

EFIC in Action

Experiences from an on-going clinical trial

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Progesterone for the Treatment of Traumatic Brain Injury

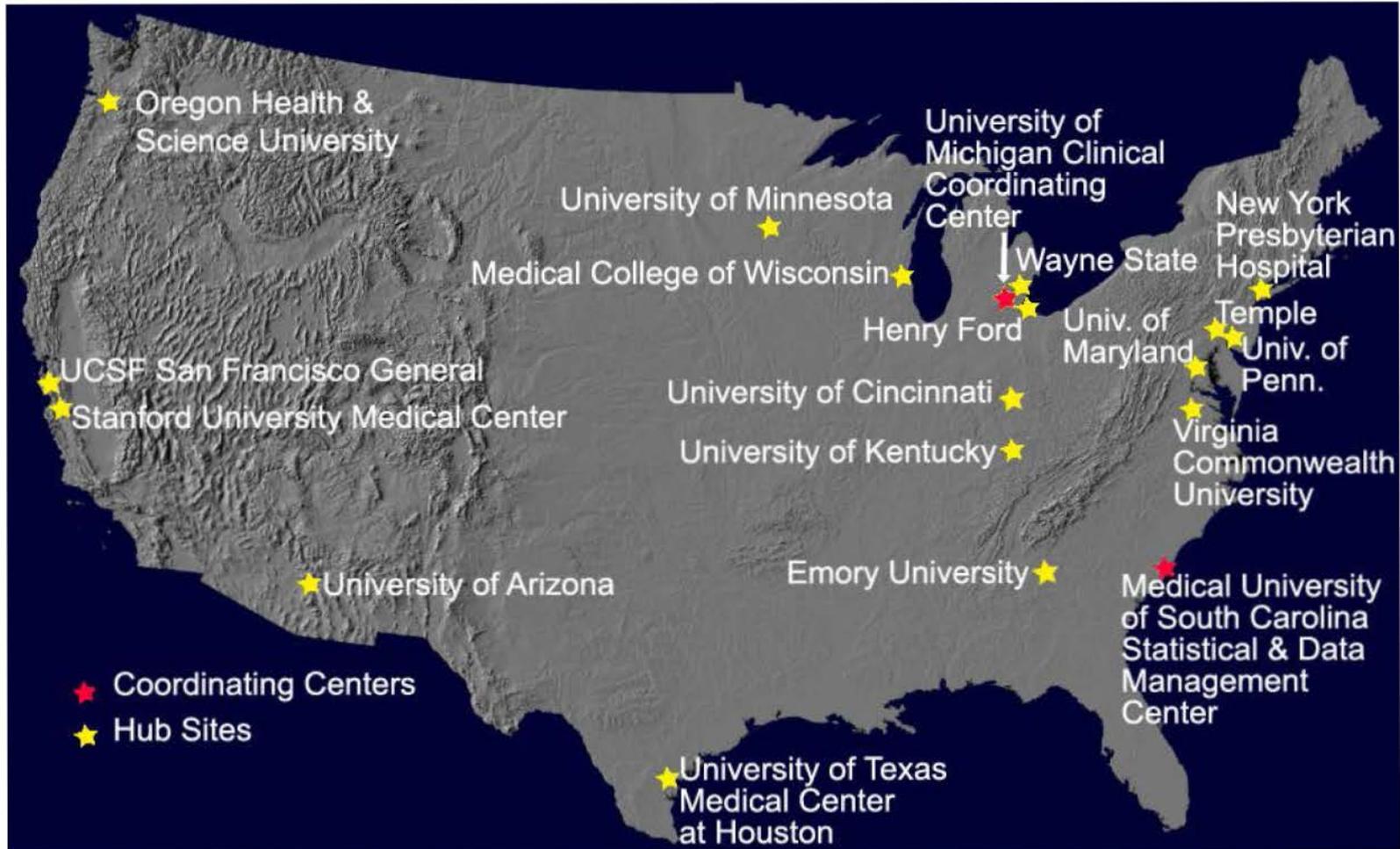
Project Number: 1U01NS062778

FDA IND #: 104,188

David W. Wright, MD - Principal Investigator

- Primary Objective: Determine the efficacy of administering intravenous (IV) progesterone (initiated within 4 hours of injury and administered for 72 hours, followed by an additional 24 hour taper) versus placebo for treating victims of moderate to severe acute TBI (Glasgow coma scale score 12-4).

