



Development of Resources for HGT Programs (in Response to NIH Guidelines Change)

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Institutional Biological Safety Officer**



Recombinant & Synthetic Nucleic Acid Research Registration Documents

Protocol Review

Resource Literature

Outreach

**HGT Research
Compliance Resources**

Shipping

Biosafety Manual

Biological Agents Registration

Material Transfer Agreements

Events / Safety Fair

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Biosafety Manual **Compliance Resources** Registration

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The Perfect Storm

- (1) NIH Guidelines Change (April 27, 2016)
- (2) Changes to Administrative Support for Human Trials
- (3) Parker Institute for Cancer Immunotherapy,

Memorial Sloan Kettering Cancer Center
Stanford Medicine
UCLA; UCSF

The University of Pennsylvania

University of Texas MD Anderson Cancer Center
Icahn School of Medicine at Mount Sinai
Washington University School of Medicine

Shared aim of **accelerating breakthrough immunotherapy research. . .**



The Perfect Storm

- (4) Vice President Joe Biden:
Announcing Cancer “Moonshot” at Penn Medicine**

- (5) Carl H. June, MD:
Center for Cellular Immunotherapies –
ex vivo T-cell engineering for cancer and HIV cell
based therapies**

NIH Guidelines Change

NIH Guidelines Change

RAC Review Procedures Revised by NIH Office of Science Policy

The changes are effective April 27, 2016

NIH Guidelines Change Guidance

Changes to Administrative Support for Human Trials

“The Office of Clinical Research (OCR)”

The new registration process is being implemented:

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- Questions / Concerns from Study Teams & Compliance Personnel
- Questions from Outside Sponsors

NIH Guidelines Change

Subject: need list of items IBC approves/acknowledges

Importance: High

Hi Andrew,

“We have reached a point where everyone is asking why our regulatory binders lack approvals/acknowledgments for all submissions to the IBC. We need a list of items that the IBC will take to their monthly meetings and those that we will not receive an approval/ackn letter for. . . “

Missing “acknowledgements is being questioned by internal/external monitors and auditors. At your earliest convenience, please provide us with documentation as to what the IBC will review at their monthly meetings so it can be provided to the monitors/auditors.”

Thanks,
Sr. Clinical Regulatory Specialist
CTU Regulatory Supervisor
Center for Cellular Immunotherapies
Clinical Trials Unit
Perelman School of Medicine

Apparently growing concern regarding what the IBC will review and approve.

**Driven by compliance teams.
What IBC letters (approvals) will be provided for audit compliance?**



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NIH Guidelines Change

And, from Pharmaceutical Sponsors:

“Please let me know the composition of your IBC and how it approves protocols.

- Does your IBC follow ICG (ICH; *International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use*) GCP (*Good Clinical Practice*) procedures (including those about board membership and reviewing all aspects of the study)
- Is your IBC fully registered with the OHRP (*Office of Human Research Protections*)?
- When they meet to discuss your project is it a full committee meeting?”

How Am I Doing? . . .



Just because you understand exactly what you want there are no guarantees that others understand the same thing.

HGT Registration Guidance

IBC Review of Human Gene Transfer (HGT) Protocols & Issuance of Formal Approval Letters

(IBC Review Clarification Issued September 1, 2016)

IMPORTANT NOTICE: This is not a policy document. This Review Clarification explains procedures that have been in effect since implementation of the IBC registration and review process at the University of Pennsylvania.

