AI-Driven Transformation in Clinical Research:

From Strategic Vision to Operational Reality at NCI and Beyond

Tanna Nelson
Umit Topaloglu
James Gulley

NIH NATIONAL CANCER INSTITUTE

CBIIT, Clinical and Translational Informatics Branch (CTRIB)

Center for Cancer Research (CCR)

Transforming Clinical Research with AI

1. The AI Imperative in Clinical Research

The Challenge

INCREASING COMPLEXITY

MASSIVE DATA SILOS

CRITICAL HUMAN BOTTLENECKS

The AI Opportunity

ACCELERATE TIMELINES

HARMONIZE UNSTRUCTURED DATA

REDUCE ADMINISTRATIVE BURDEN

Our Core Principle

AUGMENTING CURATORS & RESEARCHERS—PRESERVING EXPERT OVERSIGHT WHILE SCALING CAPABILITIES.

2. Our Team's Strategic Focus

Building a Unified Cancer Intelligence Ecosystem

SEMANTIC
CDE annotation and data mapping

PRECISION MEDICINE
LLM-powered patient matching and reasoning (MATCHBox)

TRIAL AUTOMATION
The ARTI Initiative

3. Starting at the Source: Study Planning

Foundation must be built before analysis or matching

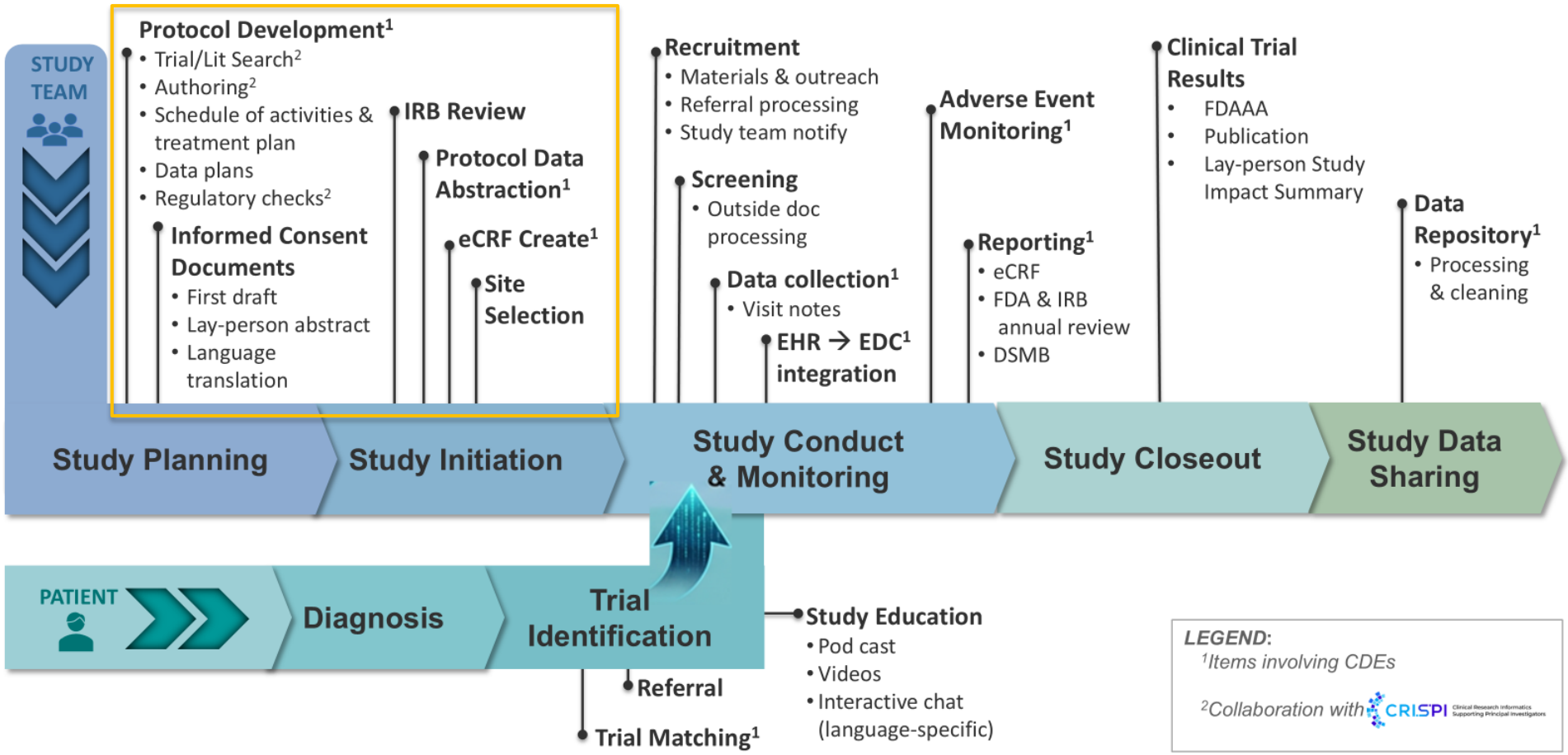
The highest-impact area for early AI intervention

PROTOCOL DEVELOPMENT & INFORMED CONSENT

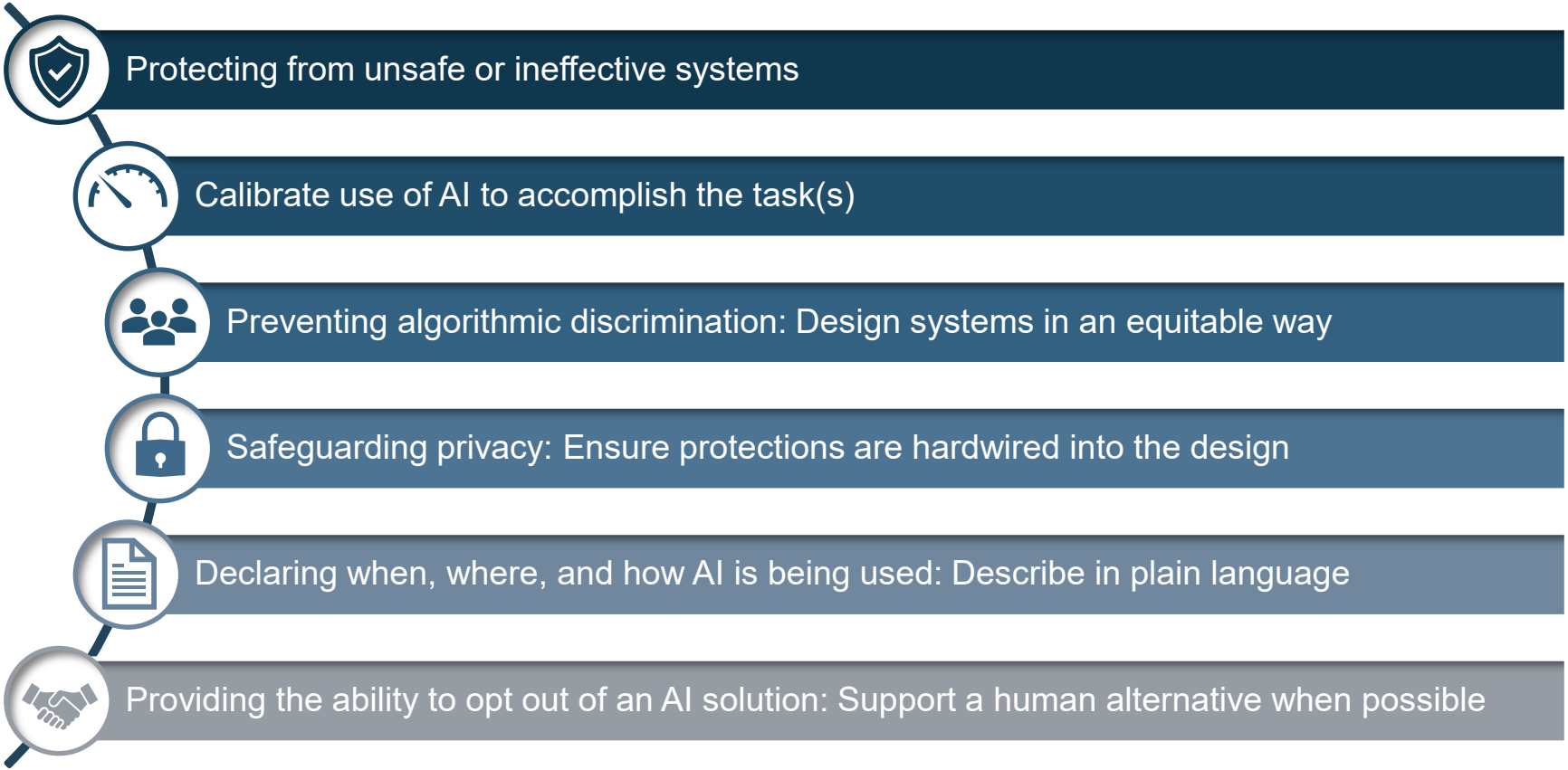
AI For Research and Translational Informatics (ARTI)