Neurological Emergencies Treatment Trials (NETT) Network



ProTECT™ III

- Enrollment began March 2010
- 34 actively participating hospitals
- 448 pts enrolled as of 3/12/2012.
- 296 enrolled under EFIC
- 152 with consent.

ProTECT™ III EFIC Process

- All sites had to submit an EFIC plan to their IRB for approval
- Sites conducted CC/PD per the IRBs recommendations
- Results of CC/PD were submitted to the IRB
- IRB either approved or requested additional activities

ProTECT™ III Protocol

- If a LAR is present within one hour of the patient's arrival to the hospital, standard consent procedures will be employed.
- In cases where rigorous attempts to identify a LAR are not successful within 1 hour post patient arrival to the hospital, subject will presumptively be enrolled using the exception from informed consent rule.
- Once the subject has been randomized and study drug initiated, the research team should continue to search for the LAR to obtain consent.

ProTECT™ III Companion Study

- ProTECT™ III includes an empirical ethics companion study protocol that will focus on:
- Measuring the effectiveness of community consultation (CC)
- This ethics research is aimed at assisting ProTECT™ in obtaining high quality CC, and using the unique opportunity provided by ProTECT™, to collect data that can inform the challenges researchers and ethicists face regarding the meaning and conduct of CC.

ProTECT™ III Companion Study

Ethics team includes:

- Rebecca D. Pentz, PhD, Professor of Research Ethics at Emory University
- Kevin Weinfurt, PhD, Associate Professor and Chair, Interdisciplinary Medical Decision Making Initiative at Duke University
- Jeremy Sugarman, MD, MPH, MA, Harvey M. Meyerhoff Professor of Bioethics and Medicine, Johns Hopkins University
- Jill Baren, MD, University of Pennsylvania,
- Michelle Biroș, MD, University of Minnesota

ProTECT™ III Companion Study

- Two research ethics goals:
 - (1) develop an instrument to assess quality of CCs; and
 - (2) assess the effectiveness and quality of different methods of CC.
- These goals will be accomplished with a two-stage design:
 - 1st stage-Collecting descriptive data using surveys, in-depth interviews and observation of CC from another EFIC trial (RAMPART).
 - 2nd stage- choose 4-5 IRBs to study during ProTECT™, assessing the effectiveness of different CC methods and testing a CC evaluation measure. quality of different methods of CC.

ProTECT Survey

- Length- 21 questions
- Domains
 - Knowledge of PROTECT study
 - Attitudes toward PROTECT and use of EFIC
 - Views of CC session in which they participated
 - Demographics
- Attitude questions on 5-point Likert scale

ProTECT™ Survey Results

Overview

Number of Hubs reporting:	13
Number of activity reports:	87
Number of participants:	5,799

Types of community involved

Percent geographic community:	75%
Percent condition-oriented community:	23%
Percent both types of community	2%

Type of consultation activities

Existing Group Meeting	45%
Focus Group	14%
Town Hall	7%
Face to Face Interview	3%
Internet Survey	0%
Phone Survey	1%
Unscheduled Feedback	0%
Other	1%

Participant Demographics

Age (average)	42 years
Age <18 years	#DIV/0!

