Quality Improvement

Patrick Herbison

Quality Improvement Specialist

Division of Human Subjects Protection

DHSP Quality Improvement Activities Including Site Audits, Consent Observations and Essential Documentation Binders

Objectives

- Audits – Site Quality Improvement Audits
- Other Quality Improvement Activities

Audits - Process

- Select a study
- Inform the PI/study team
- Collect the data
- Write report based on regulations and policy
- Report includes a corrective action plan (CAP)
- Work with team on acceptable responses to CAP

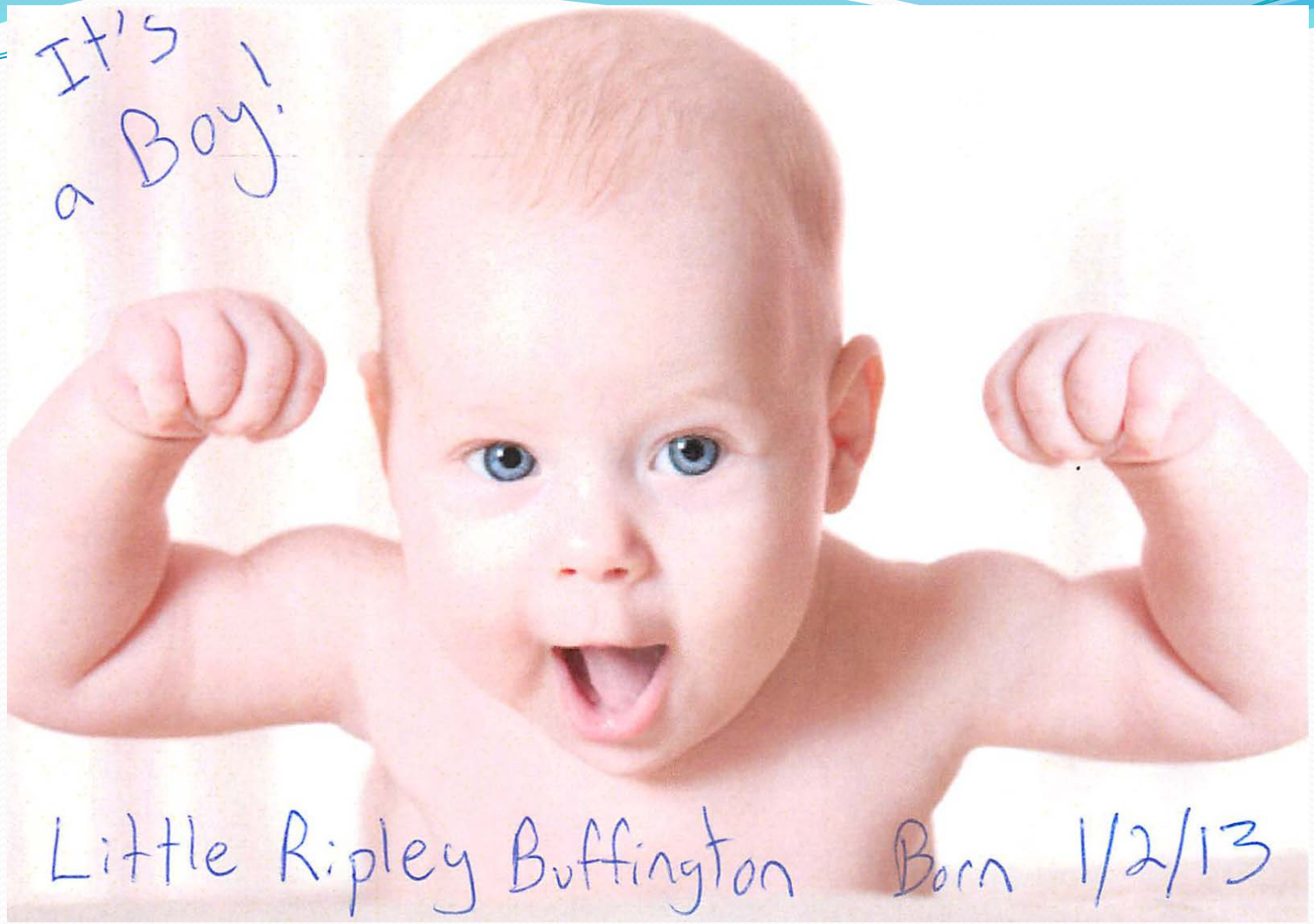
Audits - Purpose

- Demonstrate oversight of IRB approved studies
- Protect the rights of the subjects
- Ensure regulations and policies are being followed
- Increase consistency across studies and departments
- Fix problems
- Prevent future problems
- Improve the quality of research documentation

