ProtoType: A New Tool for Authoring and Managing Clinical Protocols Developed at the CC

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Agenda – Topics to Discuss

- Why ProtoType?
- What is ProtoType?
- Overview of ProtoType’s Features
- Value Added for the Researcher
- Where We’re Going - Future Development
Why *ProtoType*?

History…

- ProtoType was homespun by NIH investigators who envisioned a system that would handle all aspects of the protocol life cycle.
- ProtoType was originally outsourced for development to Stellar Systems.
- After two years of outsourcing, ProtoType was transitioned to in-house development.
Why ProtoType?

ProtoType was created for several reasons...

- Writing a clinical protocol is hard work.
- Currently, there is little standardization between protocols.
- NIH policies and regulations can change requiring updates to several forms in the protocol.
- Paper protocols are large, and costly to print out many times.
- Training tool – Learning how to write a protocol is awkward and difficult.
What is ProtoType?

ProtoType is an assisted protocol authoring tool that…
✓ Maximizes use of IT.
✓ Employs a paperless system.
✓ Standardizes protocol authoring while offering flexibility.
✓ Provides a standardized template for investigators.
✓ Improves resource allocation.
✓ Enhances integration of protocol with care.
✓ Facilitates the process for all.
  • Increases speed of protocol writing and review.
  • Consolidates other protocol-management programs.
What is ProtoType?

- Training Tool
- Protocol Review (CDs, SDs, IRBs, etc.)
- Centralized, Interactive Editing
- Standard Language Repository
- IND Wizard
- Reference and Image Manager
- Facilitate New Policies and Regulations
- Informed Consent

ProtoType
Features of *ProtoType*

- Fully customized documents tailored toward individual IRBs.
- Investigators focus on authoring - ProtoType takes care of the rest.
- Full version history of the entire protocol for both internal and external review.
- Support for full collaboration among investigators in every aspect of protocol authoring.
Ease of Use

✓ Single Sign-on (NIH standard login).
✓ Full Microsoft Word Compatibility.
✓ Portable images (cut & paste from anywhere).
✓ Protocol image library for use throughout the protocol.
✓ Robust Reference Management.
  ✓ Supports import from Quosa Reference Manager, and PubMed.
Creating a Protocol

The “Research Type” and “IRB” fields determine the format, or layout, of the Protocol.

When the “Save” button is clicked the protocol will be formatted specifically for NEI’s Clinical Trial format.
### Protocol Layout

**Protocol Type**

### 1.1 General Protocol Info

#### 1.1.1 Protocol Overview

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Combination Antibody Therapy with APOLIZUMAB [1D10] and RITUXIMAB [CD20] in Relapsed Lymphoma and CLL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbreviated Title:</td>
<td>Apolizumab and Rituximab</td>
</tr>
<tr>
<td>IRB:</td>
<td>NEI</td>
</tr>
<tr>
<td>Research Type:</td>
<td>Clinical Trial - Phase 1</td>
</tr>
<tr>
<td>Is this a multi-site collaboration:</td>
<td>No</td>
</tr>
<tr>
<td>Ionizing Radiation Use:</td>
<td>None</td>
</tr>
<tr>
<td>Investigational New Drug/Device:</td>
<td>To Be Determined</td>
</tr>
</tbody>
</table>

**Does the protocol involve a Tech Transfer Agreement:**
- **No**

#### 1.1.2 Time Frame

| Start Date: |  |
| End Date: |  |

Containers can be further broken down into Components. These are the basic sections of a protocol and typically deal with a single idea.
Using Standard Language

Pre-Loaded Standard Language

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.
Welcome to ProtoType
 Principal Investigator

My Protocols
  Associate Investigator
  — Principal Investigator
  Protocol Specialist
  CC Protocols
  All Protocols

Number  Abbreviated Title  Principal Investigator  State  Ver.
203     Caffeine Intake     Lightfoot, Philip N.    Draft - Initial  1

203     Caffeine Intake     Lightfoot, Philip N.    Draft - Initial  1
06-EI-0046  anti-CD11a and uveitis  Nussenblatt, Robert B., M.D.  Amendment B  34

ProtoType V3.1
©2007 Office of Protocol Services, Clinical Center, NIH.
[ Contact Webmaster ] [ Accessibility ] [ System Requirements ]
Edit Features
Opening the Editor

Click the Edit button to edit information within the component.

3. Precis - Abstract

Reinforcing properties of alcohol are in part mediated through endogenous opioids. Mesolimbic dopamine (DA) release is a key signal for drug reward, and endogenous opioids are thought to exert their effects by modulating the activity of this system. A functional mu-opioid receptor (OPRM1) A118G single nucleotide polymorphism (SNP) alters the affinity of the mu-opioid receptor for its endogenous ligand, is in some studies associated with increased risk for alcohol and heroin addiction, and confers differential pain sensitivity and subjective responses to alcohol. This prompts the question whether the differential subjective response to alcohol observed as a function of the OPRM1 A118G genotype reflects differential activation of the mesolimbic DA release.
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Transmembrane Glycoprotein (gp120)

Transmembrane Glycoprotein (gp41)

Viral Membrane (lipid layer)
3. Precis - Abstract

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Help Features
Opening Help Language

Time Frame: Start & End Dates

Enter the proposed Start Date. The proposed Start Date of the protocol, an estimate, is the date on which the entering of participants could begin. and the End Date. The End Date of a protocol—an estimated date—is the anticipated point at which no human subjects will be further involved. -- these will be estimates.

