Enrolling Non-English Speaking Participants in Clinical Research: Regulatory and Practical Considerations

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Dr. Roberto Torres
Director of Business Development, Puerto Rico Consortium for Clinical Investigation
About Schulman IRB

- Established in 1983
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- Compliant with FDA, OHRP and Health Canada requirements

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- **Institutional biosafety committee (IBC) services** for clinical, pre-clinical and non-clinical research
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About Today’s Presenters

Michele Russell-Einhorn, JD
VP of HRP Services and Institutional Official, Schulman IRB

- VP Oncology; VP Human Research Protection Services
- Co-Chair, Subpart A Subcommittee, SACHRP
- Founding member, NCCN IRB Directors Forum
- Previously served as Senior Director, Dana Farber Cancer Institute, Office for Human Research Studies
- Lawyer by training
About Today’s Presenters

Dr. Roberto Torres
Director of Business Development
Puerto Rico Consortium for Clinical Investigation (PRCCI)

- Before joining PRCCI, served as Director of Operations at a Global Site Management Organization
- Past experience also includes conducting behavioral research in infectious diseases as well as Operations Manager and Research Coordinator roles for cancer, blood disorders, and Phase I oncology studies
- Bachelors degree in Science and Psychology
- Masters degree in Organizational Management
- Doctoral in Health Administration
- Publications on Informed Consent and Communication with LEP
- Research interest in research related to possible adverse events associated with communication and language barriers during informed consent processes and standards of care practices
Objectives

- Define the regulatory requirements for enrolling non-English speaking subjects
- Describe the unique planning and processes necessary when working with non-English speaking subjects
- Discuss practical ways researchers can plan for and work with non-English speaking subjects
Regulatory Considerations
Belmont Report

Principle of Justice

Subject selection criteria should be fair and appropriate.

No group should be unduly burdened by the benefits and risks of the research.
Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
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Concerns Regarding Non-English Speaking Participants

- A participant or LAR who does not speak English may not fully understand the information presented
- Thus consent might not be informed, and consent might not be legally effective

Excluding participants simply because of a language barrier is a questionable practice

- Ethical mandate for equitable selection of subjects: exclusion of subjects who do not speak English can bias the research and inappropriately exclude populations who could benefit from research
Excluding Non-English Speakers

- Federal Guidance regarding enrollment of non-English speakers in research is limited

- IRB policies vary widely in terms of the depth and detail of guidance documents and policies

Best practice to permit this only where there is a sufficient justification to limit the population based upon language
Possible Reasons to Exclude Non-English Speaking Subjects

- Early phase clinical trials without a prospect for direct benefit, that will enroll only a limited number of subjects
- Studies without a prospect for direct benefit and with procedures that are greater than minimal risk
- Assessment tools, surveys, questionnaires or psychological tests that are only available in English
- Enrollment required in situations where translators will not be readily available (satellite clinics, after regular working hours, emergencies, etc.)
- Expectation based on experience that non-English speakers will rarely present to the clinic where enrollment will take place
PROCEDURES

- Am I eligible to create a Baseline Profile? You can create a Baseline Profile if you are:
  - 18 years of age or older
  - A U.S. resident
  - Able to speak and read English or Spanish
  - Not working on Project Baseline, including the Baseline study
  - Willing and able to provide your health information, including your health records and insurance claims data
  - Willing and able to sign this form

Source: https://baseline.google.com/enroll/start
Regulatory Requirements

- Regulatory Elements 45 CFR Parts **46.116** and **46.117**
- FDA requirements 21 CFR Parts **50.25** and **50.27 (b[2])**
- **Revised regulations**: Additional elements
Regulatory Requirements

Information must be presented “in language understandable to the subject”

AND

In most cases, “informed consent be documented in writing”
Consent for Non-English Speaking Participants: Long Form Consent

Subjects who do not speak English should be presented with a consent document written in a language understandable to them

