



*A Web Based Protocol Writing System*

# An Overview

By: Jon McKeeby

National Institutes of Health, Clinical Center  
Department of Clinical Research Informatics  
and Protocol Management Services  
Bethesda, Maryland  
February, 2008

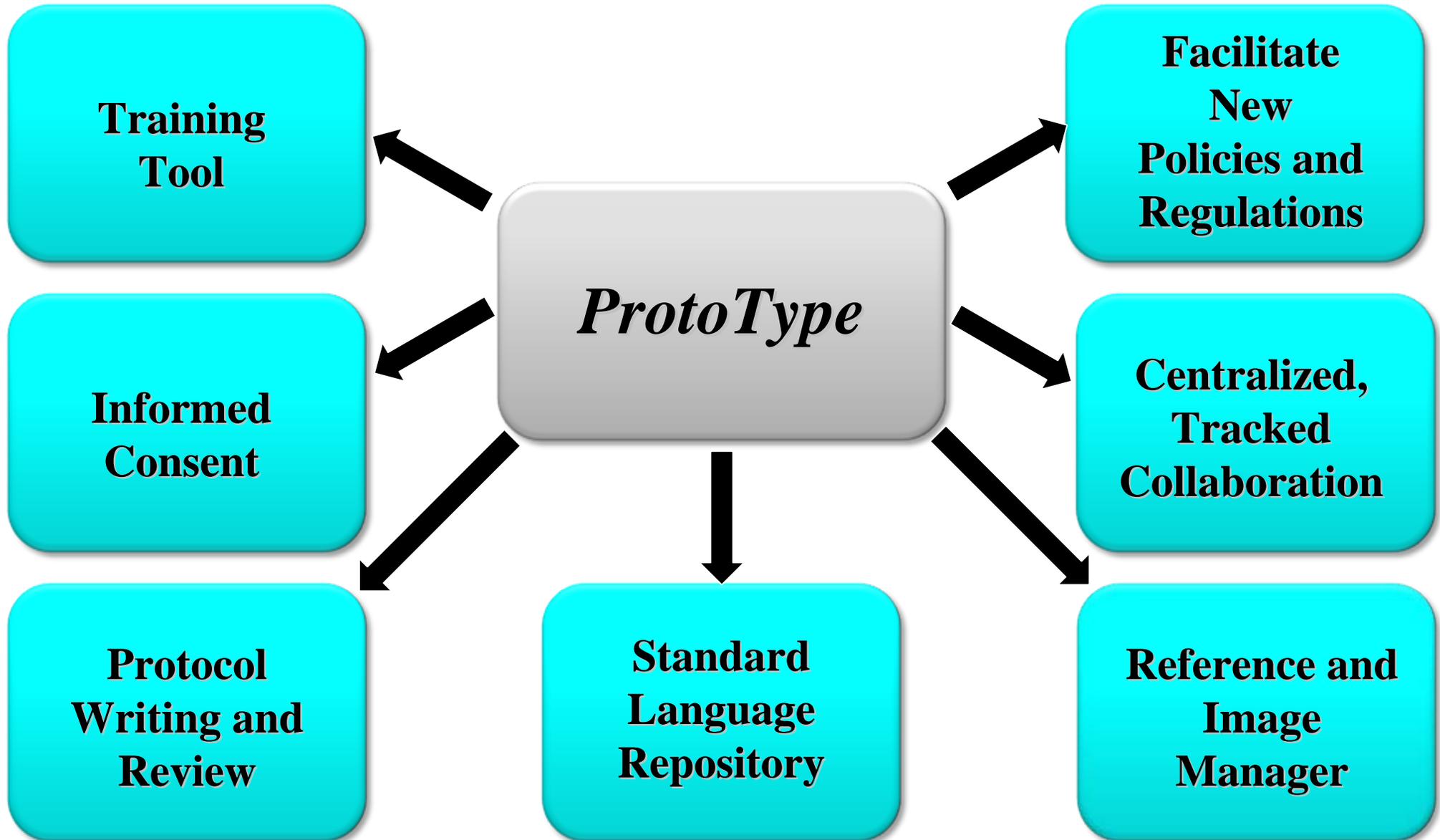


# What is *ProtoType*?

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*?



# 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.

# Features of *ProtoType*

- ✓ Fully customized documents tailored toward individual IRBs.
- ✓ Investigators only need to 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.

