Advancing International Pediatric Clinical Research

PART THREE

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

28 June 2022
9:00-11:00 AM EDT

This series is supported by an FDA Scientific Conference Grant.
Our Vision
Improve the integrity, safety, and rigor of global clinical trials.

Our Mission
Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.
Where we started & why this is important:

- Children **deserve access** to safe and effective medicines
- Children **historically excluded** from or underrepresented in research
- **Pediatric population widely dispersed** so clinical trials must be conducted in multiple jurisdictions
- **Persistent ethical issues**: while governing ethical principles may be generally agreed upon, differences in interpretation and application of principles exist
- Differing or nonexistent pediatric **regulations**
- Challenges in **trial initiation and conduct**
- The **pediatric patient and family voice** is not routinely solicited nor included in research life-cycle.
- **Children are not routinely offered a seat at the table.**
Project objectives

Broadly, sought to identify and propose solutions to regulatory, ethical, and operational challenges

- Current global landscape of pediatric research governance, focusing on legislative, regulatory, and guidance gaps and inconsistencies
- Identify current initiatives to improve pediatric research globally
- Identify challenges related to decision making by and on behalf of children
- Address benefit and risk considerations that create barriers and inefficiencies in transnational research with children.
- Identify meaningful ways to engage patients/families/community members

- Diverse leadership (Academia, EMA, Industry, participant advocates)
- 80+ members from all stakeholder groups with geographic diversity
Webinar Series: Advancing International Pediatric Clinical Research

- Funded in part through an FDA scientific conference grant award
- 5 virtual webinars; each session planned to be hosted twice, with similar content and different speakers and panelists, to allow for wide attendance and participation.
- An offshoot of the MRCT Center’s Promoting Global Clinical Research in Children project
Advancing international pediatric clinical research—looking ahead

1. **Informing the future from COVID-19 lessons learned:**
   6 October 2021 & 7 October 2021

2. **Time to Listen—Hearing from young people in clinical research;** 2 February 2022

3. **28 June 2022 : Assent and Consent in the Field: Culture, Context, and Respect**

4. **Fall 2022: Regulatory convergence to facilitate international cooperation**

5. **Early 2023: TBD**

**Today:**

Please see ”Bio Book” for extended introductions to the speakers and panelists
Prioritizing Young People’s Voices in Clinical Research

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN’S HOSPITAL and HARVARD

The International Children’s Advisory Network Inc. (iCAN) is a tax exempt organization as described in Section 501(c)3 of the Internal Revenue Code. The views and opinions expressed in this video reflect those of the individual presenter and do not imply endorsement or reflect the views or policies of any organizations or entity. The MRCT Center is supported by voluntary contributions (www.MRCTCenter.org) and by grants.
Advancing International Pediatric Clinical Research

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

Keynote Speakers

Dr. Dylan Graetz
Dr. Victor Santana

St. Jude Children’s Research Hospital,
Department of Global Pediatric Medicine,
Department of Oncology Solid Tumor Division

This series is supported by an FDA Scientific Conference Grant.
MRCT Center Pediatrics Webinar
Assent and Consent in the Field: Culture, Context & Respect
Lessons Learned Conducting Pediatric Clinical Research in Resource Limited Settings

Victor M. Santana
Dylan Graetz
St. Jude Children’s Research Hospital
Guiding statement:
Research with children in resource-limited settings requires consideration of socioeconomic inequalities and cultural and linguistic differences.

Points to consider
- Community and Leadership hierarchies
- Influence of gender dynamics
- Verbal consent in setting of low literacy
- Social status of the researchers
- Guarding against therapeutic misconception
- Notion of assent
- Finite resources to operationalize processes
Family
“A family's understanding of disease is not (only) biological but involves spiritual and social elements (more than medical factors), which alone will not determine decision making for participation in research”.
Ethical and Policy Issues in Research Involving Human Participants
Volume I
Report and Recommendations of the National Bioethics Advisory Commission
Bethesda, Maryland August 2001
Assent and Consent in the field: Culture, Context & Respect

- Scoping review of the literature (50 articles)
- Summary of key recommendations
- Identified thematic areas where guidance is available
- Pointed to gaps in addressing individual-based consent, age related adaptations such as participation of adolescents and assent process and documentation
A proposed global framework for pediatric cancer communication research

Dylan E. Graetz, MD, MPH; Ana Cacaros-Serrano, PhD; Venkatraman Radhakrishnan, MD, DM, MSc; Carmen E. Salaverria, MS; Joyce B. Kambugu, MD; and Bryan A. Sisk, MD, MSCI

Commentary

Assent and Consent in the field: Culture, Context & Respect
Assent and Consent in the field: Culture, Context & Respect

• Child involvement
  • When and how to involve the child?
  • Should all children be involved?
  • Age of consent/assent?

• Clinician Time
  • How do you build trust without time?
Assent and Consent in the field: Culture, Context & Respect

- Decision-maker
  - Preferred decision-making role
- Analysis of risks/benefits
  - Experience of a family
- Multidisciplinary team
• Literacy/Education
  • Is written consent appropriate?

