Protocol Drafting Guidance

DEVELOPED BY THE OFFICE OF HUMAN RESEARCH AFFAIRS

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| Document Version Date Tracking:   * **This guidance may be used as a template protocol if all guidance text is replaced with your study specific content** * Study teams are responsible for Version Tracking of all documents. * The OHRA will not rely on a file name version or date. We rely on a version that appears within the actual document. * As you develop Version 1 you can update the date in the file name. When you and your team are satisfied with Version 1 and are ready to submit for Ancillary Reviews, apply the latest Version 1 file date to the V1 date line on the cover page. This will become the documented version and date for initial review. * Any significant revisions after version 1 is approved should be date tracked with the intent to use the Version 2 date line. * If you need to make updates for minor or administrative changes its okay to update the date of version 1 instead of moving to version 2. All dates applied to version 1 should be recorded on the V1 line. * It is NOT recommended to incorporate the version into the header or footer since it is very easy to forget to update and create inconsistencies. Managing your versions on the cover page is sufficient | |
| V1: 04/2021 | V6: |
| V2: 02/2022 | V7: |
| V3: | V8: |
| V4: | V9: |
| V5: | V10: |

*[Automatic Table Of Contents is supported and may be inserted from the References Tab but not required]*

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| SYNOPSIS | |
| **Tracking IDs** | Please compile all assigned tracking numbers for this project (R&D Tools, Tool Factory, OHRA, Data Governance Etc.) |
| **Full Title**  **(Scientific)** | Please be careful to make each protocol title unique enough to distinguish from other similar projects |
| **Short Title**  **(Public Facing)** | Please be sure to follow up with OHRA to update any titles that change or are added over time |
| **Type of Project Description** | Please replace this text and describe your project as one of the following:  - Observational Research - Interventional Research - Operational/QI Project  - Data Analysis Plan- Expanded Access for Drug or Device |
| **Primary Objective** | Please briefly describe the primary objective of this project |
| **Anticipated Duration** | If possible, identify the planned launch timing and the desired timing to release results |
| **Primary Target Population** | (General public? Members of an existing program? Patients at a specific clinic? UHC members? M&R? UHG Employees?) |

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| PERSONNEL – Full name, Credentials, Affiliation, Email address | |
| **Principal Investigator** | There should be ONE principal investigator who signs the PI assurance |
| **Owner / Coordinator** | Typically, the PI delegates certain administrative tasks to a support lead. Please name that person and provide their contact information. |
| **Clinical Lead** | This person should have clinical expertise in the area being studied. |
| **Data Scientist** | The data scientist/statistician will be considered an internal sub-investigator. |
| **Operations Architect** | This role may be specific to Optum Labs. If other roles are present for your study please create space to identify them |
| **Internal**  **Sub-Investigators** | Do not re-name people named above |
| **External**  **Sub-Investigators** | Do not re-name people named above |

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| COLLABORATING ENTITIES | |
| **Study Sponsor** | Please identify the Internal UHG Supporting Business, Division, or Segment for this project |
| **Funding Sponsor** | Name your source of funding. If your project is funded internally by Optum Labs, please engage Dan Cummings or Mike Pontius to develop a budget plan |
| **Regulatory Sponsor** | (IND or IDE holder for FDA regulated drugs and devices under investigation) |
| **Partners** | Identify external partnering entities in the research such as businesses, health systems or universities |
| **Vendors** | If your research requires any vendors, please engage Eric Lawrence during protocol development |
| **Research Sites** | Please identify all locations (clinics, labs, etc.) where participants will be enrolled or expected to appear to engage in research activity. Please identify by Name & Address or indicate virtual participation. This information will inform the Regulatory and Compliance reviewers of any state laws that need to be considered. |

# Background & Significance

This section does not need to follow a specific format, but the following information should be included somehow:

## Project Purpose & Vision:

Explain why you are doing this project and what you envision doing with the results. Please include references to supporting sources that contextualize the history behind project in terms of healthcare delivery or outcomes and existing research on the topic. This will set the stage for understanding the focus area or problem that this project is aimed to address.

## Focus Area or Problem:

Identify the specific problem you are trying to solve with this research. If the study is more exploratory in nature, identify the focus area for exploration.