- The full English language consent can be translated into another language
- The form may be read to the subject or the subject’s legally authorized representative (LAR)
- Shall be given to the subject or LAR with adequate opportunity to read it before it is signed
- FDA recommends the translation of the long consent form
Consent for Non-English Speaking Subjects: Short Form Consent

- **45 CFR 46.117(b)(2)** permits oral presentation of informed consent in conjunction with a short form written consent document and a written summary of what is presented orally
  - A witness to the oral presentation is required
  - Subject must be given copies of the short form document and the summary
Short Form Consent

Signature Requirements

- Short form document should be signed by the subject or subject’s LAR
- Summary should be signed by the person obtaining consent
- Short form document and summary should be signed by the witness
  - A translator may serve as a witness
Short Form Consent

- Long form English consent may serve as the written summary (OPRR 1995 guidance document)
- Witness must be fluent in English as well as the subject’s language (OPRR 1995 guidance document)
- Witness and translator can be the same person (OPRR guidance document)
- Short form should be used for unexpected situations, not when it is expected that non-English speakers will be enrolled in the research (FDA guidance 1998)
The witness may be the translator (OPRR 1995 Guidance Document)

FDA recommends translation of the full consent form (1998 FDA guidance)

FDA notes that “routine ad hoc translation of the consent document should not be substituted for a written translation”
Consent is an ongoing process

- Translation of the long form consent or provision of a short form is only the beginning of the responsibility to ensure ongoing comprehension and the ability of the participant to be in the study.
Waiver of Documentation

- IRB may waive documentation for consent if the research is minimal risk
- And consent procedures would not normally be required outside of the research context

OR

- The main risk of the study would be potential loss of confidentiality and the consent document would be the only record linked to the subject

45 CFR 46.117(C), 21 CFR Part 50.27(C)
The IRB approves:
- The full English language informed consent
- The English version of the short form consent
- The translation of the short form consent (this can be expedited if the English version was approved by the convened IRB)
Template Short Form Consents

- OHRP has a templated short form consent

FDA requires the following language in a consent:

“A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”
Optional Research

- A short form consent should include signature lines for optional research studies.
Signatures

A short form consent should include signature lines for:
1. The participant
2. An LAR
3. Assent line
4. Signature of parent
Revisions to the Common Rule

- Revisions to the Common Rule include **one new basic element**
  - Notice about possible future research use of information or biospecimens stripped of identifiers
- **Additional elements of consent**
  - Notice about possible commercial profit, and whether subject will share in this profit
  - Notice about whether clinically relevant research results, including individual research results will be given to subjects, and if so, under what conditions
  - Notice about whether research might include whole genome sequencing (for research involving biospecimens)
Practical Applications
Puerto Rico Consortium for Clinical Investigation

**PRCCI Vision**
To promote and enhance clinical research & development for the benefit of patients, the Puerto Rican economy and global scientific innovation.

**PRCCI Mission**
To improve the impact, quality, and speed of clinical research in Puerto Rico through: Building a Collaborative Network of investigators, Establishing Best Practices for the conduct of clinical trials, and Educating Patients, Sponsors and Researchers.

Source: istock.com/Grafner
**Important Definitions**

- **Back Translation**: Process of translating written materials from one language to another and then, in a separate process, translates the document back into the original language.
  - This process is performed to evaluate the quality and integrity of the information being translated.

- **Certified Translator**: A professional translator who has successfully completed a certification program or exam providing them with certified translator credentials.

- **Interpreter**: Person who accompanies researchers, in real time, to convey verbal information to another person in their native language.

- **Medical Interpreter**: An interpreter who is familiar with medical terminology.

- **Non-English Speaking**: Unable to comprehend English language.

- **Translator**: Person who converts written materials from English to another language.

- **Witness**: An individual who is fluent in both English and the necessary foreign language who will be physically present during the consent process to observe the process and sign consent forms.

- **LEP**: Limited English proficiency.

