Informed Consent: Understanding and Engaging Patients in Clinical Trials

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Faculty Disclosure

In compliance with ACCME Guidelines, I hereby declare:

I do not have financial or other relationships with the manufacturer(s) of any commercial services(s) discussed in this educational activity.

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Director and Associate Professor, Tufts CSDD

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Agenda

- The spirit of informed consent

- Informed consent form review – how are we doing?
  - *CISCRP P&I 2013 study; CISCRP 2014 meta analysis of published literature*

- Ongoing consent initiatives
The Spirit of Informed Consent

• Informed consent serves two purposes:
  
  – It honors and respects volunteer autonomy by requesting their permission to proceed after a balanced and informative discussion
  
  – It meets a variety of legal and regulatory needs
Public and Patient Baseline Awareness

How would you rate your general knowledge about clinical research?

(Percent report having ‘No Knowledge’ and ‘Very Little Knowledge’)

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>57%</td>
</tr>
<tr>
<td>North America</td>
<td>41%</td>
</tr>
<tr>
<td>Europe</td>
<td>54%</td>
</tr>
<tr>
<td>South America</td>
<td>62%</td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>65%</td>
</tr>
<tr>
<td>18-34 year olds</td>
<td>83%</td>
</tr>
</tbody>
</table>

Source: CISCRP, 2013 Perceptions & Insights Study; N=5,701 Respondents
# Evolving Public Perceptions

<table>
<thead>
<tr>
<th>(Percent who indicated ‘Strongly or Somewhat Agree ‘ that people who participate in clinical trials:</th>
<th>CISCORP 2013 (US)</th>
<th>Harris Interactive 2005 (US)</th>
<th>Percentage point change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Get access to the best doctors</td>
<td>61%</td>
<td>46%</td>
<td>+15</td>
</tr>
<tr>
<td>Get access to the best possible treatment</td>
<td>62%</td>
<td>48%</td>
<td>+14</td>
</tr>
<tr>
<td>Learn more about their condition and health</td>
<td>84%</td>
<td>76%</td>
<td>+8</td>
</tr>
<tr>
<td>Make a contribution to science</td>
<td>88%</td>
<td>86%</td>
<td>+2</td>
</tr>
<tr>
<td>Have a chance to receive free medicines and care</td>
<td>76%</td>
<td>65%</td>
<td>+11</td>
</tr>
<tr>
<td>Are like experimental test subjects NOT people</td>
<td>34%</td>
<td>46%</td>
<td>-12</td>
</tr>
<tr>
<td>Are gambling with their health</td>
<td>23%</td>
<td>49%</td>
<td>-26</td>
</tr>
</tbody>
</table>

Source: CISCRP, 2013 Perceptions & Insights Study; N=5,701 Respondents
### How difficult was it to Understand the Informed Consent Form?

<table>
<thead>
<tr>
<th></th>
<th>OVERALL</th>
<th>FEMALE</th>
<th>MALE</th>
<th>NA</th>
<th>SA</th>
<th>EU</th>
<th>Apac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all difficult</td>
<td>43%</td>
<td>50%</td>
<td>35%</td>
<td>48%</td>
<td>6%</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td>Not very difficult</td>
<td>38%</td>
<td>36%</td>
<td>41%</td>
<td>40%</td>
<td>31%</td>
<td>35%</td>
<td>20%</td>
</tr>
<tr>
<td>Somewhat difficult</td>
<td>15%</td>
<td>11%</td>
<td>18%</td>
<td>10%</td>
<td>37%</td>
<td>35%</td>
<td>49%</td>
</tr>
<tr>
<td>Very difficult</td>
<td>4%</td>
<td>2%</td>
<td>6%</td>
<td>4%</td>
<td>26%</td>
<td>6%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Compared to past surveys, a higher percentage considers the informed consent form difficult to understand. Whereas 13% of study volunteers rated their informed consent forms as ‘Somewhat Difficult’ or ‘Very Difficult’ to understand in 2005, 19% did so in 2013.

