included in the measures
  - PROMIS, Beck Depression Scale, or the Hospital Anxiety and Depression Scale
    - You will need to use the PHQ-2 as well as the measure you selected

CDE Details and CRF Preparation

1. Until April/May 2020 you will be able to access the CDE details and CRFs through a Box account that NIH will set up.

2. The Contractor will create a Pain CDE website in April/May 2020. All of the CDE details and CRFs will be posted on the website.

3. The contractor will post the Core and Supplemental HEAL CDE details and CRFs

   - Investigators must include the Core HEAL CDEs

4. Download the CDE details and CRFs and instrument Notice of Copyright documents (if instrument is copyrighted, you will not see a CRF, you will see a Notice of Copyright)

Contractor's CDE Timeline

1)Core CDE HEAL Questionnaires CRFs and CDE Details

2)Core Demographics CRF and CDE Details

Due Date: December 17, 2019

1)Supplemental/NIH Approved Questionnaires CRFs and CDE Details

Due Date: Spring 2020

PI Action Items

1. If you haven't provided PRISM the list of questionnaires you are planning on collecting, please provide them as soon as possible.

    A. The contractor will prioritize creating CDE details and CRFs for the Supplemental/NIH Approved Questionnaires that we know PIs are planning on using in their studies

Thank you. Questions?

Contact Information:

Laura.Wandner@nih.gov

What is a CDE? What is a Case Report Form (CRF)

- CDE
  - Standardized question and potential answers
  - Semantic value with a CDE name, definition and permissible values
  - Example:
    - CDE Name: “Tobacco current use indicator”
    - Definition: “Indicator for whether the participant/subject regularly uses tobacco products…”
    - Data type: “Alphanumeric”
    - Input Restriction: “Single Pre-Defined Values Selected”

- CRF
  - A specialized document in clinic research
  - The document should be study protocol driven, robust in content, and have the ability to collect the study specific data.

Example CRF

CDE Detailed Report

This report contains detailed information about the selected CDEs.

Note: If at least one CDE was selected from a copyright- or trademark-protected instrument/scale then all of the CDEs from that instrument/scale are included in this report.

Disease: Stroke
Sub-Domain: General Health History
CRF: Behavioral History

Item count: 19 (19 distinct CDEs)

CDE ID	CDE Name	Variable Name	Definition / Description	Question Text	Permissible Value
C00714	Behavioral history assessment date and time	BehavrlHistAssmtDateTime	Date (and time, if applicable and known) the participant/subject behavioral history was taken.	Date behavioral history taken	
C00710	Tobacco current use indicator	TobcoUseCurntInd	Indicator for whether the participant/subject regularly uses tobacco products (e.g., cigarettes, cigars, chewing tobacco or pipe) at the present time.	Current tobacco use?	Yes;No;Unknown;
C00711	Tobacco prior use indicator	TobcoPriorUseInd	Indicator of the participant's/subject's past regular tobacco (e.g., cigarettes, cigars, chewing tobacco or pipe) use prior to the past 12 months	Past tobacco use?	Yes;No;Unknown;
C00703	Tobacco use started age value	TobcoUseStrtAgeVal	Age in years when participant/subject started using tobacco products (e.g., cigarettes, cigars, chewing tobacco or pipe)	Age started tobacco use	

*This is NOT our Core HEAL CDE form

Example CRF

Demographics

[Study Name/ID pre-filled

Site Name:

Subject ID:

1) *Gender (Choose one):
   - ☐ Male
   - ☐ Female
   - ☐ Unknown
   - ☐ Unspecified
   - ☐ Not reported
2) *Genotypic sex:
   - ☐ XX
   - ☐ XY
   - ☐ XXX
   - ☐ XYY
   - ☐ Unknown
   - ☐ Unspecified
   - ☐ Other, specify:
3) *Date of birth
4) *Ethnicity ("X" ONLY one with which you MOST CLOSELY identify):
   - ☐ Hispanic or Latino
   - ☐ Not Hispanic or Latino
   - ☐ Unknown
   - ☐ Not Reported
5) **Intracranial aneurysm pertinent ethnicity
   - ☐ Japanese
   - ☐ Finnish
   - ☐ Eastern Asian
   - ☐ European
   - ☐ Persian
   - ☐ Arab
   - ☐ Southeast Asian
   - ☐ South Asian
   - ☐ Pacific Islander
   - ☐ Amerindians
6) *Race category (Choose all those with which you identify):
   - ☐ American Indian or Alaska Native
   - ☐ Asian
   - ☐ Black or African-American
   - ☐ Native Hawaiian or Other Pacific Islander
   - ☐ White
   - ☐ Unknown
   - ☐ Not reported
7) Race expanded category:
   - ☐ Black African American
   - ☐ Black Afro-Caribbean
   - ☐ North American Indian
   - ☐ Inuit
   - ☐ Far Eastern Asian
   - ☐ Black African
   - ☐ South/Central American Indian
   - ☐ Alaskan Native
   - ☐ South Asian
   - ☐ Western Asian

*This is NOT our Core HEAL demographics form

Example CRF and CDE

Behavioral History

[Study Name/ID pre-filled

Site Name:

Subject ID:

iDate behavioral history taken (M M/D D/Y Y Y Y):

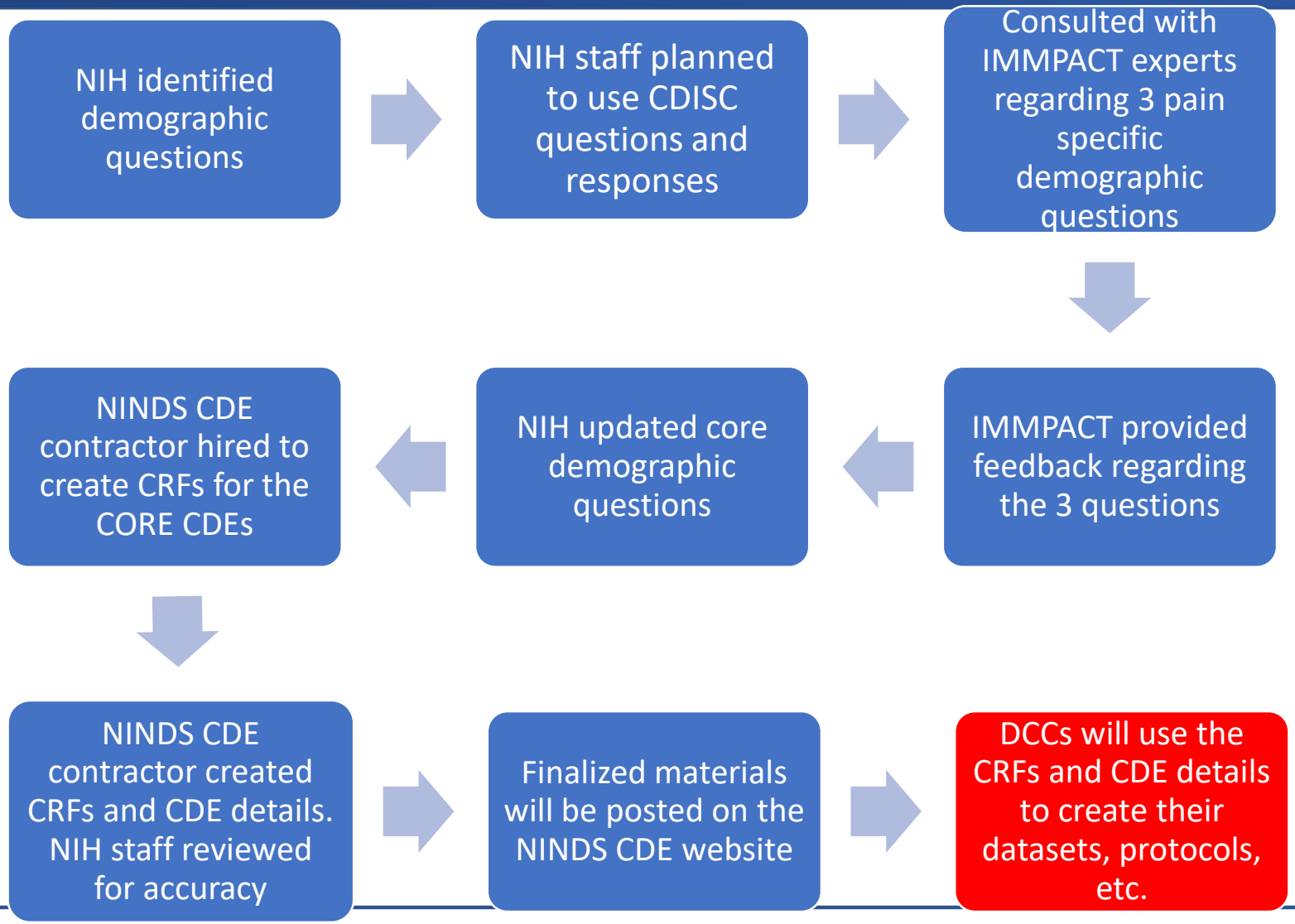
SMOKING HISTORY

1) iCurrent tobacco use? (Regular use of cigarettes, cigars, chewing tobacco or pipes within past year)
   - ☐ Yes
   - ☐ No
   - ☐ Unknown
2) iPast tobacco use? (Regular use of cigarettes, cigars, chewing tobacco or pipes prior to the past year)
   - ☐ Yes
   - ☐ No
   - ☐ Unknown

CDE Details (subset of attributes of the CDE shown below):

CDE ID	CDE Name	Variable Name	Definition / Description	Question Text	Permissible Value	Data Type	Instructions	Population	Classification (e.g., Core)
C00710	Tobacco current use indicator	TobcoUseCurntInd	Indicator for whether the participant/subject regularly uses tobacco products (e.g., cigarettes, cigars, chewing tobacco or pipe) at the present time.	Current tobacco use?	Yes;No;Unknown;	Alphanumeric	History can be obtained from participant/ subject, family member, friend, or chart/ medical record. Supplemental - Highly Recommended based on study type, disease stage and disease type.	Adult;Pediatric	Core

CDE Development Process: Core Demographic Questions



CDE Development Process: NIH Approved Questionnaires