Female	56%
Male	44%

Race

White	86%
Black/African American	7%
Asian	3%
Native Hawaiian or Pacific Islander	0%
American Indian or Alaska Native	1%
More than one race	0%
Other race	3%

Ethnicity

Hispanic/latino	6%
Nonhispanic	94%

ProTECT™ Survey Results

Overview (continued)

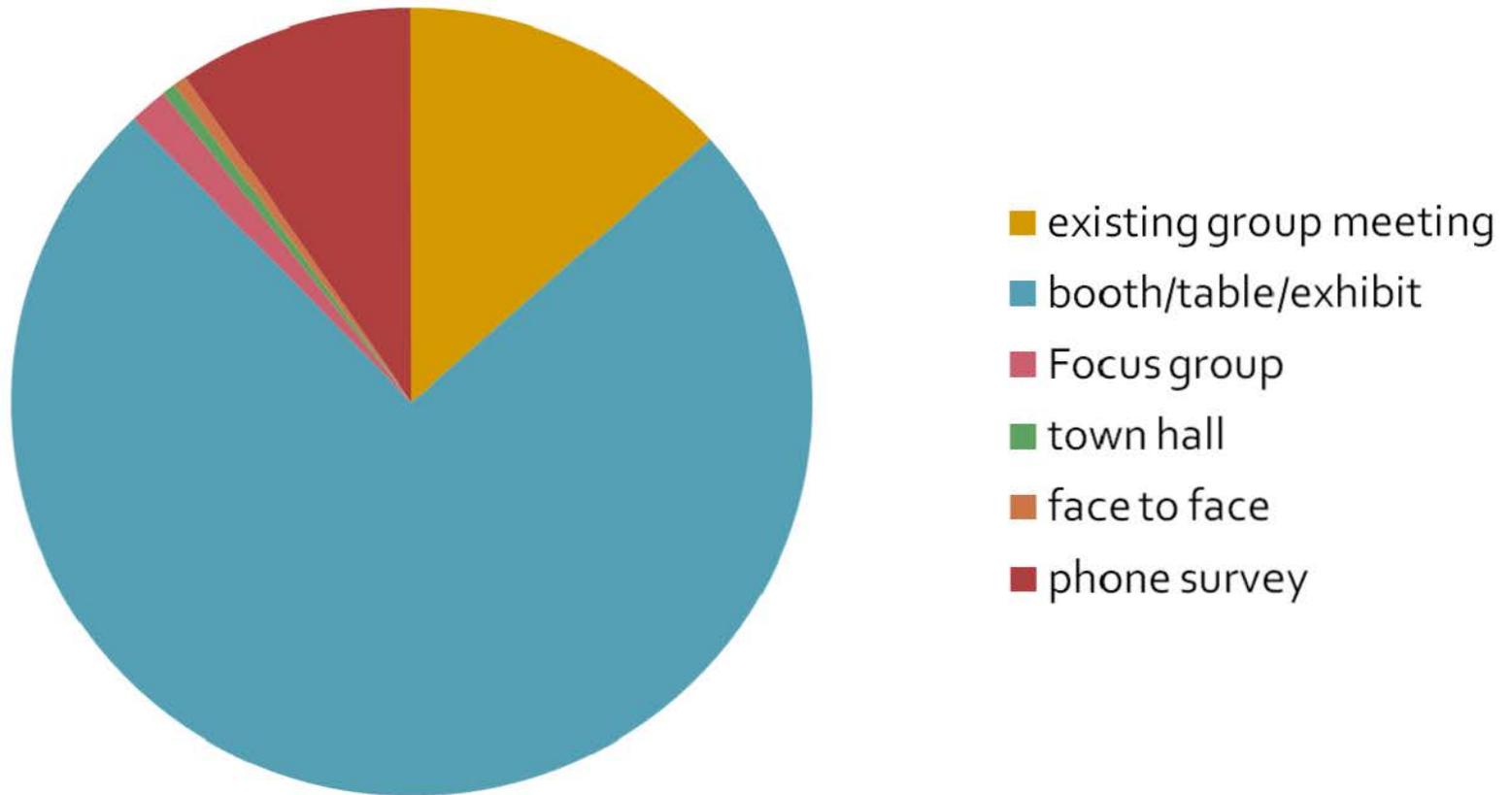
Intended event audience		intended audience versus community type (number of events)	
		geographic	condition-oriented
General	60%	90	23
Medical professionals	10%	25	8
High risk specific	8%	13	15
Age specific	8%	10	7
Civic group/leaders	7%	4	1
Ethnic/racial community	2%	13	0
Parents	1%	11	0
Religious group	0%	5	0

totals greater than 100% because some events included more than one intended audience or community type