End-to-End Clinical Trials Efficiency

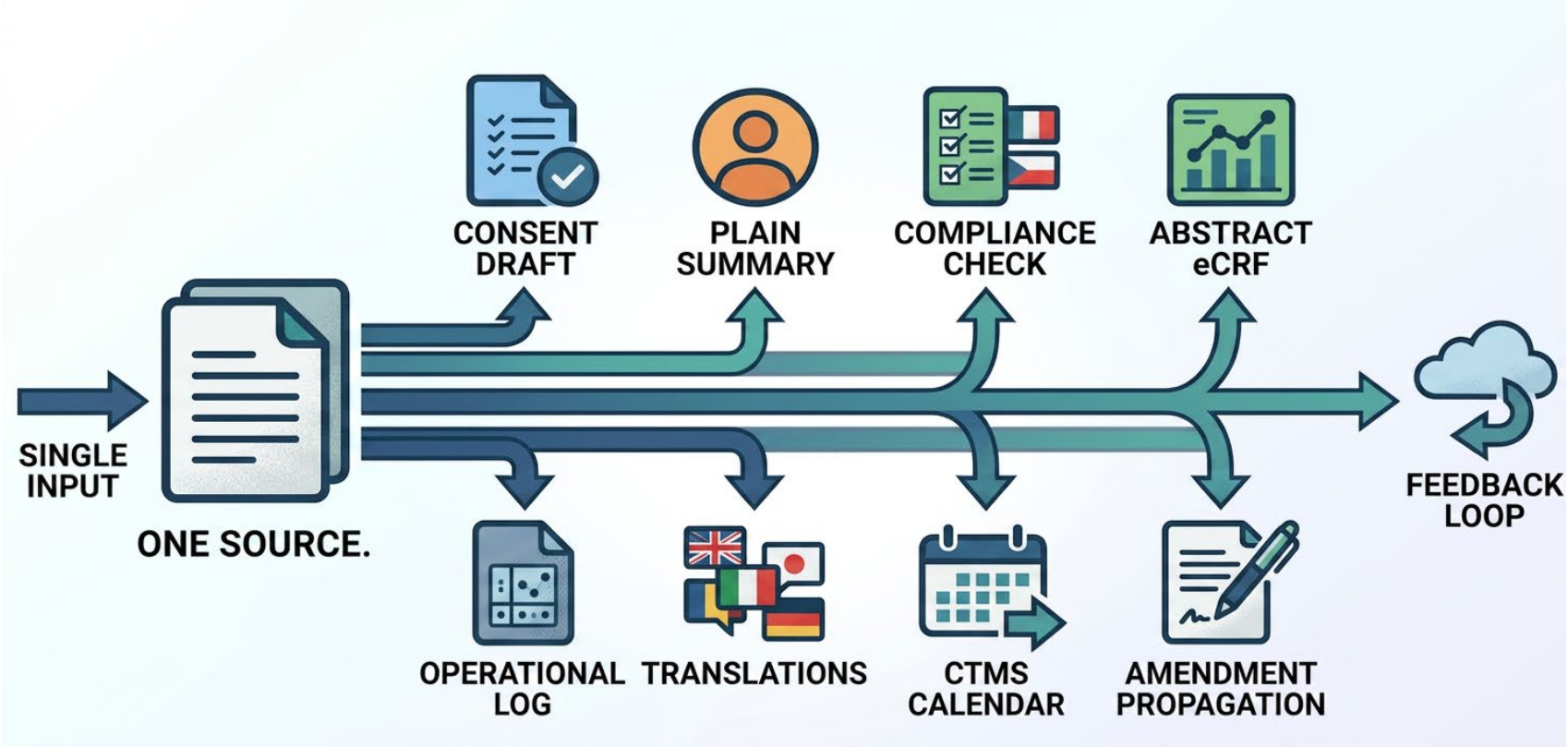
AI Opportunities Within the Clinical Trials Ecosystem



Principles for designing AI automated & semi-automated systems



Artifacts Generated from a Single Source: The Protocol



Consent Crafter

Tanna Nelson
Umit Topaloglu
James Gulley

The Case for Change: AI-Assisted Informed Consent Generation

- Informed consent is the ethical and regulatory foundation of human subjects research

Structural limitations to manual processes:

Complexity	Regulatory Precision	Readability Standards	Template Variability	Consistency
Multiple participant populations per protocol, each requiring a separate, tailored consent document	• Required NIH language must appear verbatim • Deviations from requirements creates compliance risks	Federal guidelines require 6-8th grade reading level - Difficult to achieve consistently	Multiple distinct, version-controlled templates with differing requirements	Manual processes are difficult to scale and inconsistent in quality

Building the Foundation

1 Understand the Requirements

⚖️

FEDERAL

45 CFR 46 — The Common Rule

- Federal floor for human subjects research
- Required disclosures — what, to whom, in what form
- Non-negotiable in every document

🏛️

NIH-SPECIFIC

NIH Requirements & Template

- Required formatting and structure
- Fixed legal language blocks — CoC, Privacy Act, research injury
- Institute-specific elements

📋

TEMPLATE GUIDANCE

Embedded Guidance & Edge Cases

- When optional sections apply
- How to handle conditional content
- What each section accomplishes for the participant

2 Define the Quality Standard

📄

CONTENT STANDARD

OHSRP Exemplar Review

- Reviewed consent forms OHSRP identified as exemplary
- Met regulatory requirements while communicating clearly
- Defined what good content looks like — balanced, specific, honest
- Set the target for what we were trying to replicate

📖

READABILITY STANDARD

Plain Language Research

- Even the best exemplars were written at too high a grade level
- Defined separately: Grade 6, short sentences, active voice
- No existing consent form was consistently meeting this bar
- Required its own research and enforcement strategy

💡 **Key insight:** Exemplars told us *what* to say. Plain language research told us *how* to say it. The prompt had to bridge both.