Audits - Purpose

- NOT to blame, criticize or punish

- 2nd set of eyes
- Informative (for me and the study teams)
- Update policies
- Resolve issues
- Easy solutions



TJU Policy 122.16

GENERAL GUIDELINES TO SAFEGUARD PROTECTED HEALTH INFORMATION

Baby pictures (even without a name or other identifying information)

TJU Policy 122.16

- <u>Bulletin boards:</u>
  - Bulletin boards may not contain the following:
    i. Documents with PHI of members . . .
    ii. Baby pictures (even without a name or other identifying information)
    iii. Cards and notes of appreciation

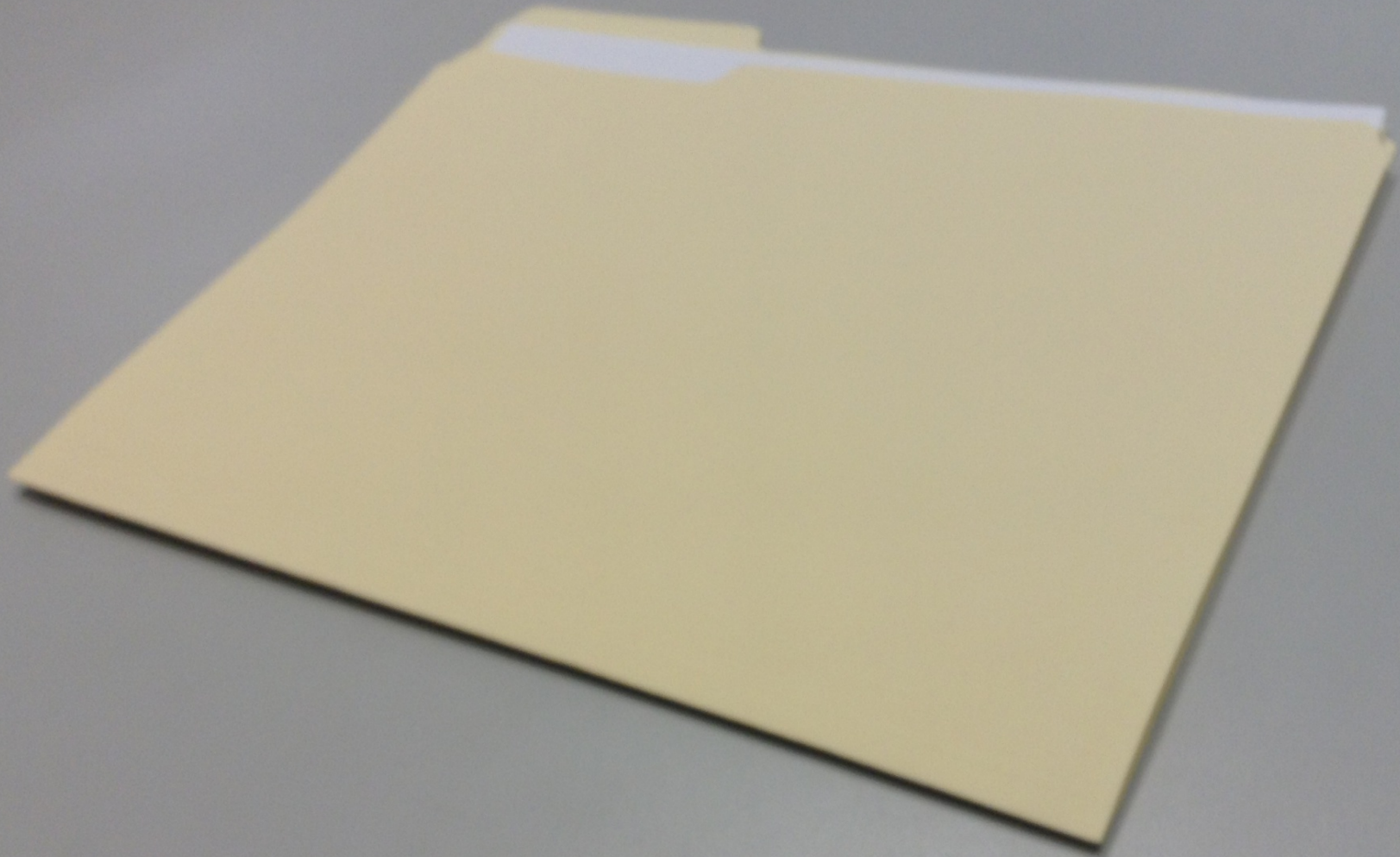
Screening and Enrollment

- Per OHR Policy GA 127:
  - Subjects must be assigned a unique number.
  - A screening and enrollment log must be maintained.
  - An eligibility checklist must be completed for each subject

Audits – Areas Reviewed

The Regulatory and Patient Binders Including:

- IRB Submissions
- Screening and Enrollment Logs
- Informed Consent Forms
- Eligibility Criteria/Waivers
- Serious Adverse Events (SAEs)
- Unanticipated Problems (UAPs)
- Data Confidentiality and Security Procedures




Fellowes
Fellowes
file folders
Fellowes
file folders

SIGNED CONSENT FORM

Thomas Jefferson University **OHR-8**
Informed Consent Document for Human Subjects Research

PI: Brennan Huff, MD **Co-I**: Dale Doback, MD
Phone: 123-456-7891 **Phone**: 123-456-7892

Medical Study Title: Study to Determine if the Observers Can Detect the Infinitesimally Small Detail Omitted from this Signed Consent Form

Lay Study Title: Study to See What's Missing from this Page

What Is Informed Consent?

You are being asked to take part in a medical research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans. Before you can make a knowledgeable decision about whether to participate, you should understand the possible risks and benefits related to this study.

*Subject Initials:*_____
Date: / /

Thomas Jefferson University IRB
Approval Date 10/13/11