## Justification of Proposed Solution:

You have identified a problem that this research is meant to solve. Discuss your proposed solution to the problem. If you are testing a product, service, device or process, why have you chosen this one (or these specific ones if comparing multiple options) over other available options? If the study is exploratory, justify your approach to collecting information about your focus area.

## Defining Population of Interest:

Briefly explain who the target population is and why they are best suited for study of this particular problem. The finer details will be explained in the eligibility criteria section later.

## Qualified Personnel:

Explain how the study team identified on page 1 are qualified and appropriate to execute this study as planned and positioned to leverage the results to achieve the project vision.

# Specific Aims & Hypotheses

## 2.1

Aim 1:

Hypothesis 1:

## 2.2

Aim 2:

Hypothesis 2:

# Preliminary Studies

Please see NIH guidance for including preliminary studies and data in your protocol. <https://www.niaid.nih.gov/grants-contracts/preliminary-data>

# Research Design & Methods

## General Design:

Please use this section to explain:

* The overall proposed experimental design elements for the project. This relates to topics such as Comparison Groups, Units, Arrangement of factors, Allocations and nature of allocation factors.

(e.g., how many arms, groups, cohorts are there? What are the basic features of each arm, group, cohort? How are the arms, groups & cohorts related? Is there a control group? What kind of control group? Is there randomization? if so, what is the randomization scheme? is there blinding? Who is blinded and for how long? What are the criteria for unblinding? Is this parallel design? Is there a plan for crossover?) a blueprint/diagram is often very helpful in this section to describe your study design

* This section should NOT be a description of the procedures to execute the project. The goal is to explain how the study has been structured to obtain data in a controlled way.
* How the experimental design being utilized aligns with answering the primary and any secondary objectives of the project. How you plan to successfully operationalize the project within the structure of the experimental design selected
* If there is potential for integration/overlap with the current clinical care landscape, describe how you will introduce the additional/revised procedures in alignment with clinical care. (i.e. Are you planning to leverage existing routine clinical appointments to execute your research?)
* How will you integrate these procedures into the current clinical care landscape?
* If the procedures cannot be integrated, please provide a plan for how to operationalize your project if there is no existing framework to build your project into. (i.e., if no existing clinical interactions exist to support your procedures, how will you arrange these interactions?)

## Study Measures & Methods

Please list and describe the surveys, interviews, questionnaires, clinical encounters, or constructed situations planned for data collection. If data will not be collected with a study measure involving human interaction, please describe the environments for data abstraction.

## Drugs & Devices

Please list and describe all drugs and devices being used in the project. If the study is not utilizing any drug or device, please clearly state that. Please note that algorithms, AI, machine learning models and similar programs may be considered “Software as a Medical Device” according to the FDA so should be explained here as well.

Please clearly identify whether each is FDA approved, being used on label, or being used off label to establish a new indication. It should be clear whether the original manufacturer or vendor will supply directly to participants or if there will be re-packaging. In the case of AI please make it clear who the developer/owner is

It is always helpful for regulatory review to have information about drugs and devices being used. Please include links to available websites, appendices for package inserts, investigators brochures, user manuals etc. as supporting documentation for your protocol.

This section will dictate whether FDA compliance assessment is needed as part of regulatory review.

## Intervention or Observation Procedures

Please explain the data collection activities and procedures from beginning to end. This section should not reiterate participant identification, recruitment, enrollment, or consent. It should be specific to what will happen for participants who successfully enrolled and confirmed to be eligible and the specific methods being used to collect data. It may be helpful to create a procedures table, flow chart or other diagram demonstrating a single participant’s journey through the project. It should be clear what is being done by the study team and what is being done by the participants. This section will drive what your consent document communicates about participation. It is advised that this section be finalized prior to beginning consent drafting. The procedures being used may trigger additional regulatory considerations to align with FDA requirements, state laws, etc.

If your project includes any genetic testing, additional regulatory review by Legal will be required. Your protocol should include an additional section specifically related to how this project is designed within the parameters of GINA law (Genetic Information Nondiscrimination Act).

## Data Sources and Variables

Your protocol should include a complete picture of all data points to be collected and where they are being collected from/how they are being collected. Using the table below to organize your variables in terms of which research Aim/Hypothesis they support and the source they come from is a common method. You may also append a separate document if you are collecting a lot of data from several places. Please provide precise definitions of how variables will be defined. For instance, when defining a “hypertension flag” you should specify the list of qualifying ICD codes, the time window used to look for those ICD codes, and whether or not there were additional criteria (e.g. two instances of a code at least 30 days apart). All data that you plan to collect should be clearly specified and should be able to describe the enrolled population and answer all proposed research questions.