Building the Pipeline

How we got the AI system to do what we needed it to do

1 FOUNDATION

Map the template into a data contract

- Reverse-engineered the NIH consent form into a typed JSON schema
- 85+ fields — each with descriptions, grammar constraints, and failure-mode rules
- Conditional logic controls which sections appear and what content fills them — driven by study-specific facts from the protocol

2 PROMPTING STRATEGY

Build a prompt that does three distinct jobs

- Establishes writing voice — who the reader is, how to write for them
- Calibrated examples for every study phase and participant type
- Encodes decision rules for hard calls — drug risk table, death disclosure, FDA status
- Requires citation of every non-obvious decision back to protocol text

3 AUDITABILITY

Require the model to show its reasoning

- Every classification decision must be traced to a verbatim protocol quote
- Stored as a structured log alongside the document — for internal quality review
- Grounding decisions in source text reduces AI fabrication

4 OUTPUT QUALITY

Send small focused batches against a stable context

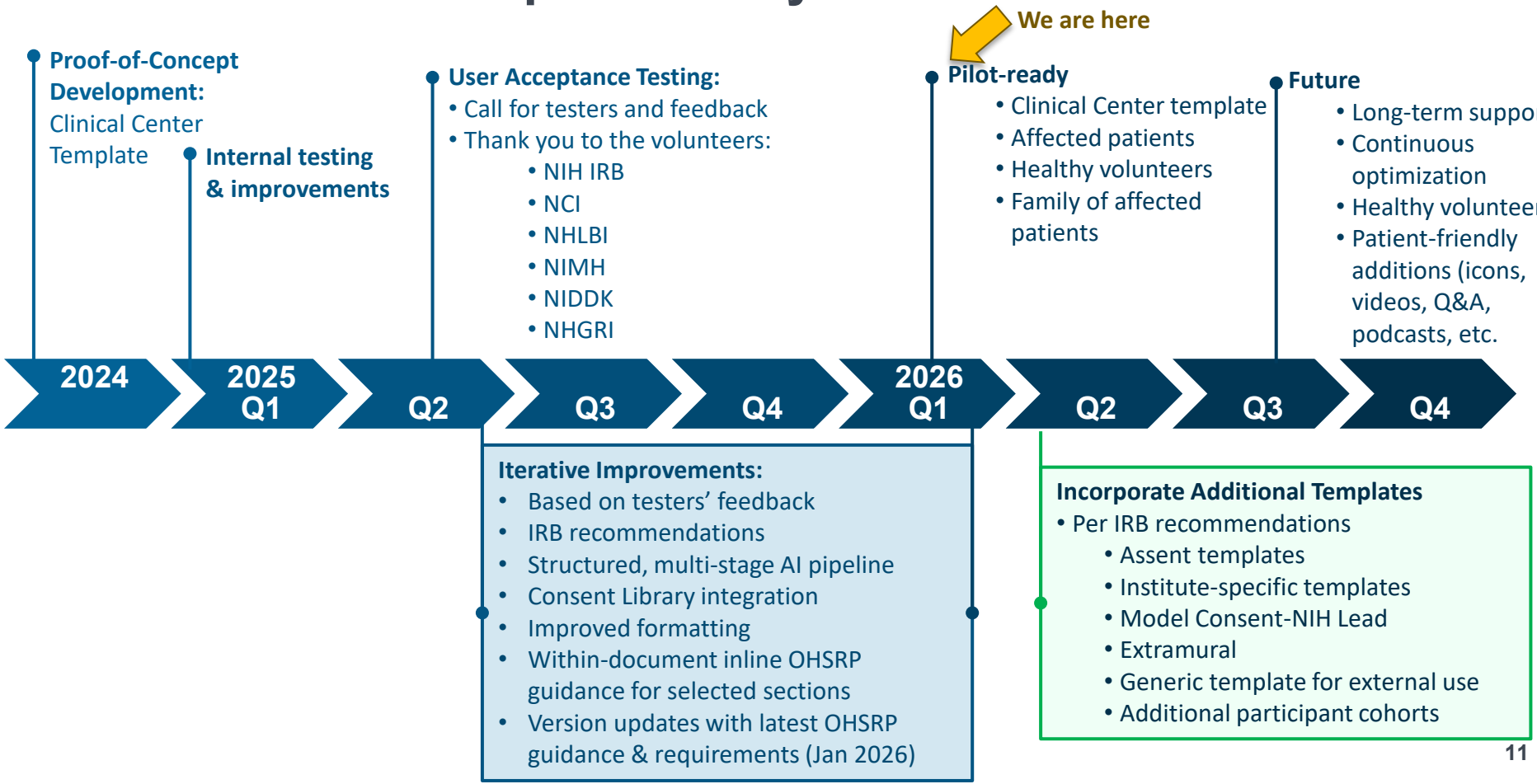
- All background material — protocol, schema, library — assembled once and held stable
- Only the field request changes with each batch
- Keeps the model focused and output consistent across all 85 fields

5 AI VS. SOFTWARE

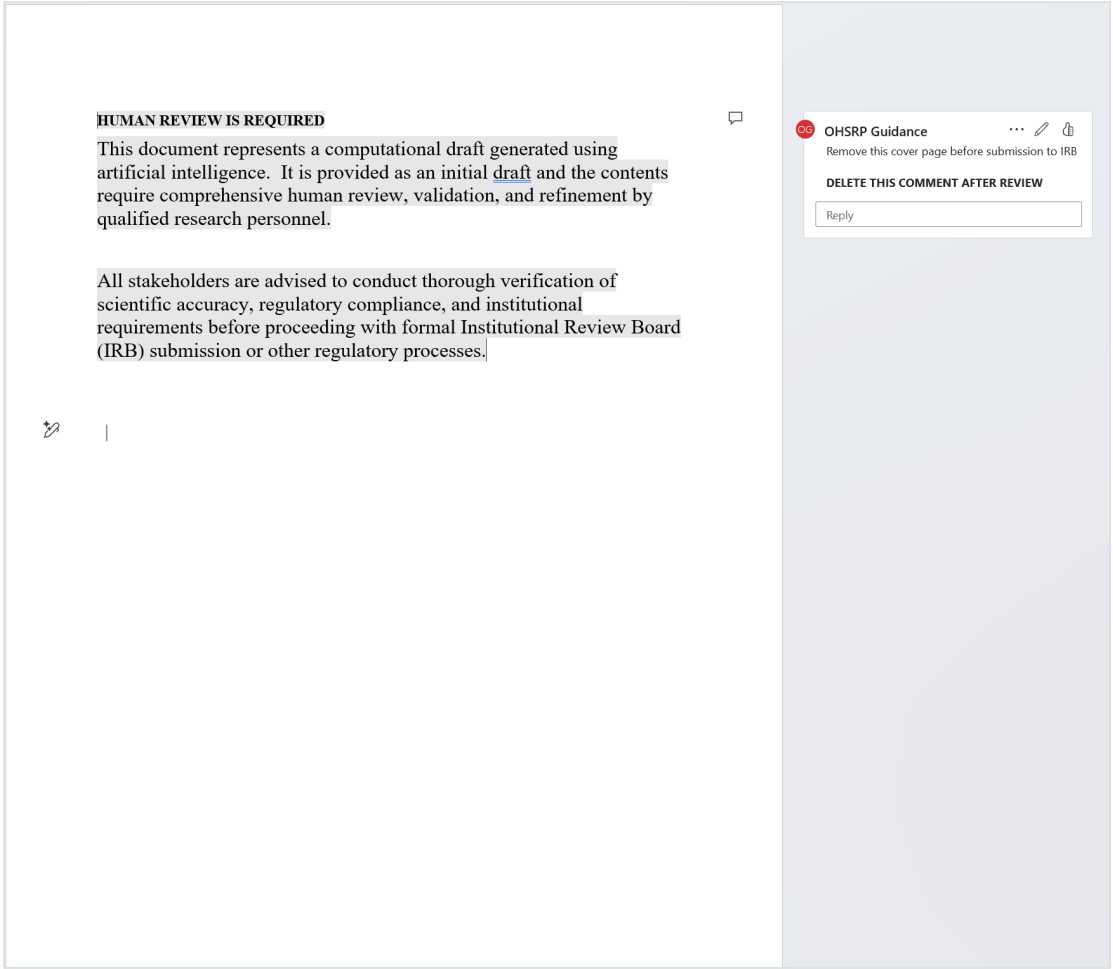
Drew a clear line between AI work and software work