# Customization and Flexibility

- ✓ Format is NIH IRB-specific
- ✓ Only relevant fields appear
  - e.g., Natural history study vs. Clinical Trial study
- ✓ Recommended language can be designated from the NIH as well as ICs for all parts of the protocol.

# Creating a Protocol

Proto Type

Philip N. Lightfoot | [Settings](#) | [Logout](#)

Home

SysAdmin

Cassettes

References

## Create New Protocol

Protocol Title  
(Limit: 250 characters)

Combination Antibody Therapy with APOLIZUMAB [1D10] and RITUXIMAB [CD20] in Relapsed Lymphoma and CLL

Abbreviated Title:  
(Limit: 30 characters)

Apolizumab and Rituximab

Research Type:

Clinical Trial - Phase 1

IRB:

NEI

Accrual Institute:

NEI

Save

Cancel

# Protocol Layout

Proto Type

John Doe, M.D. | [Settings](#) | [Logout](#)

Home

**Protocol**

Consents

Toolbox

<b>Number:</b>	200	<b>PI:</b>	John Doe, M.D.
<b>Protocol:</b>	Combination Antibody Therapy with APOLIZUMAB [1D10] and RITUXIMAB [CD20] in Relapsed Lymphoma and CLL		
<b>Version:</b>	2 (Draft - Initial: 02/06/2008) ▾	<b>Access:</b>	Read/Write
		<b>Compare:</b>	<input type="checkbox"/>

## 1. 1195 Information

**Protocol Containers are the second level of organization.**

**Protocol Pages are the top level parts of the protocol.**

- 1. Introduction
- 2. Background
- 3. Objectives
- 4. Study Design
- 5. Study Design Page 1
- 6. Study Design Page 2
- 7. Subject Enrollment
- 8. Subject Enrollment
- 9. Study Analysis
- 10. Adverse Event Reporting
- 11. Data and Safety Monitoring Plan
- 12. Human Subject Protection
- 13. Pharmaceutical, Biologic, and Device Info
- 14. References and Appendices
- 15. Consent Forms

1.1.1 Study Overview

Combination Antibody Therapy with APOLIZUMAB [1D10] and RITUXIMAB [CD20] in Relapsed Lymphoma and CLL

Apolizumab and Rituximab

NEI

Clinical Trial - Phase 1

No

None

To Be Determined

No

### 1.1.2 Time Frame

Start Date:  
End Date:

# Using Standard Language

## Pre-Loaded Standard Language

Apoluzimab

**Standard language pre-loads when the consent is created.**

### Introduction

Comment

Help

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.

# Ease of Use

- ✓ Single Sign-on
- ✓ Standard language cassettes can be used for all sections of the protocol body and consent form.
- ✓ Protocol image library for use throughout the protocol and other purposes, i.e., giving talks.
- ✓ Robust Reference Management
  - ✓ Supports import from Quosa Reference Manager, and PubMed.
- ✓ Full Word Compatibility

# Welcome to *ProtoType*

## My Protocols Investigator

ProtoType

Philip N. Lightfoot | [Settings](#) | [Logout](#)

Home

SysAdmin

Cassettes

References

### Principal Investigator

My Protocols

—Associate Investigator

**—Principal Investigator**

—Protocol Specialist

CC Protocols

All Protocols

New Protocol

Open

Copy

Delete

New Action

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](#) ]

PW\_HOME\_MY

Last Updated: 9/19/2007 12:02:47 PM

# Edit Features

## Opening the Editor

### 3. Precis - Abstract

1. 1195 Information

2. Glossary

**3. Precis - Abstract**

4. Introduction & Background

5. Hypothesis & Objectives

6. Study Design Page 1

7. Study Design Page 2

8. Subject Enrollment

9. Study Analysis

#### 3.1 Background

Click the Edit button to edit information within the component.

Edit

Comment

Omit

Help

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.

# Edit Features

## Editor Overview

Word-like visual interface.

One click inserts References and Recommended Language Cassettes

File Edit View Insert Format Tools Table Track Changes

Normal Paragraph Times New Roman 14pt B I U

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.