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| Research Question/Aim/Objective: | Data Variables: | Data Source |
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It is recommended to also include a detailed data dictionary.

### Inclusion Criteria:

* Describe the specific criteria that makes someone from the target population pool an ideal candidate eligible to contribute analyzable data to the study. The protocol section for Eligibility Screening & Medical clearance should also be clear about the specific procedures that will be used to verify that all participants meet the required inclusion criteria before they begin any study activity
* Inclusion and Exclusion criteria should be considered in context of the aims of the study, the metrics and variables that are being collected, study procedures, and potentially confounding variables that will adversely affect the overall sample.
* If your study is designed with multiple groups, arms or cohorts, be sure to name them, identify them consistently throughout the protocol and provide inclusion and exclusion for each if they differ in some way

### Exclusion Criteria:

* Describe the specific criteria that would eliminate an otherwise eligible participant
* It is not necessary to itemize the “opposites of inclusion”
* Providing some contextual information for each exclusion is often helpful especially if exclusion is clinically relevant or based on a safety consideration.
* The protocol section for Eligibility Screening & Medical clearance should also be clear about the specific procedures that will be used to verify that all participants DO NOT meet the identified exclusion criteria before they begin any study activity

## Justification of Sample Size & Power

Please describe your sample size justification and power calculation. If the study is not powered, please clearly state that and provide a justification for the selected sample size.

## Statistical Methods

Please describe the statistical methods that will be applied. An analysis plan should be included for each primary, secondary, and exploratory outcome. This analysis plan should be specific enough that a statistician familiar with the relevant methods could complete the analysis if given access to the data and statistical analysis plan with no further information. A complete analysis plan should consider the endpoints, statistical methods, hypothesis tests, multiple testing corrections, handling of missing data, adjustments for confounding variables, ascertainment of evidence of biases, and sensitivity analyses. If the study is purely descriptive, then just state the data will be summarized using descriptive measures.

Example: “Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender).”

Note that if you want to make claims of statistical significance based on the findings of the study you must prespecify the analysis in the research protocol and account for hypothesis test in your power analysis. For exploratory outcomes it is acceptable to have more open-ended analysis plans but all findings must be interpreted as exploratory or hypothesis generating.

## Control of Bias & Confounding

Please discuss the methods and controls in place to identify and reduce bias and confounding. This is usually important for projects that do not include a true randomization scheme. For example, radiographic studies might be read by a radiologist who is blind to the diagnosis. Cases might be included only if the initial presentation was within the study window; otherwise complex cases or recurrent disease might be over-represented in the sample because both old and new cases would be captured. For studies with randomization, please describe the randomization scheme (e.g. stratified, block, ratio, etc.) that was used. Please describe any blinding used in this study.

## Primary & Secondary Endpoints

The endpoints refer directly to the aims and are the specific expression of what will be compared in the study. Example: “The primary aim is to determine whether tonsillectomy increases weight gain. The primary endpoint will be the difference in weight 2 months after surgery compared to the 2 months before surgery.”

## Interim Analysis and Stopping Rules

Describe any plans to perform interim analysis on collected data prior to the primary analysis in support of publication. What is the purpose the interim analysis serves and what are the specific timepoints for interim analysis?

If the project has been designed with an intention to stop due to a particular endpoint, outcome, or failure to meet feasibility please discuss that here. Be sure to consider this in terms of stopping a specific participant from continuing (lack of response to intervention, or adverse event) as well as stopping the entire project.

All interim analyses of primary or secondary aims should be accounted for in the power analysis. Stopping rules for efficacy or futility should maintain adequate operating characteristics (power and type I error rate) of the study.

If there are no interim analyses or stopping rules pleas clearly state.

## Case Ascertainment for Synthetic Controls

If the research is designed with a synthetic control group, please be sure this is clearly noted in the General Design section and use this area to describe in more detail how the synthetic control group will be constructed and matched to the test group. Please include a description of the methods used to create the matched control group including matching methods, variables, and ratio and a plan for assessing the quality of the match. If there is no synthetic control group please state directly.