- AI fills field values, cites sources, and shows reasoning
- Software parses, validates, applies defaults, and renders the Word document
- The regulatory structure is guaranteed by code — not AI judgment

From Proof-of-Concept to Pilot System



Consent Form Draft



- Ready for human review & refinement

PRINCIPAL INVESTIGATOR: James Gulley, MD, PhD

STUDY TITLE: A Feasibility Multicenter Phase I Study of Therapeutic Drug Monitoring-Based Atezolizumab Dosing

STUDY SITE: National Cancer Institute, NIH Clinical Center

Cohort: Affected patient

Consent Version: 12/07/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

Name: James Gulley, MD, PhD, Phone: 301-480-8870, Email: gulleyj@mail.nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

You have an advanced or metastatic cancer. Your doctor thinks a drug called atezolizumab may help you. Right now, everyone gets the same amount of this cancer drug. Studies suggest most people get more than they need. We want to find out if smaller, less frequent doses still work, by using your blood tests to time each dose.

This is a an early study to see if this approach is practical and worth trying with more people. What we learn will help us decide the best way to move forward Atezolizumab is approved by the FDA to treat several cancers. The way we are giving it in this study, based on your blood levels, is not yet approved.

You will get atezolizumab through an IV. We will check your blood before each dose to time your next one. We will follow you for up to 2 years.

The drug may shrink your tumor or ease your symptoms. We cannot promise this will happen. Less frequent doses could mean fewer trips to the clinic.

The drug can cause side effects. Some are mild, but others can be serious or even life-threatening. We will watch you closely throughout the study.

You do not have to join this study. You could get atezolizumab the standard way, try other treatments, or focus on care that helps you feel better.

Taking part is your choice. You can leave the study at any time, for any reason.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with

OHSRP Guidance

The Key Information section helps prospective participants decide whether to join the study — it is not a condensed version of the full consent or a checklist of standard consent elements. Content should be organized to support understanding and decision-making for the specific population being recruited, keeping in mind their typical goals, values, and what matters most to them about this type of research.

Useful framing questions: What does this population commonly ask about during consent? What are they most interested in during participation? What concerns do they typically raise? The section should be no more than 3 pages, may use varied formats, and must be visually distinct from the rest of the consent. Content from this section may be repeated in the consent body when it aids understanding, but repetition is not required.

DELETE THIS COMMENT AFTER REVIEW

February 26, 2026, 3:44 PM

Reply

Consent Form Draft

- Ready for human review & refinement
- Headers and footers preserved
- All required information included
- ~3 minutes to generate
- 8th grade reading level
- OHSRP Guidance in comments

Please note: This is a first draft and will require modification

WHAT WILL HAPPEN DURING THE STUDY?

First, we will do tests to make sure this study is right for you. If you qualify, you will get atezolizumab through an IV for up to 2 years. We will check your blood before each dose to decide when you need your next one. After treatment, we will follow up with you.

Time Point	Description
Screening	We will do tests to see if this study is right for you. These will include a medical history review, a physical exam, blood draws, an EKG, a pregnancy test (if you can become pregnant), and a CT scan. Blood draws: You will have blood drawn from a vein. This may require a needle stick in your arm or hand. If you already have an IV in place, we might be able to use that instead. EKG: An electrocardiogram (ECG) is a test that looks at the electrical activity of your heart. You will need to lie still for about 5 minutes. We will place electrodes on your chest, arms, and legs. Electrodes are small stickers attached to wires that go to the machine. The signals are recorded by the machine. If you have a lot of hair on your chest, it may hurt a little bit when we remove the stickers. CT scan: The CT scanner is a donut-shaped machine that uses x-rays to make computer pictures of the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan, and you will be told to hold your breath. We will scan your chest, belly, and pelvis.
First two doses (the standard schedule)	You will come to the clinic and get atezolizumab through a small tube placed in a vein in your arm. This is called an IV. Your first infusion will take about 60 minutes. After that, you will stay for about 1 hour so we can watch you. Your doctor will choose one of the FDA-approved schedules for these first two doses: every 2 weeks, every 3 weeks, or every 4 weeks. Before your second dose, we will draw blood to measure how much drug is still in your body.
Dose 3 and beyond, for the first 16 weeks	Starting with your third dose, the amount of drug will be 840 mg each time. Before each dose, we will draw blood to check the drug level. A computer model will use that level to decide when you need your next

OHSRP Guidance

NOTE: This section requires modification after AI generated first-draft:

Describe, in plain language, what the participant will be asked to do — step by step. Be concise. Do not include entire study calendar.

Clearly distinguish research procedures from standard of care.

Note if randomization is involved, if inpatient stay is required, or if email communication will be used.

List all study procedures, including where they will take place (and if different procedures occur at different locations, say so).

If the research involves biospecimens, state whether whole genome sequencing will or might be performed.

If participants are co-enrolled in another NIH protocol and data or specimens will be shared between studies, include this statement: "If you are co-enrolled in another NIH protocol, data [and/or specify specimen type] collected in either study may be shared with and used for research in either study."

DELETE THIS COMMENT AFTER REVIEW

March 10, 2026, 11:54 AM

Reply

Consent Form Draft

- Ready for human review & refinement
- Headers and footers preserved
- All required information included
- ~3 minutes to generate
- 8th grade reading level
- OHSRP Guidance in comments
- Consent Library integration

Please note: This is a first draft and will require modification

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

The study drug and study procedures may affect how parts of your body work. This includes your liver, kidneys, heart, lungs, thyroid, and other glands. Your study doctor will check your blood regularly to watch for problems.

There is a risk of side effects from the study drug and procedures. Side effects are hard to predict. Doctors cannot tell ahead of time who will have them. Some side effects go away quickly. Others may last a long time. Some side effects may affect your ability to have children. Some side effects may be serious and may even result in death. Some side effects may not show up right away.

If you notice anything different about how you feel, tell your study team right away. The sooner we know, the more we can do to help. Your study doctor may be able to treat side effects. Your doctor may also change your medicines or schedule to reduce side effects.