Source: CISCRP, 2013 Perceptions & Insights Study; N=1,724 Respondents Who Have Participated
Informed Consent Form Review

• Overall, nearly six out of ten study volunteers read the informed consent form by themselves and then review it with study staff. A significantly lower percentage of study volunteers outside North America with 30% of South American, 46% of European and 23% of Asia Pacific study volunteers report doing so.

• Approximately one in four study volunteers read the informed consent form with study staff -- the highest percentage (50%) review the form with study coordinators. A significantly higher percentage of study volunteers in South America and Asia Pacific review the informed consent form with the principal investigator.

• One in ten study participants do not review the informed consent form with any one, with nearly double that percentage (18%) of study participants in South America reporting that no one reviewed the informed consent with them.

Source: CISCRP, 2013 Perceptions & Insights Study; N=1,724 Respondents Who Have Participated
What Participants Most Want to Talk About During Informed Consent Form Review

<table>
<thead>
<tr>
<th>Topic</th>
<th>Aggregate Percent of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information about how and when the results will be disseminated</td>
<td>91%</td>
</tr>
<tr>
<td>Purpose of the study</td>
<td>76%</td>
</tr>
<tr>
<td>How long research study will last</td>
<td>61%</td>
</tr>
<tr>
<td>Potential benefits</td>
<td>57%</td>
</tr>
<tr>
<td>Investigator conflicts-of-interest</td>
<td>48%</td>
</tr>
<tr>
<td>How confidentiality will be protected</td>
<td>44%</td>
</tr>
<tr>
<td>Potential risks</td>
<td>39%</td>
</tr>
</tbody>
</table>

Source: Kirkby et al (2012) compilation of results from 14 studies
After Reading the Informed Consent Form, I was…

<table>
<thead>
<tr>
<th></th>
<th>OVERALL</th>
<th>FEMALE</th>
<th>MALE</th>
<th>NA</th>
<th>SA</th>
<th>EU</th>
<th>Apac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Much less willing to participate</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
<td>0%</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Somewhat less willing to participate</td>
<td>2%</td>
<td>1%</td>
<td>3%</td>
<td>1%</td>
<td>11%</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Unchanged</td>
<td>44%</td>
<td>44%</td>
<td>44%</td>
<td>47%</td>
<td>24%</td>
<td>30%</td>
<td>23%</td>
</tr>
<tr>
<td>Somewhat more willing to participate</td>
<td>21%</td>
<td>18%</td>
<td>24%</td>
<td>19%</td>
<td>24%</td>
<td>34%</td>
<td>35%</td>
</tr>
<tr>
<td>Much more willing to participate</td>
<td>31%</td>
<td>34%</td>
<td>26%</td>
<td>31%</td>
<td>27%</td>
<td>25%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Source: CISCRC, 2013 Perceptions & Insights Study; N=1,724 Respondents Who Have Participated
Satisfaction with Informed Consent Review

• Overall, 85% of study participants say they are ‘Somewhat Satisfied’ or ‘Very Satisfied’ that their questions were answered during the informed consent form review process.

• A significantly higher percentage (approximately one-third) of study volunteers outside North America are ‘Not at all Satisfied’ or ‘Not Very Satisfied’ that their questions were answered during this review process.

• A much higher proportion of study volunteers (28%) in the 18-34 year-old age group were also less satisfied that their questions were answered during the informed consent form review.

Source: CISCRP, 2013 Perceptions & Insights Study; N=1,724 Respondents Who Have Participated
## Meta-analysis of Informed Consent Intervention Effects on Comprehension

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Study Source</th>
<th>Reported Improvement over Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extended Discussions</td>
<td>Freer ('09)</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>Aaronson ('96)</td>
<td>Low</td>
</tr>
<tr>
<td>Improved Layout of Paper ICF</td>
<td>Dresden ('10))</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>Campbell ('08)</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>Walters ('08)</td>
<td>Medium</td>
</tr>
<tr>
<td>Use of Multimedia</td>
<td>Bickmore ('09)</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Mittal ('07)</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>Hack ('07)</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Dunn ('02)</td>
<td>Low</td>
</tr>
</tbody>
</table>