Source: [University of Pittsburgh Human Research Protection Office](https://www.upmc.edu/research/human-research-protection-office)
Sponsors and CROs Can Access a Large Diverse Population in the United States

Hispanics are forecasted to make up to 25% of US population by 2030 from the current 17% (2013)

At the same time, they are currently estimated to represent only 7.6% of clinical trials participants in the US

- 2015 # of Spanish Speakers = 41 Million (14% of population)
- Followed by 3.3 Million Chinese/Diverse dialects
- 57 million people or 20% of the populations speaks a language other than English
- 25 million or 8.6% defined as LEP

Examples of Hispanic Population, Accessible within States Area, Is Also a Point of Attraction to Pharma Companies

Sponsors and CROs can access a large Hispanic patient population, which is essential for ensuring fair representation in clinical trials and ultimately better patient outcomes.

Source: Centers for Disease Control, National Institute of Health, US Census Bureau 2014 National Population Projections, PwC Analysis
PROBLEM

- Barriers of communication between physician/investigators and research participants are affecting the informed consent process during clinical trials.
Purpose of the Study

Purpose

- Qualitative case study at a North Texas Research Institution
  - Explore if communication barriers affect the understanding of LEP research participants IC process
  - Review emerging themes
  - Recordings and transcription
  - Open-ended semi-structured interview

Sample

- Providers/Principal Investigators
- LEP
- Interpreters
Significance of the Study

- Scientific research and medical innovation
  - Recruitment of diverse ethnic groups
  - Study outcomes
  - SAE & AEs
  - Ethical concerns
- Promote clear communication environments
- Increase participation
- Clean data
- Safer scientific investigations
- Leadership quality improvement processes
- IRB approval strategies
Research Questions

The central questions of this study were:

- Determine communication barriers during the informed consent process
- What other factors attributed to communication barriers
- Discover precedents that may emerge as negative procedures in the informed consent process with LEP participants
- Determine if emerging characteristics were shared among the three groups investigated
Research Design

Qualitative Case Study

- Explore communications barriers from the perspective of clinical trials participants’ experiences
- Pilot study
- Semi-structured interview
- Triangulation
- Diverse data sources (PIs, Interpreters, LEP)
- Identification of themes
- Reduce limitations and biases
- Participants
- Informed consent process
Study Data Collection

Data Collection

- Interview lasted between 30 to 45 minutes
- Semi-structured interview questions
- Private conference room
- Audio recording device
- Open statements
- Review of IRB approved ICF
- Evaluation interview process by participants (Pilot Study)
- Demographic Information

Analysis Methods

- Nvivo 9 software
## Study Findings – Principal Investigators Group

### Principal Investigators

<table>
<thead>
<tr>
<th>Organization challenges: SOC vs research</th>
<th>Lack of financial support from research sponsors</th>
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</thead>
<tbody>
<tr>
<td>Length of the ICF</td>
<td>AEs due to communication barriers</td>
</tr>
<tr>
<td>Educational level of patients</td>
<td>Cultural sensitivity</td>
</tr>
<tr>
<td>Understanding of medical procedures</td>
<td>Doctors as authority figures</td>
</tr>
<tr>
<td>Limited access to adequate interpretation and translation</td>
<td>Interpreter’s emotional involvement</td>
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<tr>
<td>Need for certified interpreters knowledgeable of specific therapeutic areas</td>
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Principal Investigators’ Expressions

“We have a less difficult time recruiting Hispanics. They trust the white coat as an authority figure, meaning they will sign anything you put in front of them.”

“If they are LEP and unsophisticated, they are going to sign anyway because they trust me as a doctor, as a good doctor. They are not going to read a paper they cannot read if the consent is in English no matter if a translator is present or not.”