## Duration

Please provide responses to all 4 areas. It is understood that projected timelines will fluctuate, however a projection is helpful for planning.

**Estimated Start of Recruitment**: when do you plan to start sending out recruitment materials? Is there a specific date? Is it just “Q2 of 2023”? If your study doesn’t involve recruitment, then please state directly.

**Estimated Enrollment Period**: how long to you plan to enroll new participants. Will you continue enrollment indefinitely until the target is met? Is there a time limit based on your funding , study goals or internal policies? If your study does not involve enrollment then please state directly.

**Active Participation time**: Think about the experience of an individual participant. What is the time frame from when they receive invitation to participate to the time they receive the final study communication?

**Projected Data Collection Cut off** : how long to you plan to collect data? Will you continue collection indefinitely until 100% evaluable data from every enrolled person is obtained? Is there a time limit based on your funding , your study goals or internal policies? If there are different phases of data collection, please explain. For example, if your study is designed to actively collect survey data from participants every 3 months for 2 years but also includes passive data collection from claims for 5 years (during the 2-year survey phase + 3 years post study observation period), this should be made clear.

## Intended Use of Learnings

Project design is significantly impacted by what the intentions for the learnings are. If learnings are being used internally, the likely affected groups may be engaged during protocol design/development to determine that the research question (or questions) are the right ones and what the data would need to demonstrate to support any claims from the learnings. In addition, the plan for statistical analysis and how the data will be evaluated should be presented to assure successful acceptance of the findings at completion of the project. This section should be used to explain how the outcomes/learnings from this project are intended to be used.

## *Internal use of findings plans and relevant enterprise segments: Examples:*

* **Medical policy (OptumCare):** fostering change in the standard clinical care space to deliver the best care possible and partner with our members/patients in their healthcare journeys
* **Medical policy (UHC):** providing evidence to support changes in healthcare coverage
* **Complex project development**: using initial findings (from either data science or pilot/feasibility work) to justify development and execution of more complex (likely human participant based) projects
* **Healthcare Provider/Clinician experience**: using individual project learnings to develop and implement practical methods to improve and enrich the clinician/provider experience for our UHG team (OptumCare, UHC, integrated/non-integrated entities)
* **Member/Patient/Citizen Scientist experience**: using both individual project learnings and overall experience feedback from any and all groups to create an environment of engagement and partnership with our patients/members/research participants

## *External presentation or publication plan: Examples*:

* **Traditional Publications**: sharing learnings (even in the non-research space) from data science and initial pilot/feasibility work when there is a generalized component to the findings (i.e. not specific to internal UHG improvement)
* **Partnerships**: using data science and/or pilot/feasibility project learnings as justification for development of larger scale efforts to impact healthcare in any and all of the current POVs in Global R&D and integrating appropriate academic/scientific partners to align with the targeted topic
* **Program Development/Delivery**: using learnings and established successes (including member/patient/participant feedback) to create platforms not only for our own members/patients but to widely benefit the community at large by making the program available.
* **Product Development/Delivery**: using learnings to demonstrate success of products (including patents and any regulatory approvals if necessary – i.e. FDA regulated devices) and transfer both internally via Ventures and externally via product marketing
* **ClinicalTrials.gov (CT.Gov) Registration Posting:** if you plan to register your study on ClinicalTrials.gov, you must have a dedicated member of your study team to manage the registration until the study is closed and results are posted. Your consent form must also disclose the registration to participants and identify whether de-identified aggregate results will be posted there.

The OHRA is currently the acting PRS administrator for UnitedHealth Group and UnitedHealthcare on CT.gov. You must contact the OHRA directly to request an access account to register your study. Please note that not all studies are required to register. However, many well-known and respected publications require CT.gov registration in alignment with the International Committee of Medical Journal Editors (ICMJE) definition of a clinical trial. It is the responsibility of the study team to understand the posting requirements for a given study. These considerations need to be made before a study begins to enroll participants. You should consider the following:

* Have you read and understood the FDA definition of an “Applicable Clinical Trial” that requires CT.gov registration and results posting per US Regulations? <https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf>
* Have you thoroughly investigated your external publications of interest to determine whether they follow ICMJE recommendations for clinical trial registration? <http://www.icmje.org/journals-following-the-icmje-recommendations/>
* Have you read and understood the ICMJE definition of a Clinical Trial that should be registered? <http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/> *(please note that ICMJE does not require posting results for studies that do not meet the FDA definition. Just prospective registration before enrollment begins)*
* Have you reviewed the [TUTORIALS](https://prsinfo.clinicaltrials.gov/tutorial/content/index.html#/) from CT.gov for [CREATING](https://clinicaltrials.gov/ct2/manage-recs/how-register) and [UPDATING](https://clinicaltrials.gov/ct2/manage-recs/how-edit) a study record?
* Have you reviewed the TUTORIALS and templates for [POSTING RESULTS](https://clinicaltrials.gov/ct2/manage-recs/how-report) on CT.gov?
* Do you have the resources (hours and manpower) required to create and maintain the registration AND translate your study results into the required format for CT.gov if results posting is planned? As noted on the CT.gov burden statement “*Public reporting burden for this collection of information is estimated to vary from 2.0 to 8.0 hours per response for registration, 10.0 to 45.0 hours per response for results information submissions, and 15 minutes to 2 hours for other submissions including certifications for delay, extension requests, and expanded access. These estimates include the time for reviewing instructions, searching existing data sources, gathering the data needed, and completing and reviewing the collection of information…*”

## Future Utilization of Collected Data or Specimens

What do you intend to do with the data collected from the project after publication? Will it be destroyed? Will it be stored for use in future protocols that have not been designed yet? If so, where will it be stored, for how long, and in what condition (identifiable? De-identified? Limited data set?)

If the project involved specimen/sample collection, are any residual samples being saved? Is there a need for biobanking? If so, where will samples be stored, for how long, and in what condition (identifiable? De-identified? coded?) Please describe those plans here. Depending on your plan, specific consent language will be needed.

# Human subjects

## Participant Safety, Risks and Risk Mitigation

Describe the reasonably foreseeable risks of all study activities.

For Drugs and Devices please provide package inserts, investigators brochures, manufacturer pamphlets or user manuals as the source documentation for risks. This section should list those risks in groups of Likely, Less Likely, Rare but Serious with information about how those risks are being minimized or mitigated

Describe the risks of the procedures required for participation.

Describe any additional risks of the project beyond interventional/procedure specific risks (i.e. use of data risks, privacy risks, commitment, and time to joining the study, any travel or other burden to joining the study, etc.)

Describe the methods, tools, and resources in place to mitigate each of these risks and ensure participant safety and protect their rights and welfare. This may include explanation of exclusion criteria to ensure safety or participant engagement that ensures safety.

If any component of this project brings elevated risk to the enterprise, please discuss those risks and mitigation plans.

## Recruitment Plan

How will you discover people who are potentially eligible?

How will you access the targeted population?

How will your population base find out about the existence of your study?

Does any member of the investigative team have direct access to the target population?

What is the recruitment strategy that will be used to inform potential research participants? If you do not have a prospective identification plan and are targeting general public, please explain the recruitment plan in those terms. How often will you reach out? Are there various methods being employed (UiR/social media/traditional print press/TV/Radio/other?)

Consider the potential of increased risk of reaching out directly (i.e. direct outreach may upset individuals for being targeted for their condition/disease)

Alternatively, describe the plan to obtain data sets or bio specimens for research that does not involve human interaction. Biospecimen plans should also include storage, care, use and disposal considerations.

## Enrollment Plan, Consent & HIPAA Authorization

After being alerted to the existence of the project via the recruitment plan noted above, how will an individual potentially eligible participant contact the researcher to enroll? Once participants have been informed of the study and show interest, how will the study obtain consent from participants? Items to consider:

* Documented Informed Consent
  + Participants are provided with a consent document that requires a signature and documentation by the research team
* Verbal Consent (“Waiver of documentation of consent”)
  + Participants are provided with an information sheet about the study. Participants are read the information sheet aloud and verbally consent to the study. (Participants are still encouraged to ask questions and voice concerns but will verbally consent to participate in the study.)
  + Verbal Consent could be in person or over the phone
* Assent & Parental Permission
* Legally Authorized Representative Consent process
* Translations and interpretations for non-English speaking participants
* HIPAA authorization – This is required if the activity in the project requires that the study team access medical records or claims. HIPAA authorization is not the same as consent. In some cases, the OHRA may approve an alteration or waiver of consent but cannot approve alteration or waiver of HIPAA authorization. Please be clear in your protocol about whether HIPAA authorization will be obtained and documented
* Alteration of consent and / or HIPAA authorization
* Waiver of Consent and/or HIPAA authorization
* Please carefully review the separate Consent Guidance on the OHRA website

## Eligibility Screening & Medical Clearance

Please explain how and when you will confirm that each participant meets inclusion criteria and does not meet exclusion criteria prior to engaging in study activity. If screening is a multi-stage process, please explain all stages.