ProTECT™ Community Consultation

13/17 Hubs= event type and # of participants

Series 1



CC Open-ended Results

Concern Themes

- Lack of consent
- Being blinded to study treatment received
- Randomization
- Study treatment unproven
- Finding effectiveness

Participants reported they needed to know more about

- Side effects
 - All of them
 - The chances of one occurring
- Progesterone
 - Dosage
 - How it works
 - How it's made
- Legality of EFIC research
- More about the other progesterone studies

CC Open-ended Results

Reasons to wear an opt-out bracelet

- Do not want to be in the study
- Allergic to eggs

Reasons not to wear an opt-out bracelet

- Would want the medicine
- Length of time too long
- Unattractive
- Shouldn't have to
- Would forget
- Would have to explain it
- Do not anticipate having a TBI
- It might get caught on something (work hazard)

CC - Geographical Community

Existing meetings/group events

- Places of worship
- Rotary clubs
- Chamber of commerce
- Police station community mtg.
- Neighborhood associations
- Community activity centers
- Basketball parents mtg.
- Homeless shelters

Booth events

- State fair
- Health expo/conf/fairs
- Hospital (ED lobby)
- College basketball games
- High school ball games
- The mall
- Univ. fitness center
- Farmers market
- Stadium events

CC - TBI Related Community

TBI related/ high risk community

- Brain injury support groups
- Women's motorcycle club
- A county cycling committee mtg.
- Cycling club meetings
- Motorcycle clubs
- Epilepsy stroll
- Senior groups

CC - Special Focus

College Community

- College ethics class
- School of nursing graduate program
- College health education classes
- Pre-med honor society
- College staff mtg.

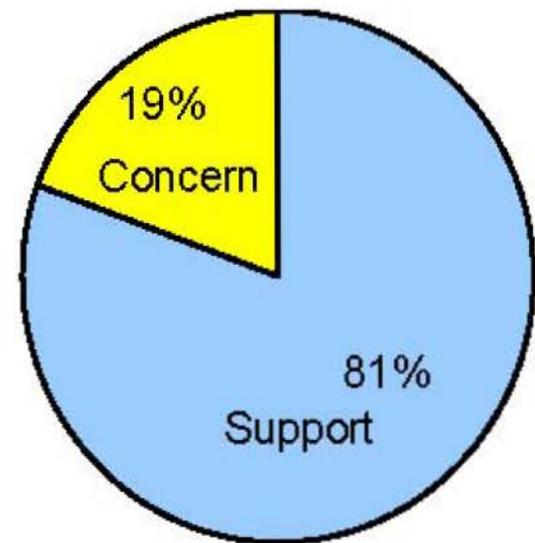
Medical Professionals:

- Hospital internal email survey
- Meeting with EMS personnel
- EMT students
- Hospital inpatient staff
- Brain injury rehab clinic

CC Closed-ended Results

Feedback Summary

Number of individual respondents	5,509
Number of closed ended responses	41,237
Number of open ended comments	961



Closed Ended Responses

PD Activity Summary

Network Activity Summary: (Hub = 17)

- Total number of events = 309
- Events in disease-related community = 23 (7%)
- # opt-outs requested = 12
 - Bracelet
 - Opt-out registry on-line (developed later)

PD – Geographical Community

Print Advertisements

- Local & National newspapers
- Local & university newsletters
- Public utility department insert
- Large local employer paycheck insert