Expiration Date 10/12/12
Annual review due 6 weeks before expiration.

Signatures:

Your Name *(please print or type)*

Patrick Herbison (Date) 1/15/13

Your Signature

Brittany Speedwell

Name of Person Conducting Consent Interview

1/23/13 (Date)

Signature of Person Conducting Consent Interview

(Date) 1/5/2013

Signature of Principal Investigator or Co-Investigator

Duke Davenport (Date)

Witness Signature

Claudio O'Malley

Name of Person Conducting Consent Interview

Claudio O'Malley (Date) 6/15/12

Signature of Person Conducting Consent Interview

(Date) 06/15/2012

Signature of Principal Investigator or Co-Investigator

Approval Date: 8/16/11

Expiration Date: 8/15/12

What Is Informed Consent?

You are being asked to take part in a medical research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans, and when the IRB approves a new consent form, you have to start using it. Before you can make a knowledgeable decision about whether to participate, you should understand the possible risks and benefits related to this study.

Thomas Jefferson University IRB

Subject Initials: ___

Date: ___

Approval Date: 4/15/12

Expiration Date: 8/15/12

Dear Dr. Jones:

The **Institutional Review Board (IRB)** has reviewed your study entitled:

"A Study to Determine if Anyone Reads Approval Letters" Control #10X.123

In accordance with Federal-Wide Assurance #00002109 to the U.S. Department of Health and Human Services, this **continuing review** was **approved** for **one year** by Board #2405 on **1/9/13** at Thomas Jefferson University following:

FULL (X) Board Review.

THIS APPROVAL REQUIRES THAT INFORMED CONSENT BE OBTAINED FROM ALL PERSONS PRIOR TO THEIR INVOLVEMENT IN THE STUDY BY THE USE OF THE LATEST APPROVED SUBJECT CONSENT FORM. EACH SUBJECT MUST RECEIVE A COPY OF THEIR SIGNED CONSENT FORM.

ALL SUBJECTS CURRENTLY ENROLLED IN THIS STUDY MUST BE RECONSENTED DUE TO THE CHANGE TO THE RISK LANGUAGE IN THE CONSENT FORM.