Possible Side Effects of Atezolizumab

COMMON, SOME MAY BE SERIOUS

These side effects happen in more than 20 out of 100 people (more than 20%)

- Feeling very tired (fatigue)
- Infection

OCCASIONAL, SOME MAY BE SERIOUS

These side effects happen in 4 to 20 out of 100 people (4% to 20%)

- Low red blood cell count (anemia)
- Diarrhea, nausea, vomiting
- Trouble swallowing (dysphagia)
- Fever, flu-like symptoms
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, or swelling of the face or throat
- Reaction during the infusion such as chills, fever, or shortness of breath
- Loss of appetite (anorexia)
- Back pain, joint pain (arthralgia)
- Cough, shortness of breath (dyspnea), stuffy nose
- Liver changes seen in blood tests: higher levels of ALT, AST, alkaline phosphatase, bilirubin, or GGT
- Higher levels of lipase or amylase in the blood
- Low potassium or sodium in the blood
- Itching (pruritus), acne-like rash, red bumpy rash

Consent Form Draft

- Ready for human review & refinement
- Headers and footers preserved
- All required information included
- ~3 minutes to generate
- 8th grade reading level
- OHSRP Guidance in comments
- Consent Library integration
- Study drug risks

Please note: This is a first draft and will require modification

You can also choose to leave the study at any time, for any reason. Whatever happens, your study team will help take care of you and plan your next steps.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved by the study team for use in other studies?

As part of this study, we are obtaining specimens and data from you. We plan to store and use these specimens and data for studies other than the one described in this consent form that are going on right now, as well as studies that may be conducted in the future. The specimens and data will be kept in a way that we will still know that they came from you (i.e., they will be identifiable to us). If we use your identifiable specimens or data for future research, our study will be reviewed and approved by an Institutional Review Board who will make sure that we are protecting your confidentiality. These future studies might help us better understand cancer or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my identifiable specimens and data to be stored and used by the study team for future studies as described above.

_____ Yes _____ No

Initial Initial

Will your specimens or data be shared with other researchers for use in other studies?

We may share your specimens and data with other researchers. The other researchers may be doing studies in similar areas to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or at commercial entities.

One way that we may share your data is by putting it into a large database called a repository, which is a way to make it widely available to the research community. If we do place your data in a repository, it will be labeled with a code, (not with your name or other information that could be used to easily identify you). Even though it will only be labeled with a code, some types of data, in particular data about your genes (called genetic or genomic data), can be used to figure out who you are, although this is difficult to do, and we think it is unlikely to happen.

The data in the repository will be widely available to anyone who wants it.

OHSRP Guidance

If your protocol offers the **prospect of direct benefit** to the participant, e.g., a study with therapeutic intent, you must include the permission statements and yes/no boxes in the sections below.

If your study has **no prospect of direct benefit**, e.g., a repository or a study with only healthy volunteers, the permission statements and yes/no boxes below are optional and may be removed.

If the **primary objective of your study is to collect and retain specimens and/or data for future use** (i.e., a repository study), you should delete the permission statements and yes/no boxes, as applicable.

If you are **only collecting data and not any specimens**, remove all references to specimens in this section.

DELETE THIS COMMENT AFTER REVIEW

February 26, 2026, 3:44 PM

Reply

OHSRP Guidance

If you might use identifiable specimens/data for future research, you must include the language in this subsection.

Reply

OHSRP Guidance

Specimens/Data SHARED Guidance:
For all studies, you **must** include both of the first two paragraphs.

Reply

Consent Form Draft

- Ready for human review & refinement
- Headers and footers preserved
- All required information included
- ~3 minutes to generate
- 8th grade reading level
- OHSRP Guidance in comments
- Consent Library integration
- Study drug risks
- Highlight areas where decisions must be made

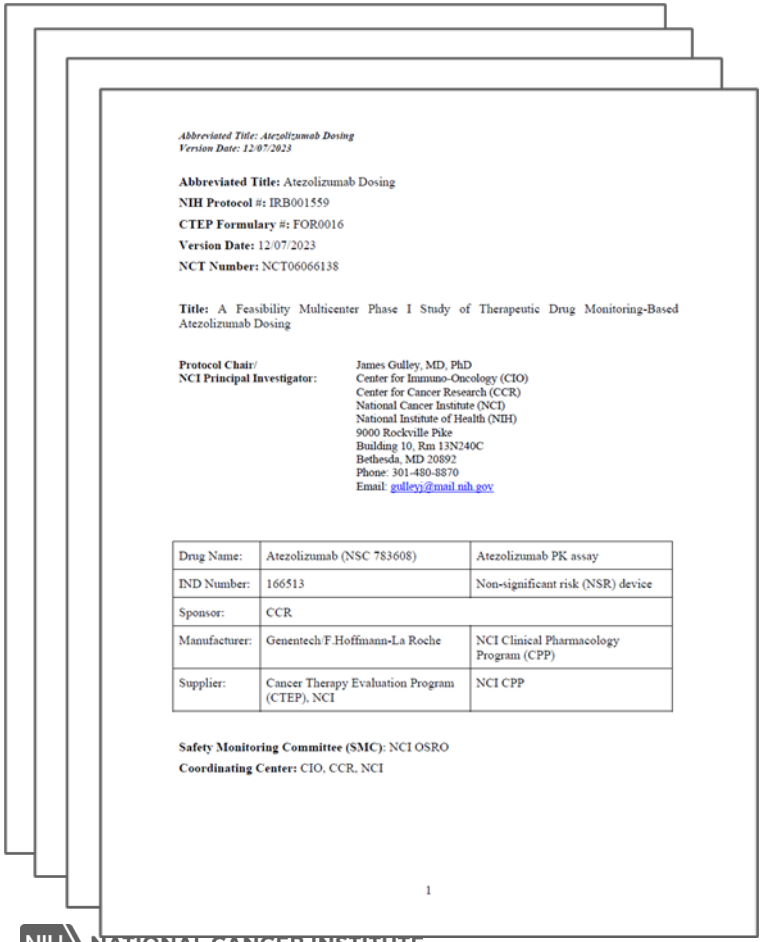
Please note: This is a first draft and will require modification

Lay Person's Research Summary

Brenda Adjei
Tanna Nelson
James Gulley

Lay Abstract: Prototype Development With Humans-in-the-Loop at All Steps

Protocol



Abbreviated Title: Atezolizumab Dosing
Version Date: 12/07/2023

Abbreviated Title: Atezolizumab Dosing

NIH Protocol #: IRB001559

CTEP Formulary #: FOR0016

Version Date: 12/07/2023

NCT Number: NCT06066138

Title: A Feasibility Multicenter Phase I Study of Therapeutic Drug Monitoring-Based Atezolizumab Dosing

Protocol Chair/ NCI Principal Investigator:
James Gulley, MD, PhD
Center for Immuno-Oncology (CIO)
Center for Cancer Research (CCR)
National Cancer Institute (NCI)
National Institute of Health (NIH)
9000 Rockville Pike
Building 10, Rm 13N240C
Bethesda, MD 20892
Phone: 301-480-8870
Email: gulleyj@mail.nih.gov

Drug Name:	Atezolizumab (NSC 783608)	Atezolizumab PK assay
IND Number:	166513	Non-significant risk (NSR) device
Sponsor:	CCR	
Manufacturer:	Genentech/F.Hoffmann-La Roche	NCI Clinical Pharmacology Program (CPP)
Supplier:	Cancer Therapy Evaluation Program (CTEP), NCI	NCI CPP

Safety Monitoring Committee (SMC): NCI OSRO

Coordinating Center: CIO, CCR, NCI

1

One page 4th grade reading level

Ready for human review & refinement

Lay-Person Summary

Project Title: Testing a Better Way to Give Cancer Drug Atezolizumab (NCT06066138)
Principal Investigators: Dr. James Gulley
Institute/Center: National Cancer Institute

What is the goal of this study?