Design Code

References Cassettes

Click on an Item to Insert It

**Feuer, 1978**  
Feuer G. Role of phospholipids in the dev  
Res Commun Chem Pathol Pharmacol. 19  
734233

**McGrath, et al., 1986**  
McGrath H, Wilson WA, Scopellitis E. Acu  
Photochem Photobiol. 1986 Jun;43(6):62  
3489242

**Mena, et al., 1979**  
Mena F, Pacheco P, Aguayo D, Martinez  
Induced contractile response of the mam  
436734

**Menezes, 1999**  
Menezes AH. Pathogenesis, dynamics, an  
16972748

**Strauss, Hill, 1970**  
Strauss B, Hill T. The intermediate in the  
Biophys Acta. 1970 Jul 16;213(1):14-25.  
4992323

**Teodorovich, et al., 2006**  
Teodorovich OV, Lutsevich OE, Galliamov  
retroperitoneoscopic operations in. Urolog  
17058676

# Edit Features

## Adding a Reference

To add a reference, mouse over the reference and click.

Reference added to the text.

The screenshot shows a word processor window with a menu bar (File, Edit, View, Insert, Format, Tools, Table, Track Changes) and a toolbar. The document text reads: "Reinforcing properties of alcohol are in part mediated through endogenous opioids, [\[\[McGrath, et al., 1986\]\]](#) 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." The reference "McGrath, et al., 1986" is highlighted in blue in the text. At the bottom of the window are "Design" and "Code" tabs.

The screenshot shows a reference list panel with a blue header and a scroll bar at the bottom. The header contains the text "Click on an Item to Insert It". The list includes the following references:

- Feuer, 1978**  
Feuer G. Role of phospholipids in the dev. Res Commun Child Neurol Pharmacol. 1973;4:734-742.
- McGrath, et al., 1986**  
McGrath H, Wilson WA, Scopellitis E. Acute photochemical photolysis. 1986 Jun;43(6):6234-6242.
- Mena, et al., 1979**  
Mena F, Pacheco P, Aguayo D, Martinez J. Induced contractile response of the mammary gland. 1979;43:4367-4374.
- Menezes, 1999**  
Menezes AH. Pathogenesis, dynamics, and epidemiology of alcoholism. 1999;43:1697-1748.
- Strauss, Hill, 1970**  
Strauss B, Hill T. The intermediate in the biophysics of the intermediate. 1970 Jul 16;213(1):14-25.
- Teodorovich, et al., 2006**  
Teodorovich OV, Lutsevich OE, Galliamov AV. Retrospective analysis of laparoscopic operations in urology. 2006;43:1705-1766.

A blue arrow points to the "McGrath, et al., 1986" reference in the list.

# Edit Features

## Adding an Image

Clicking this button displays images specific to this protocol.

The screenshot shows a rich text editor window with a menu bar (File, Edit, View, Insert, Format, Tools, Table, Track Changes) and a toolbar. The text area contains the following paragraph:

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.

Below the text is an image of a virus. The image shows a yellow, spherical viral membrane (lipid layer) with several green, spiky transmembrane glycoproteins protruding from its surface. Labels with leader lines point to the following components:

- Transmembrane Glycoprotein (gp120)
- Transmembrane Glycoprotein (gp41)
- Viral Membrane (lipid layer)

At the bottom of the editor window, there are two buttons: "Design" and "Code".