## Participant Engagement, Results, & Withdrawal

Please explain the plan for ongoing communication with participants. How will you keep them engaged? Are there timed emails? SmS text messaging? If there are tests being performed as part of procedures, how will you share their individual results with them? Will providing information back to participants have the potential to upset individuals (e.g. genomics test finds results of disease or condition otherwise unknown to the participant) If so, what plan is in place to ensure asking participants if they want to receive their results and is an information sheet necessary to describe what the results may include. If your study includes genetic testing, there is an expectation to provide access to genetic counseling for any positive results.

Please also discuss the withdrawal process. Describe the conditions under which a participant would be removed from the study.

Please explain the process for a participant to withdraw themselves. If there are any potential safety concerns for withdrawal that require additional study team oversight, please explain them here (e.g. titrating off a study drug)

There is also an expectation for studies conducted through United In Research to share the results of each project. This plan should include Informing the participants of study results when appropriate to communicate things like:

General findings, Successful outcomes of the project and plans for the future, Demographics & Enrollment numbers

What information will you share with participants?

How will this information be shared (e.g. Infographics, email, phone calls, etc.)?

When will this information be shared with participants (e.g. finish of study, sporadically, etc.)?

What is the plan for reconnecting with participants and informing them of results once the study is completed?

## Compensation / Remuneration / Reimbursement

Are you planning to pay subjects for their time spent in your project (compensation/remuneration) or cover expenses, or pay back incurred expenses, for any project related costs (reimbursement)?

Compensation/remuneration:

* + How much will participants receive?
  + Consider the amount of compensation and if the amount would lead to coercion or undue influence (the amount should not influence a participant to complete a risky or burdensome study for the compensation)
  + When will participants receive compensation (e.g. after completion, specific timepoint, specific activity completion etc.)
  + How will participants receive compensation (e.g. electronically, cash, etc.)

Reimbursement:

* + What expenses will the study reimburse (Travel expense, Lodging, Transportation, Parking)
  + When will participants receive reimbursement (i.e. timeline of when patients should expect to be reimbursed)
  + How will participants receive reimbursement (e.g. submitting receipts, etc.)

Studies that include payment will need Legal Concurrence during protocol development as well as budget confirmation. If UHG employees are being targeted, Human Capital backing for compensation will be needed. If UHC members or M&R members are being targeted, UHC concurrence will be needed during protocol development.

## Diversity Considerations:

Ensuring diversity in research should be an underlying goal of all projects. This section should discuss opportunities and limitations for diversity that are relevant to the project design, goals, and target population. The data collection section should identify an objective for ensuring diversity with a plan for obtaining race and ethnicity information and a plan for interim analysis for diversity before the enrollment period ends. The table below should be used for statistical planning when possible. If you cannot make a statistical plan for diversity this section should include a narrative discussion about considerations for diversity. A thoughtful execution of this section will reflect the following concepts:

* Has your team done any preparatory work to determine the racial, ethnic, cultural groups most effected by the problem you have identified? On a global level? Country level? State, county or clinic level?
* Has your team done any preparatory work to determine the racial, ethnic, cultural groups that your chosen participant pool is comprised of?
* In the case of limitations on diversity where research cannot be conducted with an appropriately diverse participant group, how will you represent and account for this when you present your results internally and externally?