This approval expires on 1/8/14 one year from the original approval date, unless suspended or terminated earlier by action of the IRB. At the end of the current approval, a report (Form OHR-9) must be submitted to the IRB summarizing progress on the study during that period.

If you wish to continue the study beyond the expiration of this approval, an application for continuation of your study must be submitted to the IRB at least one month prior to the expiration date.

OHR-12 Re-Consent

Re-Consent Determination (Complete if consent form has been revised):

To maintain our primary objective of human subject protection, the following subjects will be re-consented in order to provide information which may relate to the subjects' willingness to continue participation:

☐ **All subjects who received study intervention**

☐ **All active subjects (not subjects 30 days* post last treatment, in follow-up, withdrawn or off study)**

☐ **All active subjects including subjects 30 days* post last treatment (not subjects in follow-up, withdrawn or off study)**

☐ **All active subjects including subjects 30 days* post last treatment and in follow-up (not subjects withdrawn or off study)**

☐ **Subjects will not be re-consented**

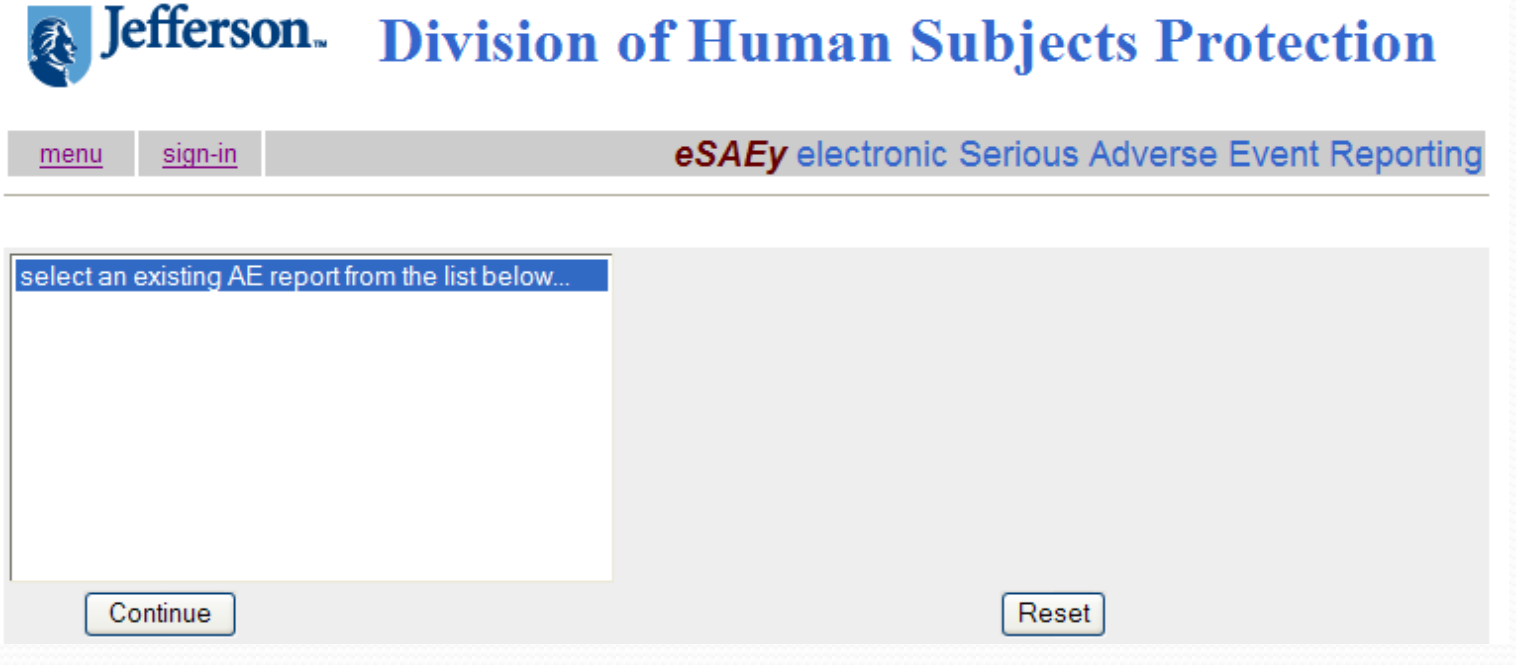
☐ **Subjects will not be re-consented, but will be informed of the change(s)**