# Edit Features

## After the Edits

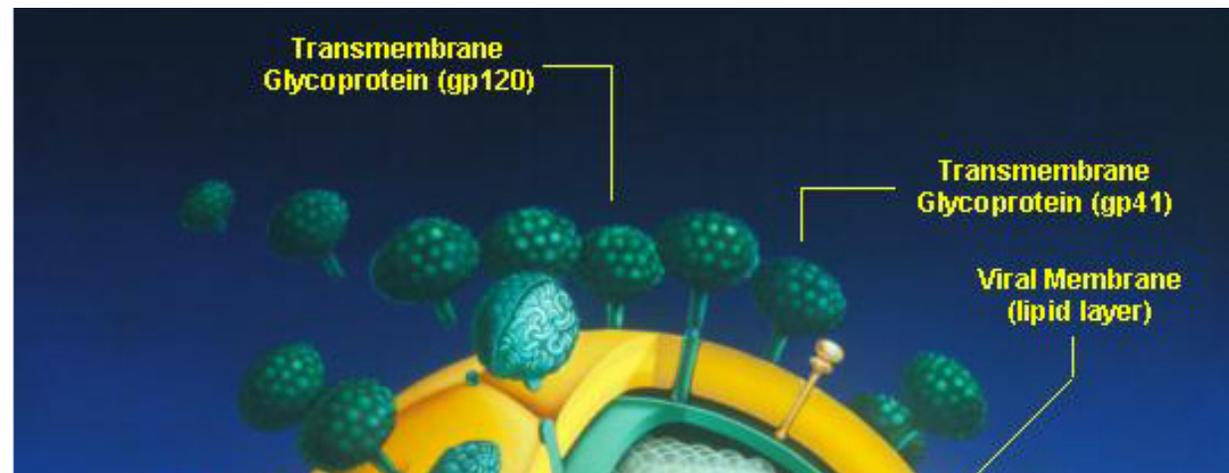
### 3. Precis - Abstract

1. 1195 Information
2. Glossary
- 3. Precis - Abstract**
4. Introduction & Background
5. Hypothesis & Objectives
6. Study Design Page 1
7. Study Design Page 2
8. Subject Enrollment
9. Study Analysis
10. Adverse Event Reporting
11. Data and Safety Monitoring Plan
12. Human Subject Protection
13. Pharmaceutical, Biologic, and Device Info
14. References and Appendices
15. Consent Forms

#### 3.1 Background

[Edit](#)[Comment](#)[Omit](#)[Help](#)

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.



# Change Tracking and Feedback

ProtoType supports three different methods for reviewing the protocol and providing feedback...

- ✓ Integrated change-tracking in the editor.
- ✓ The ability to compare protocols at different dates or different actions (i.e., comparing '06 CR against an '07 CR).
- ✓ Fully featured feedback and comment system from co-authors, reviewers, etc.

# Editing the Protocol

## Integrated Change Tracking

File Edit View Insert Format Tools Table Track Changes

Normal Paragraph Times New Roman 14pt B I U

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 John Doe, M.D., February 6, 2008 4:14 PM: - Inserted Text (CNV) is similar to those at play in atherosclerosis. If this is the case, then C directed against specific parts of the immune system.

Blue text has been edited by John Doe, M.D.

Design Code

# Version History Comparison

Comparing protocols across time.

Current Version of the Protocol

Click here to compare versions.

Version Being Compared Against

**Number:** 438      **PI:** Philip N. Lightfoot

**Protocol:** Treatment of choroidal subretinal neovascularization with agents directed against the immune response

**Version:** 139 (Draft - Initial: 01/31/2008)      **Access:** Read/Write      **Compare:**       **Compare To:** 138 (Draft - Initial: 12/14/2006)

## 3. Precis - Abstract

- 1. 1195 Information
- 2. Glossary
- 3. Precis - Abstract**
- 4. Introduction & Background
- 5. Hypothesis & Objectives
- 6. Study Design Page 1
- 7. Study Design Page 2
- 7. Study Design Page 2

### 3.1 Background

Edit   Comment   Omit   Help

There has been much interest in the possible role of the immune system in age related macular ~~degeneration.~~ **degeneration.**[Bok]  
Experimental models and patient material have, to date, suggested a role for ~~macrophages and complement.~~ **We hypothesize**  
**macrophages and complement.**[Bian] **We hypothesize** that the underlying mechanism that leads to choroidal neovascularization  
~~(CNV) is~~ **(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.**[Alber]  
However, there is little experience with CNV treatment in regards to new immunomodulatory agents. [Alder]

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 uvietis 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 uvietis 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.

Design Code

Change tracked edition ready for review.

The comment body.