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| TARGETED/PLANNED ENROLLMENT: Number of Subjects | | | | |
| Ethnic Category | Females | | Males | Total |
| Hispanic or Latino |  | |  |  |
| Not Hispanic or Latino |  | |  |  |
| Ethnic Category: Total of All Subjects \* |  | |  |  |
| Racial Categories |  | | | |
| American Indian/Alaska Native |  |  | |  |
| Asian |  |  | |  |
| Native Hawaiian or Other Pacific Islander |  |  | |  |
| Black or African American |  |  | |  |
| White |  |  | |  |
| Racial Categories: Total of All Subjects \* |  |  | |  |

## Protected Populations:

The following populations are being targeted for participation and are necessary for this project (Check all that apply): **Note- this is meant to indicate populations that WILL be targeted and their participation is required in order to make statti. It is not meant to capture incidental participants.**

UnitedHealth Group Employees -- *(Requires Human Capital support during development)*

UnitedHealthcare Members -- *(Requires UHC support. Please specify targeted plan types below. Protocol requires UHC Research Review Board approval)*

Medicare & Retirement Plan Members (M&R)

Employer & Individual Plan Members (E&I)

Community & State Plan Members (C&S)

Global Markets

Children – *(Requires age range justification, assent & parental permission process / materials. OHRA must apply additional regulations)*

Pregnant Women - project is specific to pregnancy or includes intervention that may affect the fetus *(OHRA must apply additional regulations)*

Intellectually / Cognitively / Developmentally Disabled Persons *(requires LAR considerations for recruitment, enrollment & all procedures)*

Economically Disadvantaged Persons *(requires careful consideration of compensation amounts)*

Prisoners *(Requires convened review & must include qualified prisoner representative. OHRA must apply additional regulations.)*

**Protected Populations Justifications**: *For each population please provide justification for why their involvement is necessary and explain how the project is designed to appropriately accommodate and protect them from undue influence and risk of harm.*

***UHG Employees***

*Potential participants in this group must be informed that their decision to participate or not will have no bearing on employment or other benefits to which they are otherwise entitled.*

*Studies targeting UHG employees must have considerations for timing of participation. Will participants be expected to do research activity during normal work hours? Do they need to leave the location where they report to work in order to participate? How is the project designed to accommodate employees, especially hourly employees?*

*Studies targeting UHG employees should work with Human Capital to determine appropriateness of this target population, plans for compensation, and procedures that may interfere with the work schedule. Your cover letter for initial review should indicate whether Human Capital has approved the protocol being submitted for review.*

***UHC Members***

*Targeted participants in these groups must be informed that their decision to participate or not will have no bearing on coverage or other benefits to which they are otherwise entitled. Your protocol must identify the plans being targeted. This information is used to facilitate the relationship between the related UHC segments and investigators targeting those members.*

*Studies targeting UHC members should work with UHC directly during project development to ensure access to member lists. UHC has its own specific intake form to support the collaboration of UHC and Optum Labs.*

***Children***

*The OHRA is required to apply additional regulations to your project when children are eligible due to their designation as a vulnerable population*

*Research involving children should have a pediatrician or other relevant expert on the research team*

*Eligibility of children should be defined by specific age group*

*A plan for obtaining assent and parental permission is required*

***Pregnant Women, fetuses & neonates***

*The OHRA is required to apply additional regulations to your project when pregnant women are eligible and the project is designed with objectives relevant to the pregnancy or includes interventions that may affect the fetus or neonate due to their designation as a vulnerable population.*

***Intellectually / Cognitively / Developmentally Disabled Persons***

*This category is meant to capture individuals with impaired or no decision-making ability that require a legally authorized representative (LAR). This could describe a chronic or acute condition. When these groups are targeted for research participation, appropriate accommodations for LAR support during recruitment, enrollment and all project procedures must be clearly outlined throughout the protocol.*

*If inclusion criteria dictate that all participants be able to consent for themselves and perform all study activities themselves, this population cannot be included.*

***Economically Disadvantaged Persons***

*Targeting the economically disadvantaged for research can be important for identifying and testing solutions that fit the demographic. However, when research is greater than minimal risk and targets those at an economic disadvantage, any monetary compensation structure should be carefully considered in order to avoid undue influence.*

***Prisoners***

*"Prisoner" means any individual involuntarily confined or detained in a penal institution. Targeting prisoners for research can be important for identifying and testing solutions that fit the demographic. However, US research regulations define prisoners as a vulnerable population due to their incarceration placing extreme limits on their autonomy. Please engage the OHRA as soon as possible when developing this kind of research to ensure appropriate resources are available.*