☐ **Other (Specify):**

SAEs and AEs

- Serious Adverse Events (SAEs) – Grade 3, 4 or 5 resulting in death, life-threatening experience, inpatient hospitalization (or prolongation), persistent or significant disability or incapacity, congenital anomaly or birth defect.
- An SAE is any serious event that the patient experiences during the study (unless specified in the protocol/OHR-2)

Adverse Events	Start Date mm/dd/yy	Stop Date mm/dd/yy: check box "on-going" if the AE is on-going at the time of report	Type of AE	Serious Criteria* AdEERS Submitted		Intensity/ Grade (Please √ one) To be completed by the PI	Attribution (Please √ one) To be completed by the PI	Action Taken	Outcome	PI Initials/ Date
				Yes*	No					
Heart Attack	1/15/13	1/15/13 ☐ On-going	☐ Expected ☒ Unexpected	☒	☐	☐ Mild/1 ☐ Moderate/2 ☐ Severe/3 ☒ Life-threatening or Disabling/4 ☐ Death/5	☐ Unrelated ☐ Unlikely ☒ Possible ☐ Probable ☐ Definite	☐ None ☒ Medication Therapy ☐ Procedure ☒ Hospitalization ☐ Other	☐ Recovered ☒ Improved ☐ Ongoing ☐ Death ☐ Unknown	PA 1/15/13
Stroke	1/20/13	1/20/13 ☐ On-going	☐ Expected ☒ Unexpected	☒	☐	☐ Mild/1 ☐ Moderate/2 ☐ Severe/3 ☒ Life-threatening or Disabling/4 ☐ Death/5	☐ Unrelated ☐ Unlikely ☒ Possible ☐ Probable ☐ Definite	☐ None ☒ Medication Therapy ☒ Procedure ☒ Hospitalization ☐ Other	☐ Recovered ☒ Improved ☐ Ongoing ☐ Death ☐ Unknown	PA 1/20/13



Subject #: 01-003

Adverse Event Record

Description	Start Date	Stop Date	Related	Severity	SAE?	Action Taken	Outcome
	/ /	/ /					
	/ /	/ /					
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	/ /	/ /					
	/ /	/ /					

Patient had a pretty bad reaction to study drug.

SAEs and UAPs

Type	Reporting Timeframe (Workings Days*)
UAP	10
SAE – Unrelated	5
SAE – Possibly or Definitely Related	2
SAE – Death	1 (24 Hours)
*Between site being aware and Inv. signing eSAEy report	

Lab Report Clinical Trial #123456

Name: Patrick Herbison DOB: [redacted] MR#: [redacted]

Phone Number: 215-955-4239 SS#: [redacted]

CBC

WBC Count		5.6	[4-11]	B/L
RBC Count		4.73	[4.5-6.0]	T/L
Hemoglobin	L	13.9	[14.0-17]	g/dL
Hematocrit	L	41.0	[42-52]	%

Audits – Random

- Sort of random

Audits – For Cause

- Lapse in IRB Approval
- Problems with IRB Submission Forms/Responses
- Findings in External Monitoring Reports
- Protocol Deviations/Violations
- Late Reporting of SAEs/UAPs
- Surrogate Consent/Child Assent/Vulnerable Populations
- Other
- Let me know!

Non-Waiver of Legal Rights Statement

By your agreement/your permission to participate/allow your child to participate in this study, and by signing this consent form, you are not waiving any of your/ your or your child's legal rights.

In order to be in this research study, you must sign this consent/parental permission form.

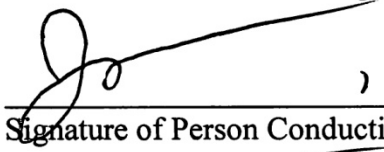
You affirm that you have read this consent form. You have been told that you will receive a copy.

