Clinical Trial
Diversification
Better Practices

TOPIC 5: INFORMED CONSENT SHORT FORM
Guidance for Gaining Informed Consent from Subjects with Low Health Literacy and/or Limited English Proficiency

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Version 1.2

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Clinical trial populations are often not reflective of the target population who will use the medicine:

• Drug safety and efficacy can vary across demographic sub-groups
• Minorities have historically been under represented in clinical trial populations
• Addressing the lack of diversity in clinical trial populations is an on-going challenge for sponsors

The status quo is being challenged:

• The racial/ethnic sub-group population is growing and will soon no longer be a minority
• Marketing approvals are expected to become more stringent as regulatory authorities request more representative trial populations
• Patients, physicians and payers are increasingly demanding evidence of sub-group health outcomes
• The drive towards personalized medicine will likely require sponsors to be more expansive in their recruitment practices

KEY QUESTION:
How can sponsors improve racial/ethnic diversity in clinical trial populations to better reflect the targeted population?

Recommendation:
The Clinical Trial Diversification initiative recommend sponsors consider the use of the Informed Consent Short Form and encourage sites to do the same in order to increase recruitment and retention of patients with low health literacy and / or limited English proficiency.
Sponsors face increasing pressure to ensure clinical trial populations reflect the disease state.

### Changing pressures to ensure representative diversity in clinical trial populations:

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory / Political</td>
<td>Regulators are increasingly focused on ensuring trial populations are representative of the indicated population</td>
</tr>
<tr>
<td>Scientific</td>
<td>The standard practice of generalizing scientific conclusions is challenged by the demand for personalized medicine</td>
</tr>
<tr>
<td>Commercial</td>
<td>In the US, traditional minority populations are growing rapidly and expected to become the majority</td>
</tr>
<tr>
<td>Social Responsibility</td>
<td>Broad recognition of the need to develop drugs with all patients in mind</td>
</tr>
</tbody>
</table>

**Current FDA guidance**<sup>[1]</sup> states:

“Although FDA has long requested race and ethnicity data on subjects in certain clinical trials, the Agency has not previously made explicit recommendations on the categories to use when collecting and reporting the data.”

**However, minority populations generally remain under-represented in clinical trial populations**<sup>[2]</sup>

- African Americans represent 12% of the U.S. population but only 5% of clinical trial participants.
- Hispanics represent 16% of the U.S. population but only 1% of clinical trial participants.

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Objectives and Target Audience

THE OBJECTIVES OF THE FOLLOWING CONTENT IS TO:
Provide sponsor companies with tools to increase clinical trial participation for patients with limited English proficiency and low health literacy/numeracy.

Content provided in this presentation is intended for sponsor company resources responsible for supporting trial operations and / or overseeing site selection/feasibility, site training, patient enrollment and informed consent form use and development, including*:

Clinical Operations
(Protocol Managers & Site Managers)

Site Monitors

Any person with responsibility for improving trial diversity

*Sponsor companies should also consider using the information contained in this slide deck within their own communications with sites and PIs
Sponsors are coming under increasing pressure to achieve representative diversity


<table>
<thead>
<tr>
<th>Year</th>
<th>White</th>
<th>Non-white</th>
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</thead>
<tbody>
<tr>
<td>2015</td>
<td></td>
<td></td>
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<tr>
<td>2020</td>
<td></td>
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<tr>
<td>2025</td>
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<td>2055</td>
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</tr>
<tr>
<td>2060</td>
<td></td>
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</tr>
</tbody>
</table>

By 2020, “minorities” are projected to account for over 40% of the nations population[^1]

By 2050, Hispanics will make up to 29% of the U.S. population[^1]

Use of non-English languages is expected to continue growing in the US\textsuperscript{[1]}

\textbf{Number of Hispanic Spanish Speakers in the U.S., Actual and Projected, 1980-2020}
\textit{(in millions among Hispanics ages 5 and older)}

\begin{itemize}
\item 1980: 10
\item 1990: 15
\item 2000: 30
\item 2010: 35
\item 2020 (projected): 40
\end{itemize}

Notes: Projections for 2010 to 2020 indicated by broken line.

Efforts to build clinical trial diversity must address the needs of patients with limited English proficiency and/or low health literacy.

In 2010, 25.2M U.S. residents (8.6%) spoke English less than "very well" (in some states, this is nearly 20%) [2]

Limited health literacy affects adults in all racial and ethnic groups [2,3]

Over 50% of U.S. adults have basic or below basic quantitative literacy and are challenged by numerical presentations of health, risk, and benefit data [4]

Each dot represents 100 Spanish people who speak English "less than very well" [1]

Consent form wording complexity and document length is associated with lower clinical trial retention rates[1]

The Short Form accompanied by a presentation may offer a more patient-friendly option for obtaining consent:

<table>
<thead>
<tr>
<th>IF…</th>
<th>THEN…</th>
</tr>
</thead>
<tbody>
<tr>
<td>A subject or their legally authorized representative: 1. Is unable to read or understand English or 2. Is unable to read due to illiteracy or blindness or 3. Has low literacy and/or numeracy</td>
<td>The Short Form process may be considered for use[2]: 1. Information contained in the consent long form must be orally presented, with assistance from an interpreter if needed, in the same quantity and quality in person or via video recording 2. Presentation must be witnessed by an impartial person not otherwise connected with the clinical investigation 3. Short form is signed after the presentation 4. Subject is provided with a translated version of the written summary (usually the long consent form) and a copy of the short form 5. Witness must sign both the short form and the written summary.</td>
</tr>
</tbody>
</table>