# Administration, Quality Control, Monitoring & Reporting

## Materials for Internal Development & Procurement

Based on your description of the project so far (design, participant identification-recruitment-enrollment, procedures) Please develop a list of materials needed to support those activities. If you are collaborating with a vendor or partner that will provide some materials, please identify them. Any internally developed materials should be drafted in collaboration with Operations Architect and writing/editing team through Scott S. Anything in this list that is participant facing will require OHRA approval unless the OHRA communicates otherwise in the initial approval letter. This should essentially be the list of documents that the OHRA/IRB will be asked to approve in support of the study

## Research Site Management Plan, Delegation & Training

Projects that involve human participants require oversight and coordination of all collaborating entities. It is the expectation of the OHRA that all projects will include a plan for site monitoring and quality control. This plan should include steps to ensure the protocol is being followed as written and that any serious issues (deviations or events that impact the safety or rights of research participants and staff) are effectively identified in a timely manner and reported to the OHRA according to current guidelines and best practices. Please describe all methods, tools , resources and schedules that will be employed to ensure protocol compliance and quality control. Your plan should align with the risk level, complexity, and planned duration of the research. Areas to consider include but are not limited to:

* + An appropriate delegation log for the PI to delegate study responsibilities
  + Routine meetings with stake holders about progress
  + Mechanisms for participant activity sites to report back to the team, ask questions, identify issues
  + Mechanisms for addressing participant complaints or issues
  + Managing Logistics of procedures occurring remotely like shipping supplies, tests and devices, virtual surveys and interactions etc.

## Deviations & Adverse Events Recording and Reporting

The quality control plan described above should adequately serve as a mechanism for identifying deviations from the protocol and adverse events that occur. All deviations and adverse events occurring on a research study should be fully documented and assessed for OHRA reporting criteria. The OHRA provides a template Issues Log for all projects. The Log template should be downloaded from the OHRA website resources library. This log is expected at the time of annual renewal for all studies that require annual renewal. The log is expected at the time of closure for all studies that do not require annual renewal. If this is a clinical trial the PI and clinical lead should identify the types of clinical outcomes that are expected (risks) and describe generally the types of clinical outcomes that would be considered adverse events. Please see the OHRA guidance “issues recording and reporting” for more details.

## Data Handling; Security, Protection, Storage and Transfer Plan

This section should be developed in collaboration with a Privacy Officer. Please describe the attributes of each system, environment, method, location that are in place to ensure all data collected remains protected and confidential for the duration of the project and whatever timeframe the data will be retained for future use. This plan should be approved by Data Governance if data will be shared with external partners.

## Financial Conflicts of Interest Reporting

The OHRA requires a cover letter to accompany all applications. The existence or absence of any conflicts should be clearly stated in the cover letter. Any conflicts that are reported to OHRA will trigger a management process that will involve the OHRA, PI, Conflicted Investigator and General Council. Depending on the details of the conflict, a management plan will be established. The plan may include restricting the role of that investigator to certain activities and disclosure of the conflict in any consent forms.

You may utilize this section of the protocol to document conflicts and associated management plans.

Investigators (persons responsible for the design, conduct, or reporting of this research protocol) must disclose any of the following financial interests / relationships with any entity that sponsors, provides support, or otherwise has a financial interest in the conduct or outcome of this research protocol (Outside Organization):

• Payments received for the past 12 months from a publicly traded Outside Organization for personal services(e.g., consulting, lecturing / speaking, service on the Scientific Advisory Board) plus the value of any current equity that when aggregated exceeds $5,000

• Payments received for the past 12 months from a non-publicly traded Outside Organization for personal services that in total exceed $5,000, or having any equity interest

• Membership on the governing board of any Outside Organization, including service on its board of directors, or having a position of authority or responsibility to act in its best interests, including being an officer, manager, partner, or limited liability company member with management responsibility

Investigators must also disclose any financial interest in a drug, device—or other product or a competing product (IP rights)—regardless of whether the IP has been patented, licensed, or assigned to UHG, if such IP is being tested, evaluated, or developed in, or if its commercial value could be affected by, this protocol.

Investigators must also disclose financial interests as related to their spouse, parents, siblings, and/or any children of any person responsible for the design, conduct, or reporting of this research.

Investigators are not required to disclose equity in mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles.

# List of abbreviations

# References

# Appendices

Please do not append any informed consent documents into the protocol. Appendices should be limited to things such as:

* Participant communications for your engagement plan
* Surveys and other data collection forms
* Data Use Agreements
* Statements of Work