Source: Nishimura et al 2013
<table>
<thead>
<tr>
<th>Factors Correlated with Satisfaction</th>
<th>Increased</th>
<th>No Effect</th>
<th>Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Situation Dynamics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited time to deliberate / feeling rushed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling overwhelmed by diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Being asked to give written consent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study staff appearing annoyed and impatient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study language positioned positively</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI and staff appearing friendly and dedicated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encouraging that questions be asked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant others, relatives or nurses present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Form Design/Layout</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewing ICF independently</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not enough detail in ICF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Too much detail in ICF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction of non-treatment-related info in ICF</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Nishimura et al 2013
### Meta-analysis of Informed Consent Form Factors Correlated with Enrollment Performance

<table>
<thead>
<tr>
<th>Factor</th>
<th>Increased Enrollment</th>
<th>No Effect</th>
<th>Decreased Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of easy-to-read consent form or tailored brochures/forms or audiovisual patient information or use of multidisciplinary educational session</td>
<td><strong>Green</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contribution of standard IC form on decision to participate</td>
<td></td>
<td><strong>Yellow</strong></td>
<td></td>
</tr>
<tr>
<td>Length and complexity of form</td>
<td></td>
<td></td>
<td><strong>Red</strong></td>
</tr>
<tr>
<td>Lack of prior clinical research knowledge</td>
<td></td>
<td></td>
<td><strong>Red</strong></td>
</tr>
</tbody>
</table>

Source: Nishimura et al 2013
# Impact of ICF on Study Volunteer Retention

<table>
<thead>
<tr>
<th>Issue</th>
<th>Overall</th>
<th>Dropped Out (n=260)</th>
<th>Completed (n=1326)</th>
</tr>
</thead>
<tbody>
<tr>
<td>It was ‘Somewhat/Very Difficult’ to understand the ICF</td>
<td>19%</td>
<td>35%</td>
<td>16%</td>
</tr>
<tr>
<td>After reading ICF, the purpose of the study was ‘Not Very/Not At All Clear’*</td>
<td>5%</td>
<td>14%</td>
<td>2%</td>
</tr>
<tr>
<td>‘Not Very/Not At All Satisfied’ questions were answered during IC review*</td>
<td>4%</td>
<td>12%</td>
<td>1%</td>
</tr>
<tr>
<td>I still did not understand parts of the study after ICF review*</td>
<td>12%</td>
<td>22%</td>
<td>11%</td>
</tr>
</tbody>
</table>

*Dropped Out vs. Completed significantly different at P<0.05

Source: CISCRP, 2013 Perceptions & Insights Study
Key Takeaways

- Volunteer satisfaction less associated with ICF document design and comprehension than with discussion, and the relationship, with study staff

- Information needs vary suggesting customized and variety of formats

- Evidence of association between informed consent process effectiveness and retention
The Spirit of Informed Consent

• Informed consent serves two purposes:
  – It honors and respects volunteer autonomy by requesting their permission to proceed after a balanced and informative discussion
  – It meets a variety of legal and regulatory needs
  – Consent is a dynamic property of partnership – the parties trust one and other to share information, to solicit and exchange ideas and feedback
2010 Focus Groups with Study Volunteers

Conducted by the CISCRP

• Readily and consistently affirm the essential role of study staff to influence decision to begin and complete participation

• Identified four core needs driving engagement:
  • Want to feel that they are in control
  • Want to be personally connected to study staff
  • Want to be treated with respect
  • Want to know that their participation will matter/mattered

• Unanimous agreement that being in a clinical trial is an unusual and profound experience that leads study volunteers to affiliate with a unique community
Top Reasons Why Volunteers Chose to Participate

- 85% Receive medical care and attention
- 83% Gain access to medical experts
- 79% Learn about my disease
- 71% Receive my trial results after the study has ended
- 68% Receive regular updates about the research during my trial

Source: CISCRP, 2013 Perceptions & Insights Study, N= 1,724 Respondents who have participated
## Top Five Motivations to Stay in a Study

<table>
<thead>
<tr>
<th>Motivation</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free care and procedures I received</td>
<td>20%</td>
</tr>
<tr>
<td>Information I learned during my participation</td>
<td>23%</td>
</tr>
<tr>
<td>My relationship with study staff</td>
<td>26%</td>
</tr>
<tr>
<td>Desire to keep honor my commitment</td>
<td>34%</td>
</tr>
<tr>
<td>Compensation I received</td>
<td>37%</td>
</tr>
</tbody>
</table>

Source: CISCRP, 2013 Perceptions & Insights Study, N= 1,724 Respondents who have participated
How often did you receive updates while enrolled in your clinical research study?