This study tests if we can give a cancer drug in a new way. We want to see if we can use less drug but still fight cancer well.

Who can be in this study?

People who:
- are 18 years old or older
- have cancer that has spread
- can do daily tasks with little help
- have good enough organ function

What will happen during this study?

You will:
- get the cancer drug through a vein
- have blood drawn before each dose
- have scans every 12 weeks
- may have an optional tumor biopsy

How long will I be in this study?

- You will get treatment for up to 2 years
- You will come to the clinic every 2 to 6 weeks for your drug, then every 3 months after 16 weeks

What are some risks of this study?

You might:
- feel tired or weak
- get infections
- have nausea, vomiting, or diarrhea
- have pain or bruising from blood draws
- be exposed to radiation from scans

What are the benefits of this study?

For you: The drug may shrink your tumor or help with your cancer symptoms.

For others: This study may help us find better ways to give this drug to other people with cancer.

Do I have to be in this study?

- **Your taking part in the study is voluntary**
- **Withdrawal:** You can stop taking part at any time if you change your mind.
- **Alternatives:** You could get the standard cancer treatment your doctor suggests instead of joining this study.

Will I be paid or have costs in this study?

You will not be paid for this study, and costs depend on your local study site.

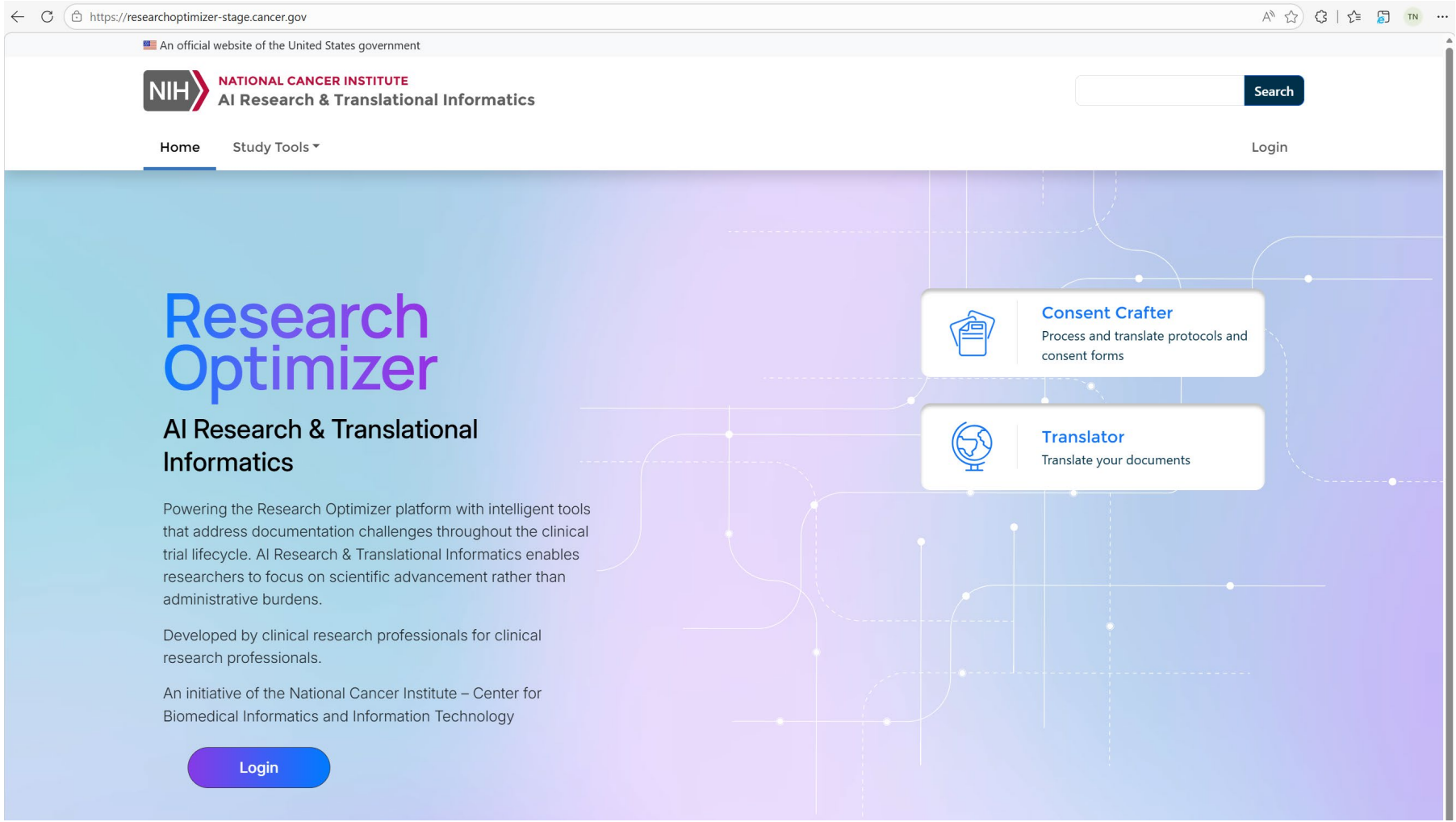
Please review more details on the next pages.