Online Advertisements

- Twitter
- Facebook
- Craigslist
- Hospital website
- University website (athletic department page)
- ProTECT study local website

PD – Special Focus

Print advertisement

- Local Spanish journal

Radio Advertisement

- Vietnamese radio

Booth

- EMS expo

PD - TBI Related Community

Brochure/Flyer/Poster Distribution

- Brain injury rehab clinics
- Motorcycle clubs
- Senior centers

Booth

- Senior day (local event)
- Epilepsy stroll

PD – Geographical Community

TV/Radio Advertisements

- Radio announcements
- Radio interviews
- TV morning & evening news programs

Brochure/Flyer/Poster Distribution

- Sporting events
- libraries

Booth

- Sporting events
- Farmers markets
- State fair

Patients' Experiences in Emergency Research (PEER)-PROTECT

- Emory University, led by Drs. Neal Dickert and Rebecca Pentz
- Conducting an interview study with subject and decision-makers for subject who have been enrolled in the PROTECT™ III research study under EFIC.
- Goal 100 interviews

Human Subjects Protection Committee (HSP)- NETT

- 2 EFIC trials so far (RAMPART/ProTECT)
- Wanted a way to vet EFIC and ethical issues
- NETT established the HSP committee which meets monthly
- Michelle Biros, MD, Univ. of Minnesota-moderator

Interesting Cases

- ProTECT Subject enrolled under EFIC while family was present within the first hour -- The family arrived 30 minutes after the patient arrived to the hospital, but were determined to be too intoxicated to give consent.

HSP Committee Discussion

- Allowing EFIC enrollments when family members lack capacity removes the temptation to try to enroll subjects that would otherwise be lost by obtaining consent from family members that cannot meaningfully or legally engage in a consent process. At the same time we recognize that this interpretation creates a temptation to determine that the family lack capacity to serve as LAR in order to allow enrollment under EFIC. This is largely mitigated by the requirement that consent still needs to be obtained as soon as possible after an EFIC enrollment, and it is anticipated that enrollments of this type will be rare.

HSP committee Recommendations

- However, the following additional safeguards and guidelines were recommended:
 - a. The study team is responsible for carefully assessing the capacity of a family member before determining that the individual is not capable of being an LAR. Such a determination must be based on reliable historical or clinical information.
 - b. If family are present within 60 minutes, but lack capacity to serve as LAR, the study team should notify the on-call hotline investigator prior to enrolling using EFIC. The intent is to make sure this rule is being interpreted correctly, and to make sure these interpretations are highly transparent and can be tracked.
 - c. Whenever a study team enrolls using EFIC in situations where the family were present within 60 minutes but lacked capacity to serve as an LAR, the study team will present the case on a subsequent conference call of the HSP working group. The intent is to allow the HSP working group to track such enrollments and recommend improvements to this interpretation or implementation as needed.

IRBs Response

- I agree with the guidance from the consortium. It is certainly reasonable not to attempt consent from a representative who is unable to consent. Their discussion of balancing the potential to overestimate incapacity seems sound to me as well. Having reviewed the protocol, I do not think this is a reportable event insofar as this does not deviate from the procedures you describe. All of the attempts to gain consent, contact persons to consent on behalf of the patient, etc. were followed. I would say that you were unable to find someone who was able to consent for the patient. If someone who might otherwise consent on behalf of the patient is impaired to the extent that she cannot consent, we would do the patient a disservice if we relied on her impaired judgment to either enroll or not enroll in the study...better in such a situation to enroll the patient under EFIC.

Questions????

- [Protectiii.com](https://protectiii.com)

Interesting Cases

- The patient was enrolled under EFIC with the mother present. The mother did not want to give consent, and wanted to wait for the wife of the patient to arrive. The mother verbalized no objection, but did not want to be the LAR.

Interesting Cases

- Consent was signed by someone who stated he was the subjects brother
- After the subject improved and was approached for consent he stated that the person who gave consent was “Harley Brother”, not a biological brother.