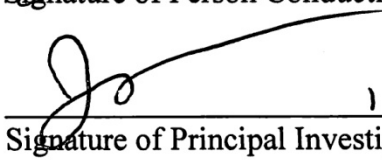
Signatures:

_____
Your Name *(please print or type)*

_____(Date)
Your Signature

Justin Case, MD
_____
Name of Person Conducting Consent Interview


, MD
_____(Date)
Signature of Person Conducting Consent Interview


, MD
_____(Date)
Signature of Principal Investigator or
Co-Investigator

THOMAS JEFFERSON UNIVERSITY INSTITUTIONAL REVIEW BOARD
Continuing or Final Review of Research Protocols Involving Human Subjects

OHR-9
12/2012
1 of 1

TYPE OF APPLICATION: (X) CONTINUING REVIEW ( ) FINAL REPORT

INITIAL REVIEW WAS: (X) FULL or ( ) EXPEDITED *(Noted on approval letter)*

TITLE OF PROTOCOL: Giving Multiple Unapproved Drugs to People with Several Critical Conditions

	Since Last Approval	**Total to Date**
13. Number of serious adverse events occurring at TJU in the past year currently noted in consent form :	0	0
14. Number of serious adverse events occurring at TJU in the past year not currently noted in consent form:	0	0

Vulnerable Individuals

From Regulations/Policy

- Children
- Decisionally impaired
- Terminally ill or very sick
- Low income
- Low education
- Drug users
- Prisoners
- Pregnant women
- Disabled

From Jefferson Studies

- Brain injury
- Cancer
- Possible Cancer
- Children
- Heart Failure
- Parkinson's
- Aortic Aneurysm
- Pregnant women with weakened hearts
- Emergency Surgery
- Depression
- Septic shock

CHILD'S ASSENT TO PARTICIPATE IN A CLINICAL TRIAL

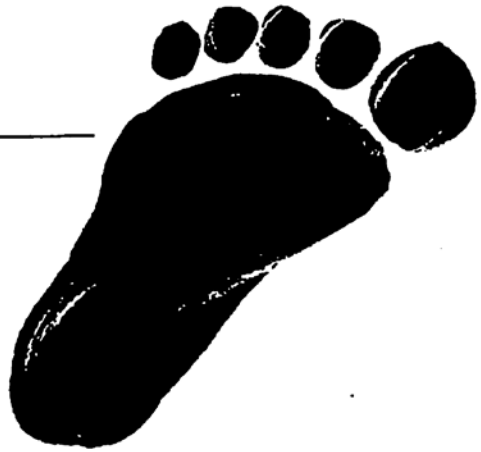
PROTOCOL TITLE: Study to Determine if Child Assent can be Properly Documented