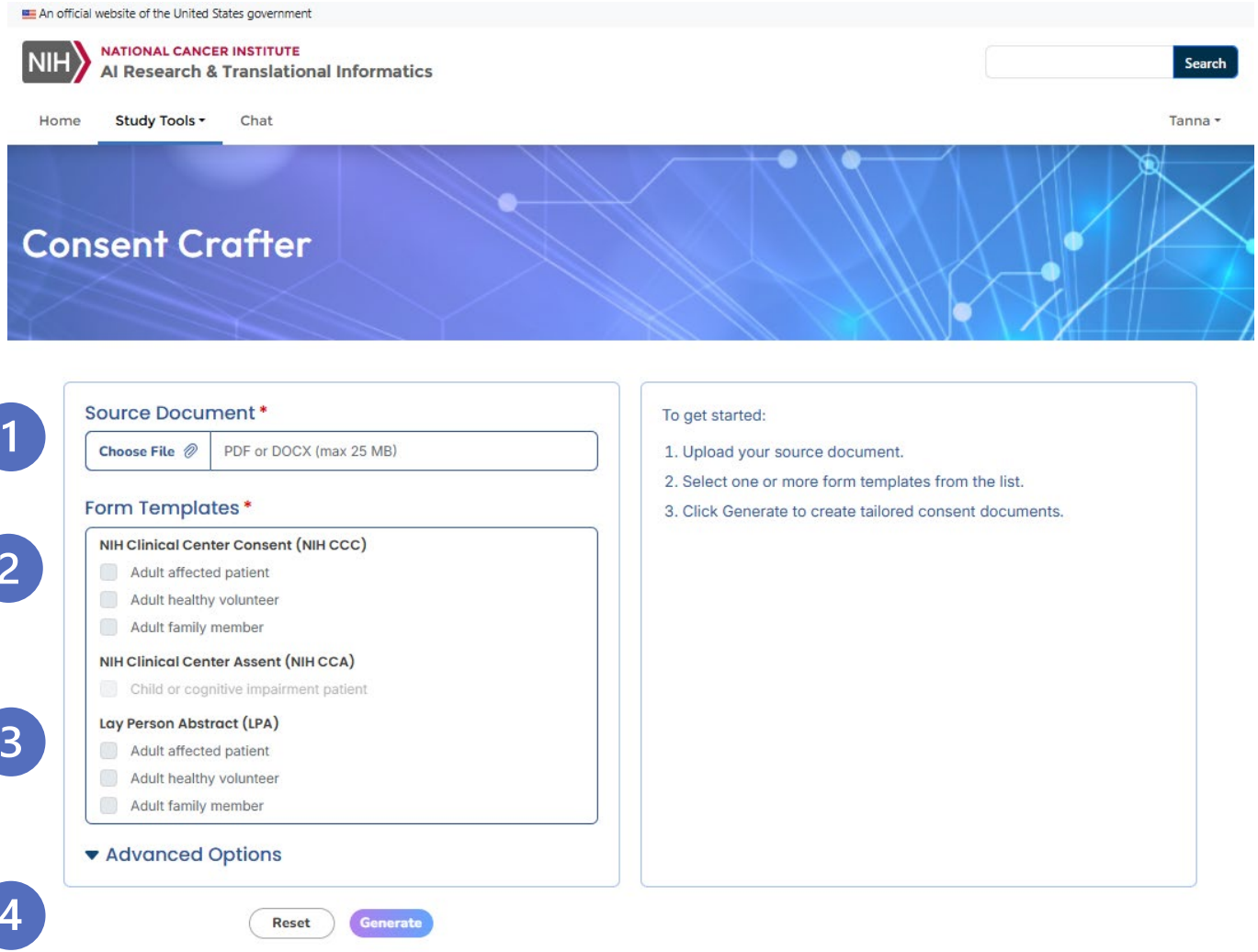
If you have questions or want to join the study, contact Dr. James Gulley:
Email: gulleyj@mail.nih.gov | **Phone:** 301-480-8870

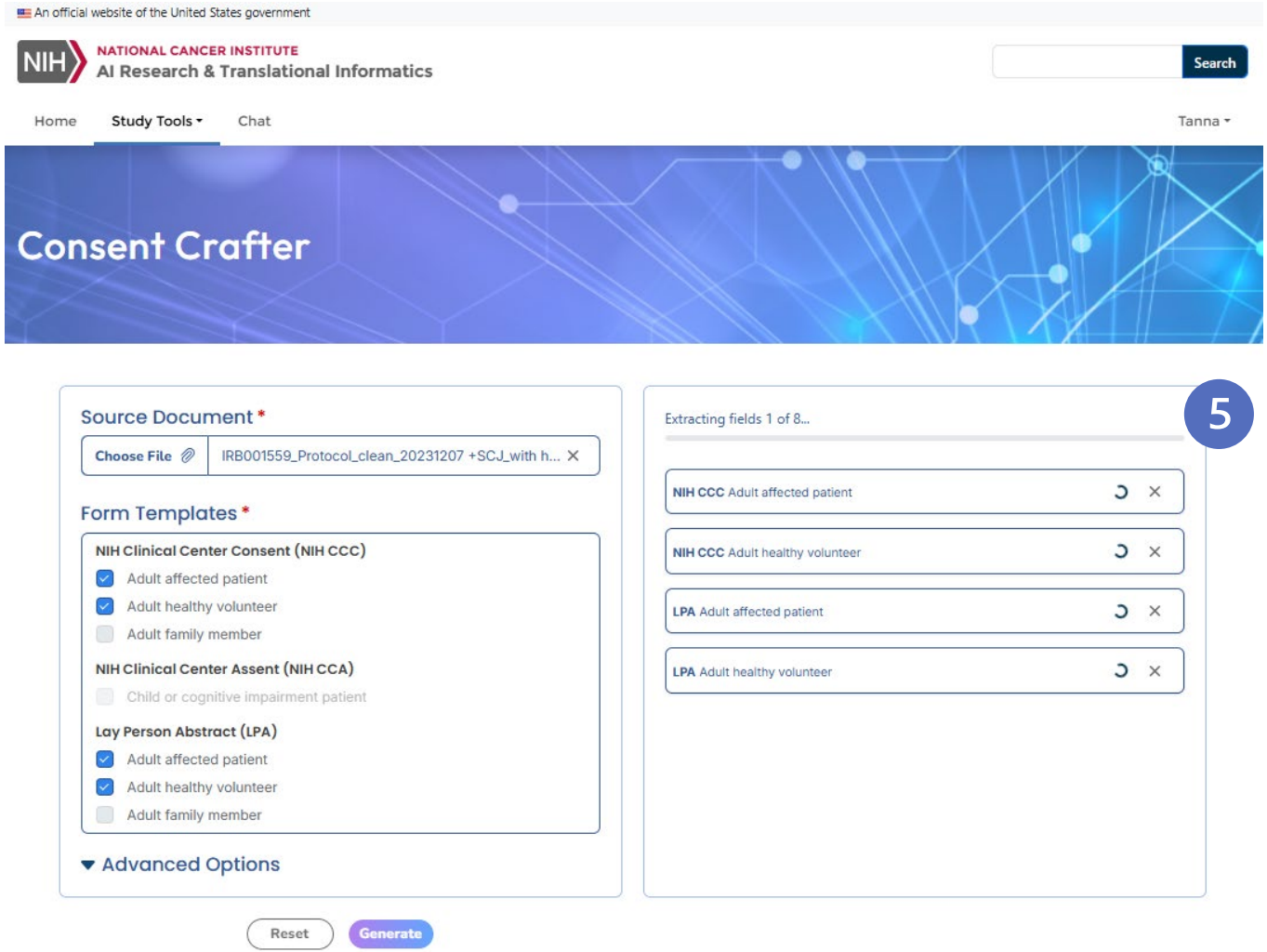
https://politilab.wustl.edu/research/project-score/study-aims/