<table>
<thead>
<tr>
<th></th>
<th>OVERALL</th>
<th>FEMALE</th>
<th>MALE</th>
<th>NA</th>
<th>SA</th>
<th>EU</th>
<th>Apac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don’t remember</td>
<td>21%</td>
<td>24%</td>
<td>18%</td>
<td>22%</td>
<td>8%</td>
<td>20%</td>
<td>8%</td>
</tr>
<tr>
<td>Never</td>
<td>18%</td>
<td>20%</td>
<td>16%</td>
<td>19%</td>
<td>6%</td>
<td>14%</td>
<td>7%</td>
</tr>
<tr>
<td>Multiple times per week</td>
<td>35%</td>
<td>31%</td>
<td>39%</td>
<td>31%</td>
<td>78%</td>
<td>44%</td>
<td>74%</td>
</tr>
<tr>
<td>Monthly</td>
<td>26%</td>
<td>25%</td>
<td>27%</td>
<td>28%</td>
<td>8%</td>
<td>22%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Source: CISCRP, 2013 Perceptions & Insights Study, N= 1,724 Respondents who have participated
What did you do after finding out that you did not qualify for a study?

- 35% Searched for Another Clinical Trial
- 23% Decided not to Participate
- 42% Nothing

Source: CISCRP, 2013 Perceptions & Insights Study, N= 1,647 Respondents who wanted to, but did not, qualify
## Lay Language Results to Volunteers

<table>
<thead>
<tr>
<th>STUDY VOLUNTEERS</th>
<th>RESEARCH PROFESSIONALS</th>
<th>REGULATORY AGENCIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 90% want to know the results of their clinical trial&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• 98% of study staff would like to provide results to their volunteers&lt;sup&gt;4&lt;/sup&gt;</td>
<td>• Declaration of Helsinki obligates sponsors and research professionals to offer study results (2013; Guideline 26)</td>
</tr>
<tr>
<td>• 91% never hear back from study staff or sponsor&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• 95% of research ethics board chairs strongly support (Canadian survey)&lt;sup&gt;5&lt;/sup&gt;</td>
<td>• FDAAA 2007 results disclosure required on ClinicalTrials.gov; TEST Act of 2012 (H.R. 6272) seeks to expand requirements</td>
</tr>
<tr>
<td>• A top five reason why patients participate</td>
<td>• PhRMA and EFPIA: a key principle of responsible data sharing (July 2013)</td>
<td>• EU Clinical Trials Regulation requires narrative summaries beginning mid-2016</td>
</tr>
<tr>
<td>• If not informed, 68% would not participate in future trials&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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The Trial Results Communication Process

- **Informed Consent**
  - Sponsors include explanation that volunteers will receive a trial result summary in plain language

- **Last Visit**
  - CISCRP provides sites with “Thank You” communication for distribution to volunteers at last visit; explains timing for receipt of trial results

- **Reminders Every 6 Months**
  - CISCRP provides sites with post-trial education for their volunteers at intervals, until results are ready; includes updates on expected trial end date

- **Trial Results posted ClinicalTrials.gov**
  - CISCRP engages editorial panel and provides sites with lay-language summary of trial results in print, audio and webpage formats to be delivered to study volunteers

**Set Expectations**

**THANK Volunteers**

**Ongoing Communications**

**Report Results**
Top 50 Sponsors Planning and Executing Results Communication Programs
CONTRIBUTION AND COMMUNITY

Partnership with Patients and the Public

AWARENESS AND EDUCATION

ENRICHED PARTICIPATION EXPERIENCE

A Model of Patient Engagement
Q&A and Thank You!

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Founder and Chairman, CISCRP