“I place trust in interpreters to understand and translate the communication and documents clearly, the communication barriers begin if the interpreter starts crying in front of the family: a negative message is portrayed to the family.”
Study Findings – Interpreters Group

### Interpreters

| Understanding role of interpreters during the IC process | Patients see doctors as the person to cure their child |
| Knowledge of clinical trials | Providers’ time spent discussing ICF |
| Perceptions of communication barriers | Ad hoc interpreters |
| Reservations about patients’ understanding of the ICF | Communication is a complex process and situational experience |
| Physicians established as a persuasive role | Communication is more than language |
| Provider vs researcher roles | Country of origin, meaning of words, and religion |
Interpreters’ Expressions

“Communication barriers are present all the time. Even though I speak Spanish or English to someone else does not mean the information is getting through clearly.”

“American healthcare has its own elements, sometimes, when we are trying to explain, is hard because those elements do not exist in other countries.”

“Communication does not have to do with language or grammar. By using one term or another, the origin from Mexican Spanish to Argentinean Spanish and all the Latin American cultures of Spanish speaking cultures communication can still be a barrier.”

“Research does not mean the same from here to South America. If you want to cross the communication barrier gap, investigators have to cross the cultural gap. Every person has different beliefs.”
Study Findings – LEP Group

**Limited English Proficiency**

<table>
<thead>
<tr>
<th>Perception of doctors as authority</th>
<th>Problems understanding research language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s illness: parents want their child to be cured</td>
<td>Length of document and high level of words</td>
</tr>
<tr>
<td>Doctors have the knowledge to cure</td>
<td>Do not know what research is</td>
</tr>
<tr>
<td>Role of patients invited to participate in a clinical trial</td>
<td>Communication is a situational experience</td>
</tr>
<tr>
<td>Challenges to understand clinical personnel/NO interpreters</td>
<td>Cultural &amp; religious beliefs</td>
</tr>
<tr>
<td>No documents in the primary language</td>
<td>Trust</td>
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</table>
LEP Expressions

“An interpreter was with the doctor, but I could not understand what the interpreter was saying. The conversation was confusing; our language was not the same.”

“I remember my child was very sick. I took him to the hospital, and the doctors found a virus. I was taking her to the ear doctor and they explained to me about the virus and made me sign some forms. I believe the study was done to learn more about the condition that my child had.”

“Sorry, I do not understand the difference between standard of care and research. I just brought my child to the appointments they gave me at the clinic. I do not know what clinical trials are.”

“I was confused. I was not able to understand what the doctor wanted to do to my child. The doctor showed me some papers and I signed them.”
My Recommendation: Key Process for LEP Trial Participation

1. **Identify Patient**
   - Review databases to identify patient based on protocol criteria

2. **Study Patient Medical History**
   - Review patient history, identify possible language barriers

3. **Review Protocol and ICF**
   - Review ICF to determine use of short form or full translated form

4. **Interpreter Needed**
   - Identify interpreter and communication method (F to F, video)

5. **Consent Patient Meeting**
   - Determine how interpreter will be involved

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Puerto Rico Consortium for Clinical Investigation
Address Root Causes

- Develop strategies and systems among LEP by strengthening interpreter services
- Improve interpreter’s coordination
- Translated materials
- Training for healthcare providers/investigators
- Develop dedicated services for interpretation during clinical trials
- Provide patients with written materials
- Create mechanisms to schedule an interpreter automatically before research visits
- Train staff on team communication, use of interpreter’s services, cultural competency
Recommendations

- Recognize communication barriers
- Train interpreters on specific therapeutic areas
- Documents written in the primary language of the patients
- Need for resources, certified interpreters, personnel, translation budgets
- Need for IRBs’ regulatory policies for LEPs’ documentation and interpretation
- Holistic view of clinical trials communication process
- Continue training and reinforcements
- Development of cultural approaches education
Recommendations (cont’d)

- SOC vs Clinical Trial
- Promote difference from SOC to research consents
- Differences between cultures and countries towards research
- Develop systems to routinely monitor participants’ safety
- Develop safety reports
- Create routine forums for analyzing cases of LEP enrolled in clinical trials to better understand root causes and high-risk scenarios
- Develop strategies for improvement and error prevention
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