HGT Registration Guidance

The IBC must review & approve the following submissions:

1. New Human Gene Transfer Protocols

- (a) An **Initial Assessment** letter
- (b) **Recombinant nucleic acid registration** approval letter with **registration number**

2. All HGT Protocol Amendments

- (a) Approval letter for the submitted protocol amendment

3. All Informed Consent (ICF) modifications

- (a) Approval letter for the submitted ICF amendment

4. All 3-year registration renewals

- (a) **Recombinant nucleic acid registration** approval letter with **new registration number**

HGT Registration Guidance

The IBC must review & approve the following submissions:

5. All unanticipated SAEs (Medwatch; SAE Report Form; etc.)

- (a) Notify the IBC of any serious adverse event reported to the FDA. You must submit a copy of your FDA cover letter and report summary to the IBC. An acknowledgement letter will not be provided.
- (b) After administrative review, a determination will be made if the event must be reported to the NIH OSP. If a report to the NIH OSP is warranted then the study team will be notified and a copy of that report will be provided to the study team via email.

HGT Registration Guidance

The University of Pennsylvania IBC requests submission of all attendant materials for registered studies:

All other revisions, documentation, communications not limited to but including:

Administrative letters, Closure requests, Continuing review submissions to IRB, Deviations, DSMP submission or revision, DSMB meeting minutes, Enrollment closures, Exception requests, IND transfer letters, Investigator's brochure revisions, IRB annual review requests, Study holds, etc.

The IBC is not tasked with review and approval of attendant materials. An acknowledgement and/or approval letter will NOT be provided.

What Is Next?

The first HGT Trial using CRISPR tools at Penn

Edward Stadtmauer – *Phase 1 Trial of Autologous T Cells Engineered to Express NY-ESO-1 TCR and CRISPR Gene Edited to Eliminate Endogenous TCR and PD-1 (NYCE T Cells).*

NIH RAC Public Review – June 21, 2016

IBC Review and Approval – January 23, 2017 through June 26, 2017

IRB review and approval – (not yet approved) September 28, 2017

What Is Next?

FDA Approves Personalized Cellular Therapy for Advanced Leukemia Developed by University of Pennsylvania and Children's Hospital of Philadelphia

*Pioneering CAR T-cell Studies Led to First-ever Cancer Cell and
Gene Therapy Approval*

August 30, 2017



What Is Next?

School of Veterinary Medicine has been breaking new ground in using immunotherapies to treat cancer in dogs

Patients have traveled from as far as Seattle to participate in clinical trials

“Long term, my hope is that immunotherapies are ultimately going to enable us to move toward a cure”

Compliance & Oversight Challenges

- **Provide Resources and Educate, Educate, Educate.**
- **Increased Number of Individuals / Entities Involved.**
- **Lack of Background / Experience.**
- **Need to Be Responsive, Proactive, Efficient, Timely**
- **Planning For The Future.**

Compliance & Oversight Challenges

- “While recombinant DNA has become ubiquitous, new emerging technologies – ranging from new genome editing tools to novel RNA applications – are presenting interesting challenges to our current biosafety framework”

(NIH Workshop: Honoring the Past Charting the Future. July 18 & 19, 2017)

Planning For The Future

- How long will the NIH Guidelines remain relevant within the current rapidly evolving policy and regulatory landscape?
- Emerging Biotechnologies – “Unique Biosafety”
- Adapting Quickly to Changing Technologies
- “Technologies are evolving more rapidly than anticipated.”
- Zn++ fingers > TALENS > CRISPR > Base Replacement > ? ? ?

(NIH Workshop: Honoring the Past Charting the Future. July 18 & 19, 2017)

Planning For The Future

- How do we address the immediacy that our clients expect?
- How do we guard against “traditional approach dooms us to crisis management and reactionary approaches?”
- Differences in the use of terminology and definitions. Lack of common language.
- Future face of Biosafety Oversight > non-traditional areas using biological materials / biological tools
- Adaptability is very important.

(NIH Workshop: Honoring the Past Charting the Future. July 18 & 19, 2017)

*(Andrew B. Maksymowych. 2017. IBC Best Practice Meeting, State College, PA.
August 28 & 29.)*



Planning For The Future



Future Challenges:

Proactive, Responsive, Resourceful, Imaginative

Communication, Adaptability, Timeliness, Reinvention

Thank You