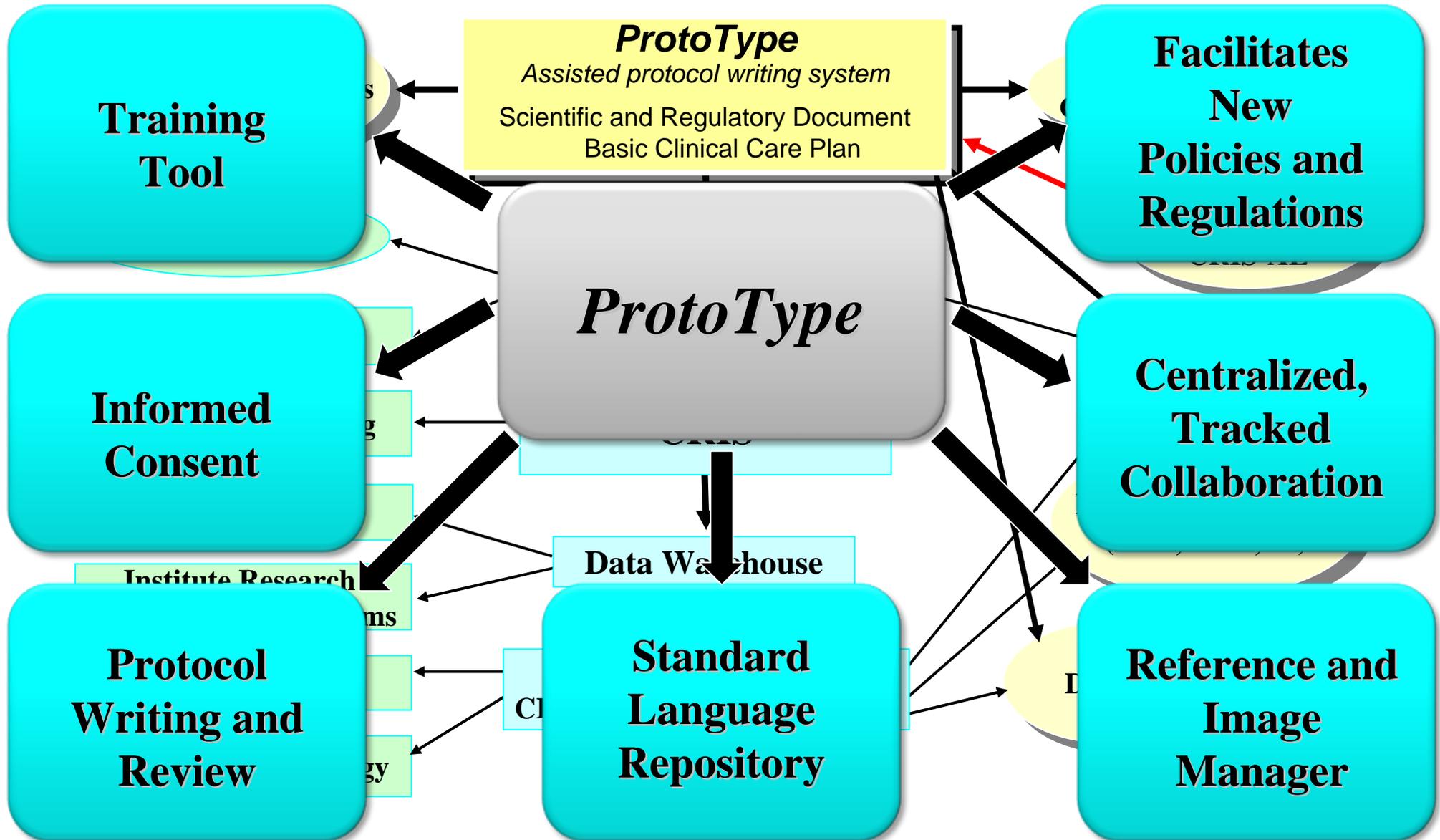
# Value Added for the Researcher

- ✓ Standard Language Cassettes for protocol body and consent forms
- ✓ Online archive of all protocols
- ✓ Amendments immediately incorporated into protocol
- ✓ Protocol moves electronically to IC, IRB, CC, etc.
- ✓ 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 - List of amendments and protocol changes

# Coming Soon, Spring 2008

- ✓ Robust formats for several IRBs.
  - ✓ CNS IRB
  - ✓ NIAID IRB
  - ✓ NIDA IRB
- ✓ Integration with IC Systems.
  - ✓ PTMS and IRIS
- ✓ Table of contents and page numbering in protocol exports.
- ✓ Improve collaborating site interface.

# Where We're Going



# *ProtoType*

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>

# ***ProtoType* Contacts**

**Phil Lightfoot**  
**(301) 496-3343**  
**[plightfoot@mail.nih.gov](mailto:plightfoot@mail.nih.gov)**

**Kim Jarema**  
**(301) 435-2401**  
**[kjarema@mail.nih.gov](mailto:kjarema@mail.nih.gov)**

# Thank You

**Dr. Jon McKeeby**

**Kim Jarema**

**Phil Lightfoot**