INVESTIGATOR(S): Adam Abrams, Babbette Billingsly

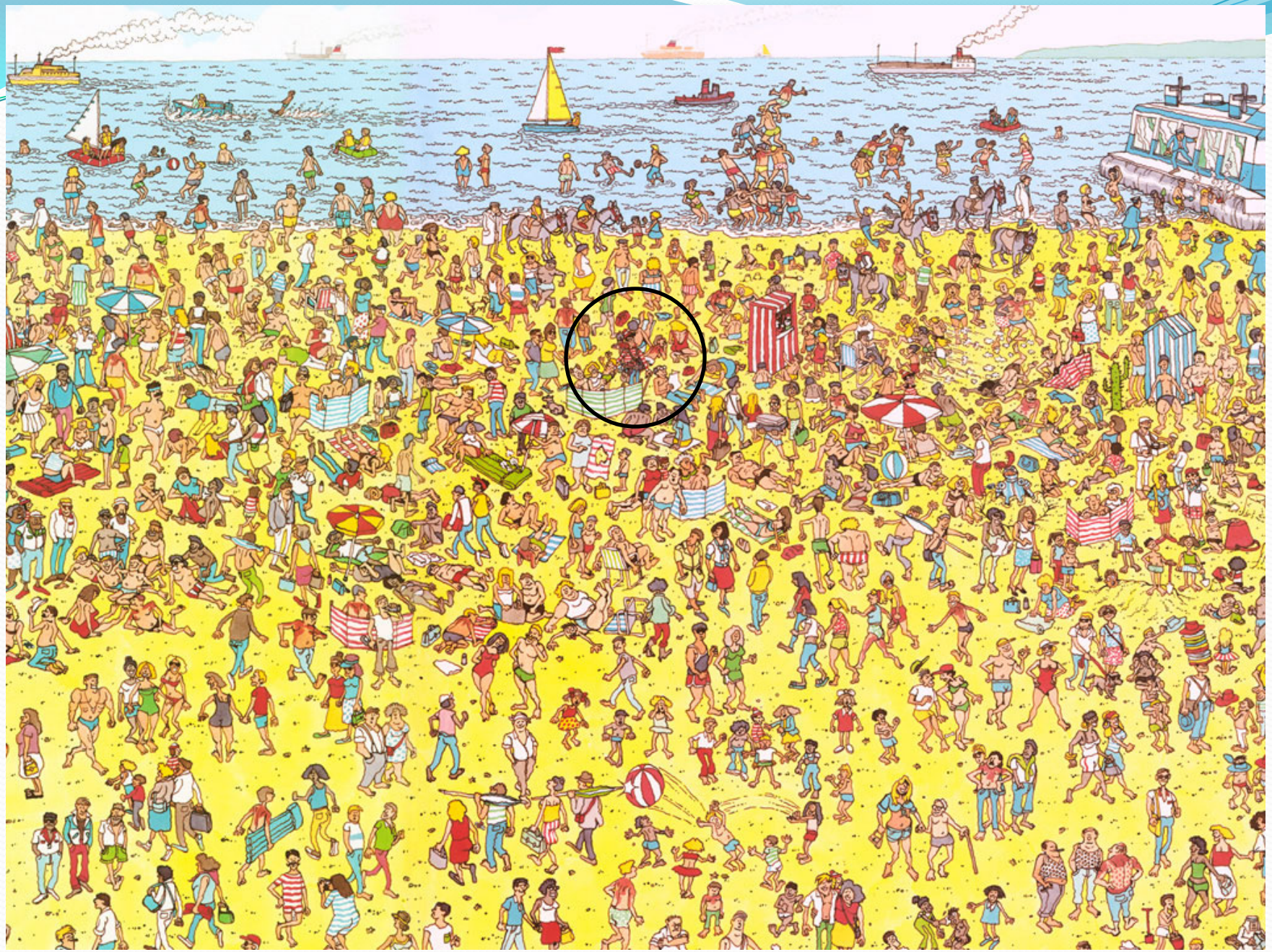
The doctor has asked you if you want to be in a research study. The doctor has told you and your parent(s) about the study and everything that will happen to you. You can ask any question you have any time you want to. You do not have to be in this study if you don't want to. If you start the study and decide to stop, that is ok. The doctor may write about this study, but your name will not be used. Children age 7 to 17 should be asked to assent or if they are able, to sign the parental permission form (TJU Policy 506).

I Baby Boy Jones want to be in this study.

Baby Boy Jones
Subject's Signature



1/2/13
Date



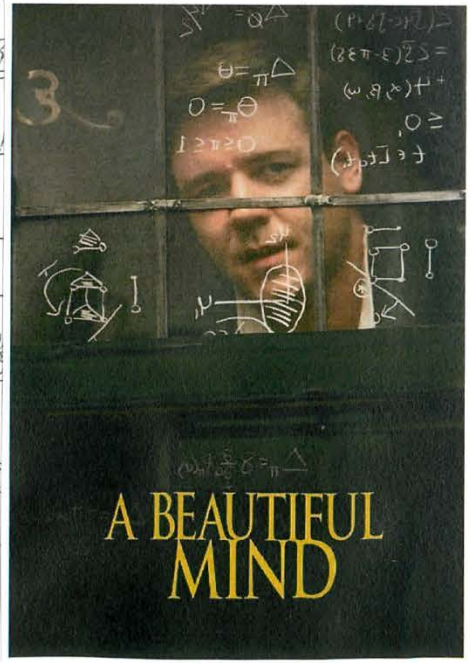
CONFIDENTIAL

ICF/Assent – Subjects

☐ NA – See comment in Initial and Continuing Reviews, Protocols and ICFs/Assent Section

* If applicable, complete if consent was required, but consent documentation was waived.