[1] CISCRP Public and Patient Perceptions & Insights Series 2015, subjects were approximately twice more likely to drop out than complete if they reported that it was 'Somewhat/Very Difficult' to Understand the Informed Consent Form.
Informed Consent
Patients with Limited English Proficiency (1/2)

Different processes should be considered when languages are anticipated versus unexpected:

**EXPECTED LANGUAGE**

- Translated Informed Consent Form (ICF) can be IRB-approved and readily available
- Either long form or short form with written summary can be translated prior to study initiation
- PIs should provide IRBs with description of how interpreters will be made available during consent process
- During Site Feasibility and Selection, sponsors may proactively request translation needs

**UNEXPECTED LANGUAGE**

Non-English speaking patient identified as eligible but no IRB-approved translation of long form or short form with written summary are available.

**Options:**

- Assess length of enrolment period and have patient return at later date once forms are translated and approved
- Use IRB approved generic short forms that have already been translated into multiple languages (PI must consult with IRB to determine there is sufficient justification for not waiting for a translated long form to be approved by the IRB)

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Informed Consent
Patients with Limited English Proficiency (2/2)

Short form procedure for obtaining and documenting informed consent when the language is unexpected[1]:

1. Determine if there is sufficient justification to consent patient without a translated long form:
   Investigator and IRB determine criteria to justify when to consent patients without waiting for translated long form. Investigator then considers each circumstance and whether the consent process will provide sufficient information for the patient to make an informed decision.

2. Obtain and document the subject’s informed consent:
   Prerequisite: Translated, IRB-approved generic short form must be available in a language understandable to the patient.

   PI, with the assistance of an interpreter if needed, provides oral presentation of information in the consent long form. Impartial third party witness must be present who is fluent in the oral presentation language.

   Patient signs and dates short form and is given the IRB-approved translated short form and a copy of the IRB-approved English version of the long form (written summary).

3. After subject has been enrolled, the Investigator must[1]:
   Notify IRB of enrollment if the IRB has not been notified.
   Promptly obtain translated copy of IRB-approved English version of the long form.
   Promptly submit to IRB for review and approval.
   Provide to subject as quickly as possible. (21 CFR 50.27)

Informed Consent
Subjects with Low Literacy and Numeracy[1]

Sponsor, clinical investigator and IRB should consider whether any modifications to the informed consent process are necessary to ensure that the informed consent process is understandable:

Elements of informed consent may be presented to the subject or the subject’s legally authorized representative

When doing so, the IRB may want to consider approving the use of the short form and written summary.

The presentation must also be witnessed and witness signature entered in ICF.

Subject or legally authorized representative must sign the ICF.

Subject who cannot write may “mark” the ICF, where allowed by local law; Investigator to document reason for mark versus signature in subject’s chart.

Summary of Differences Between Short and Long Consent Forms

**CONSENT SHORT FORM**

- 2-3 pages
- Translated versions only need to be prepared once (Generic content)
- Easier for the subject to comprehend
- May enable non-English speaking patients to be enrolled in trials as quickly as English-speaking patients

**CONSENT LONG FORM**

- Varies (can be over 20 pages) General & study specific content
- Versions need to be created for each study and each language
- Complex language
- High numeracy especially describing risks

**Short Form signature summary:**

<table>
<thead>
<tr>
<th>RESPONSIBLE</th>
<th>SIGN AND DATE</th>
<th>PROVIDE DOCUMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigator</td>
<td>Copy of IRB-approved English version of long form (written summary)</td>
<td>File copy of signed short form and English version long form</td>
</tr>
<tr>
<td>Subject</td>
<td>Short form</td>
<td>IRB-approved, translated short form, English version of long form, and later, translated long form.</td>
</tr>
<tr>
<td>Witness (Interpreter may serve as witness but not person obtaining consent)</td>
<td>Short form and copy of IRB-approved English version of long form (summary)</td>
<td></td>
</tr>
</tbody>
</table>

Considerations for Sponsors

1. Once a sponsor has a pre-translated generic short form approved by the IRB or site, that form can be used for multiple studies.

2. Study teams should assess what languages are spoken by those likely to be enrolled at any particular site.

3. Sites should be encouraged to secure appropriate interpreter services in the anticipated languages and be available throughout the course of the research.

4. Witnesses should be fluent in the language of the oral presentation - interpreters may act as witness.

5. Translations must be provided by qualified translators - certifications are recommended.

6. Sponsors will need to ensure funds for site interpreter services and, if applicable, production of video materials.

7. Sponsors may discuss informed consent process for non-English speaking patients and those potential subjects with low health literacy/numeracy. Clear documentation of process should be in place prior to site initiation. Sponsors can assist sites with developing the standard process.
Many IRBs have already made available Short Form templates that are pre-translated into multiple languages:

**Western IRB**[1] (includes 14 translations)

**Copernicus**[2]

**Local IRBs**
(e.g. Tufts[3], Northwestern[4], University of Minnesota[5], etc.)

The following template has been provided as an example of a Short Form template and may be adapted by sponsor organizations.

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See TransCelerate Website for electronic version.