Accessing the Tools

Research Optimizer

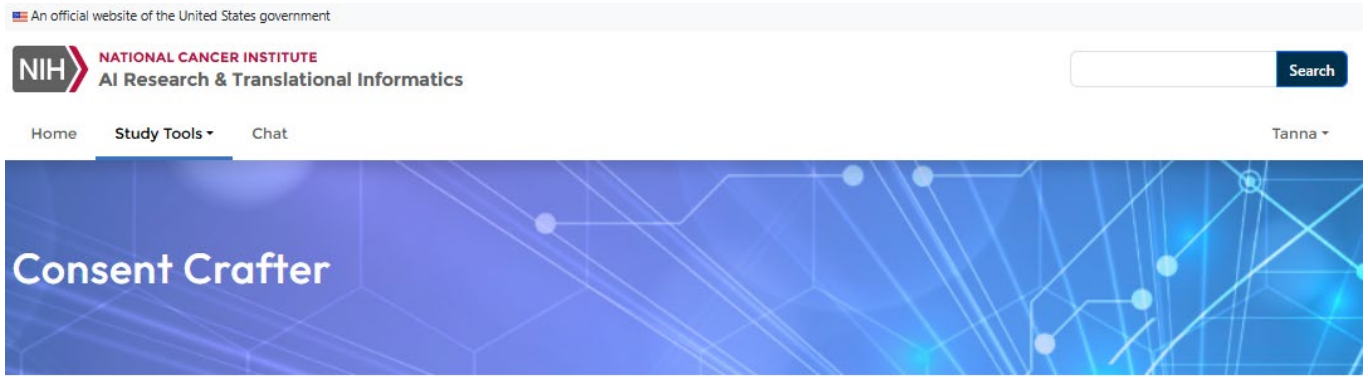

https://researchoptimizer-stage.cancer.gov
An official website of the United States government
NIH
NATIONAL CANCER INSTITUTE
AI Research & Translational Informatics
Search
Home
Study Tools
Login
Research Optimizer
AI Research & Translational Informatics
Powering the Research Optimizer platform with intelligent tools that address documentation challenges throughout the clinical trial lifecycle. AI Research & Translational Informatics enables researchers to focus on scientific advancement rather than administrative burdens.
Developed by clinical research professionals for clinical research professionals.
An initiative of the National Cancer Institute – Center for Biomedical Informatics and Information Technology
Login
Consent Crafter
Process and translate protocols and consent forms
Translator
Translate your documents

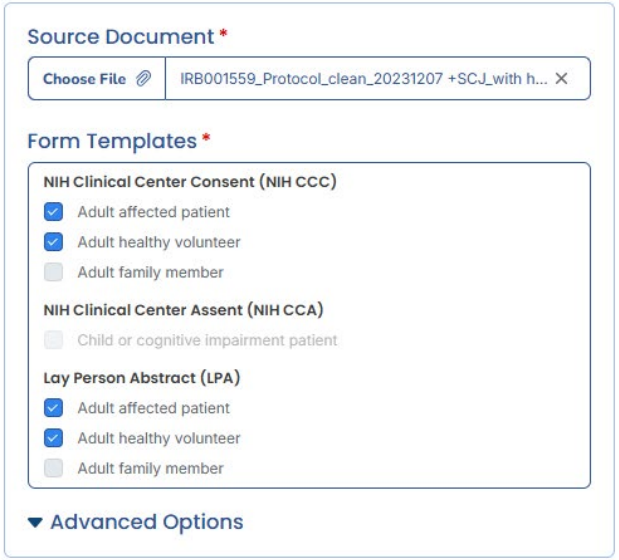

An official website of the United States government
NIH
NATIONAL CANCER INSTITUTE
AI Research & Translational Informatics
Search
Home
Study Tools
Chat
Tanna
Consent Crafter
Attach Protocol
1
Source Document *
Choose File
PDF or DOCX (max 25 MB)
Select study group
2
Form Templates *
NIH Clinical Center Consent (NIH CCC)
Adult affected patient
Adult healthy volunteer
Adult family member
NIH Clinical Center Assent (NIH CCA)
Child or cognitive impairment patient
Choose Lay-Person Summary
3
Lay Person Abstract (LPA)
Adult affected patient
Adult healthy volunteer
Adult family member
Advanced Options
Click Generate
4
Reset
Generate
To get started:
1. Upload your source document.
2. Select one or more form templates from the list.
3. Click Generate to create tailored consent documents.

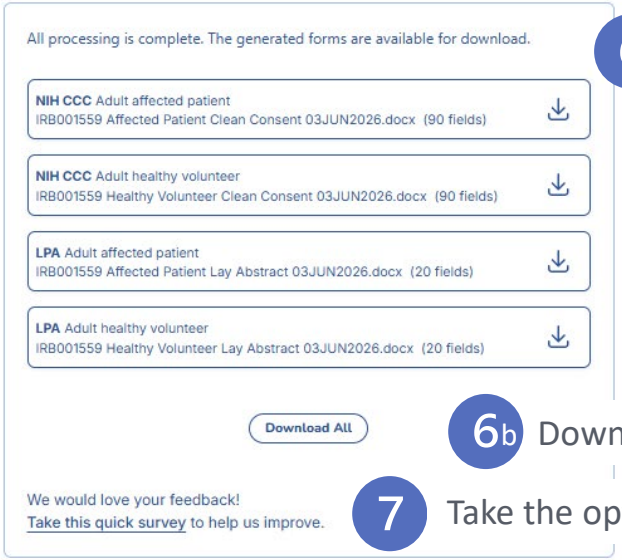


5

Monitor progress
(can take ~3 minutes







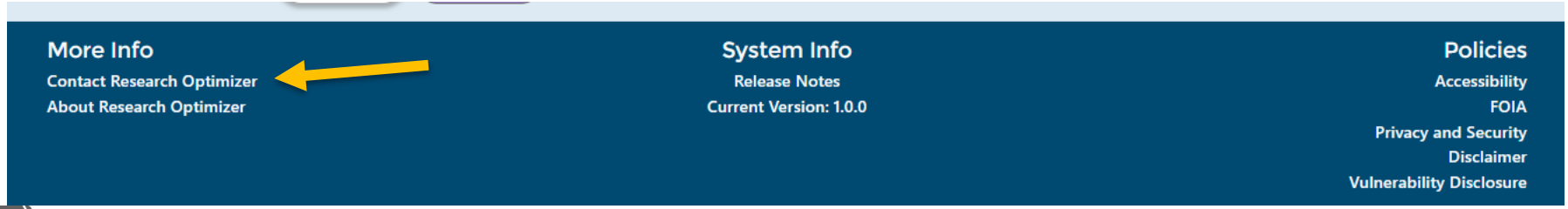
6a Download individual documents

6b Download all as a zip file

7 Take the optional survey

How to Access Research Optimizer Platform

- https://researchoptimizer-stage.cancer.gov/tools/consent-crafter
- If working remotely or teleworking, must be on VPN
- Authentication Required
- Agree to Terms of Use
- Issues, Feedback, Questions: ctribresearchoptimizer@mail.nih.gov



Known Issues and Future Development

Issues

- Exceeded usage limits – Resolved
- Finish tasks even when usage limit reached – Resolution soon

Piloting Across NIH

- Consent Generation
- Lay-Person Research Summary
- Spanish Language Translation

Active Development

- Pre-IRB Protocol Advisor – 26Q4
- Protocol data abstraction – 27Q2
- Digital Protocol Composer – 27Q3

Acknowledgements

Center for Cancer Research (CCR)

- Brenda Adjei
- Stacie Jeter
- Aubrey Wachter
- Tammy Cole

NIH Institutional Review Board

- Jonathan Green
- Nicole Grant
- Tiffany Gommel

Center for Biomedical Informatics and Information Technology (CBIIT)

- Ye Wu
- Kai-Ling Chen
- Byong Park
- Alejandro Vega
- Linmin Pei
- Angela Carson
- Lucia Alzaga
- Julie Hom
- Alex Gordon
- Li Wang
- Hannah Stogsdill
- Sarma Seetamraju
- Hong Cheung
- Pavan Malhotra
- Lichao Duan
- Trancy Truong
- Manpreet Singh
- Adil Asheer
- Krish Seshadri
- Srujan Boppana

Clinical Research Informatics Supporting Principal Investigators (CRISPI)

- Yang Fann
- Nic Dobbins
- Nick Webber
- Steevenson Davidson
- Andrew Schroeder
- Alexandra Hershey
- Daphne Techathuvanan
- Geoffrey Marsh

Thank you!

Contact Information:

Tanna.Nelson@nih.gov

Umit.Topaloglu@nih.gov

Questions?