Subject ID#	502406	500229	500317	502491	504437
Does Signed ICF Have IRB Stamps	Yes Yes Yes	M Yes M Yes	Y Y Y	Y Y	Y Y
Did the Subject Initial and Date All Pages	Yes Yes Yes	Yes Yes	Y Y Y	Y Yes	Y Yes
*If Surrogate, OHR-8B Used	NA NA NA	NA NA	NA NA NA NA	NA NA	NA NA
Date Signed and Dated by Subject	M 1/3/13 M 9/8/13 B 7/19/13	M 8/15/13 M 1/7/13	M 1/15/13 B 8/7/13 M 8/7/13 B 11/11/13	M 1/17/13 M 8/8/13	M 1/22/13 M 8/19/13
Date Signed and Dated by the Person who Conducted the Consent Discussion	M 1/3/13 M 9/20/13 B 7/19/13	8/15/13 1/7/13	1/15/13 8/7/13 8/7/13 9/24/13	1/17/13 8/8/13	8/19/13
Date Signed and Dated by Investigator or Co-Investigator	1/3/13 10/21/13 B 8/19/13	8/19/13 1/7/13	1/15/13 B 8/19/13 M 8/19/13	1/17/13 8/19/13	
*Approval and Expiration Date(s) of All Applicable ICFs/Assents	XX/XX/XX – XX/XX/XX 7/11/13 – 10/17/13 10/18/12 – 10/17/13	7/11/13 – 10/17/13 12/18/12 – 10/17/13	10/18/12 – 10/17/13 7/11/13 – 10/17/13 8/13/13 – 10/17/13	10/18/12 – 10/17/13 7/11/13 – 10/	
*Approval and Expiration Date(s) of ICFs Used for Consent/Assent	XX/XX/XX – XX/XX/XX B 1/3/13 – 10/17/13	7/11/13 – 10/17/13	10/18/12 – 10/17/13 7/11/13 – 10/17/13		
*Was ICF/Assent Signed in Approval-Expiration Window	Consider Approval Letter Date Yes Yes	Yes Yes	NO – But Line Struck Out Y	Yes Yes	
Were Study Personnel Submitted to IRB	Copy signatures from OHR-1 (and 12's) Y	B NA CC NA NA CH CC CH Yes Yes	CC NA NA NA CC CC CC CC Yes Yes Yes Yes	CC NA CC Yes CC	
*Date of First Research Activity	Check OHR-2/Protocol 1/3/13	4/17/13	1/15/13	1/17/13	
Is it Documented that Subject Received a Signed and Dated Copy of ICF/Assent	? Yes Yes	? No ? No	?	No	
*Authorization to Use PHI	Blurb				



Audits – CAP

- Corrective Action Plan (CAP)

Observation	Recommended Action	Response
The form wasn't signed.	Please sign the form.	We signed the form.

Audits – By Request

- Pre-Monitoring Visit
- Pre-FDA Inspection
  - Includes mini training on inspections
- Study Team Request
  - When an issue is suspected
  - High staff turnover

Other Quality Improvement Activities

- Consent Observation
  - Painless
  - Feedback on what works for others
- Study Binders
  - Help in setting up patient binders/folder
  - Required forms/logs
  - Binder with sections for all study related materials

Questions?

Contact Info

Patrick Herbison

patrick.herbison@jefferson.edu

215-955-4239

FDA Inspections - Purpose

To ensure:

- Compliance with regulations
- Accuracy and reliability of data
- The rights of research subjects are protected

FDA Inspections

- FDA will look at everything from internal audits PLUS
  - Protocol adherence
  - Source documents vs. case report forms (CRFs)
  - Test article accountability
  - Labs
  - Regulatory Documentation

FDA Inspections

- Any study conducted under an Investigational New Drug application (IND) or Investigational Device Exemption application (IDE)
- Most inspections are triggered by New Drug Application (NDA)

Additional Factors

- High enrollment (especially in a short time)
- Few adverse events
- Results different from other sites
- Patient complaints
- Investigators with many studies
- Investigator on study outside of specialty
- Sponsor reports poor quality data or other difficulties

Observations and Reports

- Form FDA 483, Inspectional Observations (End of Inspection)
- Establishment Inspection Report (EIR) – Final Report
- Classification of EIRs
  - OAI – Official Action Indicated
  - VAI – Voluntary Action Indicated
  - NAI – No Action Indicated
- Site responds with corrective actions and preventative actions (CAPA) within 15 days
- Close out letter

Possible Consequences

- Study put on hold
- Re-inspection
- Rejection of study data
- Warning letter (Not following regulations)
- Restriction/Disqualification of investigator
- Increased risk to subjects