The Start Date is the date that entering participants could begin. The End Date is the point at which no human subjects would be further involved.

Note: ProtoType will not allow you to save with a start date that occurs after an end date.

A note about Duration:
The term "duration" may mean different things in different contexts. Protocols with end points such as the appearance of renal failure or myocardial infarction would be of indefinite duration, unless a date is specified for ending all follow-up. Duration also has been defined as the time during which new subjects are entered into the protocol.

At NIH, the duration of a protocol is the length of time required to enroll subjects and to complete the protocol to the point at which subjects are no longer involved. A protocol is considered active until the PI notifies the IRB An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. [ICH E6] of his or her intent to terminate the study. (Note that protocols often exceed their expected duration because suitable subjects are not accrued as rapidly as initially anticipated.)
ProtoType supports three different methods for reviewing the protocol and providing feedback…

✓ Integrated track changes in the editor.

✓ The ability to compare protocols at different dates or different actions (i.e., comparing ‘07 CR against an ’08 CR).

✓ Fully featured feedback and comment system from co-authors, reviewers, etc.
There has been much interest in the possible role of the immune system in age-related macular degeneration. Experimental models and patient material have, to date, suggested a role for macrophages and complement. We hypothesize that the underlying mechanism of choroidal neovascularization (CNV) is similar to those at play in atherosclerosis. If this is the case, then immunomodulatory agents directed against specific parts of the immune system.

Blue text has been edited by John Doe, M.D.
# Version History Comparison
Comparing protocols across time.

## 3. Precis - Abstract

### 3.1 Background

There has been much interest in the possible role of the immune system in age related macular degeneration. Experimental models and patient material have, to date, suggested a role for macrophages and complement. We hypothesize that the underlying mechanism that leads to choroidal neovascularization (CNV) is similar to those at play in atherosclerosis. If this is the case, then CNV treatment should be amenable to new immunomodulatory agents directed against specific parts of the immune system. However, there is little experience with CNV treatment in regards to new immunomodulatory agents.

Old Text Crossed Out And In Red.

New Text Colored Yellow.
Protocol Feedback
Comment Creation

Protocol: Apolizumab and Rituximab
Container: Methods

Protocol Component

This pilot study has permitted enrollment of up to 12 adults with non-infectious intermediate or posterior uveitis who require treatments to maintain visual function. This extended protocol began with an evaluation of the safety and potential efficacy of intravenous (IV) daclizumab treatments for uveitis while reducing or eliminating standard medications commensurate with the standard of care. As subcutaneous (SC) daclizumab treatments become available, eligible participants will be offered continuing daclizumab treatments using the new SC formulation, though they may elect to remain on the IV treatments. If the therapeutic benefit is sustained using

Protocol Component Comment

Should consider expanding the study to include 24 adults. This will help ensure sufficient participants remain at the end of the study.
Value Added for the Researcher

✓ Recommended Language Cassettes for protocol body and consent forms.
✓ Online archive of all PI’s protocols.
✓ Amendments immediately incorporated into protocol.
✓ Protocol moves electronically to IC, IRB, CC, etc.
✓ IRB can recommend language changes.
✓ Tracks states of the protocol, i.e. Amendment, Continuing Review, and Termination.
✓ Template updated based on NIH policies/regulatory changes, i.e. COI.
✓ Continuing review report - Summary of amendments and protocol changes.
Coming Soon

- Integration with IC Systems.
- Improved collaborating site interface to assist 1195 prep.
- Adverse Event Reporting.
- Assisted Compliance with Public Law 110-85.
- NIDDK, NHGRI, and other templates
- ... and many more.
Where We’re Going

ProtoType

Assisted Protocol Writing System
Scientific and Regulatory Document
Basic Clinical Care Plan

Protocol Mapping System
Cost/Resource Projections
Protocol Monitoring

NLM
ClinicalTrials.gov
PL 110-85

Adverse Events Reporting System
CRIS-AE

Regulatory Agencies
(FDA, OBA, etc.)

Conflict-of-Interest
Report of Investigators
(to ICD)

ProtoType
Protocol
Review
(SDs, IRBs, etc.)

Standard Language Repository

Centralized, Interactive Editing

Training Tool

Facilitate New Policies and Regulations

IND Wizard

Reference and Image Manager

Informed Consent

Facilitate New Policies and Regulations

Centralized, Interactive Editing

IND Wizard

Regulatory Agencies
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✓ Elaine Ayres (OD)
✓ Dr. Ekaterina Tsilou (NEI)
✓ Dr. Juan Lertora (CC)
✓ Dr. James Cimino (OD)

And many more….!
We encourage you to use ProtoType

To visit ProtoType go to…
http://prototype.cc.nih.gov

The link is also available from the OPS website…
http://intranet.cc.nih.gov/ops/links.html
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