• Physical space
  • Private room? Bedside communication?
Assent and Consent in the field: Culture, Context & Respect

- Community
  - Spiritual community
  - Stigma
- Referral network
  - Traditional healers
Assent and Consent in the field: Culture, Context & Respect

- Role of medical providers
  - Deference

- Autonomy
  - Relational autonomy
Assent and Consent in the field: Culture, Context & Respect

- A model for communication, including consent, with a foundation of cultural context and respect
Advancing International Pediatric Clinical Research

PART THREE

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

PANEL DISCUSSION

Moderator
Dr. Martine Dehlinger-Kremer
Vice President of Scientific Affairs,
Pediatric Subject Matter Expert
Drug Development Solutions,
ICON PLC

Guest Speaker
Dr. Ruben Cuttica
Hospitals General De Niño's
Pedro de Elizalde
Argentina

Guest Speaker
Dr. Haleema Saeed
Shaukat Khanum Memorial Cancer Hospital & Research Centre
Pakistan

Guest Speaker
Dr. Muhammed Afolabi
London School of Hygiene & Tropical Medicine
England

This series is supported by an FDA Scientific Conference Grant.
Moderator

Dr. Martine Dehlinger-Kremer
Vice President of Scientific Affairs,
Pediatric Subject Matter Expert
Drug Development Solutions, ICON PLC
Advancing International Pediatric Clinical Research
Assent and Consent in the Field: Culture, Context, and Respect

MRCT Webinar
June 28, 2022

Dr Martine Dehlinger-Kremer
VP Scientific Affairs, Paediatric SME
Center for Paediatric Clinical Development
Drug Development Solutions
Clinical Trials on Minors and Consent

Consent

• Process by which volunteer/patient voluntarily confirm willingness to participate in a trial, after having been informed of aspects of the trial that are relevant to its decision to participate

Clinical Trials on Minors

• Parenteral/Legal Guardian consent is required
  • Frequently from the 2 parents unless the local jurisdiction requires only one parent
• Child to be involved in process of informed consent
  • Age-appropriate assent / consent
• Re-consent required if minor reaches age of legal competence
The Process of Informed Consent - Informed Consent from the Legally Designated Representative

- Informed Consent must be sought from the parents/legally designated representative on the child’s behalf
- Specific, written informed consent must be obtained prior to enrolling a child in a trial
- The person providing the information should be experienced in providing tailored research information, competent in communicating and working with children and young people, and providing them and their legal representatives with the time and space to reach a decision without pressure
- The information should be given to each parent, or legally designated representative, both in oral and written form
- The information be provided in a "comprehensive, concise, clear, relevant, and understandable" manner
- Parents/legally designated representative should be explicitly informed of their right to refuse to the child's participation, and to withdraw the child from the clinical trial at any time without any resulting detriment for the child and without having to provide any justification
Informed Consent of Families with Different Cultural Background

- Information to be adapted to the language skills and understanding of the child and the parents/legal representative
- Cultural differences may lead to misunderstandings
- Where appropriate, the investigator should arrange for translations: a translator and/or a cultural mediator to be available in the planning of the study and during the process of informed consent and assent / agreement
- This person should be familiar with medical terminology, experienced in the language, social habits, culture, traditions, religion and particular ethnic differences
Continued Consent Process during the Clinical Trial

Consent, assent and agreement, is a dynamic, continual process

Could be achieved by

- Brief discussion during trial visits and documented
- The discussion is part of the ongoing dialogue between minors, parents and investigators and should focus on new information that arises from the trial and may affect the willingness of the parents and minor to continue
- Especially in long-term trials, the investigator should follow up on a regular basis and document the evolving maturity of the child, his or her ability to assent or agree, and act accordingly

Should not only be obtained prior to enrolling a minor in a trial, but also sustained during the trial

The child should be involved in this process
Minor’s Participation in the Informed Consent Process

- Each minor should participate in the informed consent process together with the parents/legally designated representative, in a way that is appropriate to his or her age and maturity.

- Minors are to be treated as persons who have the potential from an early age to express altruism and play an active role on decisions for their own lives, within their familial and social environment.

- The central role of parents in the protection of their child should be recognized.

- To provide age-appropriate information and assent/agreement forms, separate material should be used for children, using language and communication tools (visuals, cartoons, videos etc.) appropriate to the participants’ age and maturity. It is strongly recommended to check the information material for sufficient understanding in the relevant population.
Adolescent Who is no Longer a Minor

– Once an adolescent is no longer a minor, or when he or she is an “emancipated minor”*, he or she should be asked to provide written informed consent as soon as practically reasonable, as for any adult capable of giving consent

– Informed consent is no longer required from the parents/legally designated representative

– The withdrawal of informed consent by the adolescent shall not affect the activities already carried out and the use of data obtained based on informed consent before its withdrawal

– The legal age to give informed consent varies, i.e., follows the specific jurisdiction requirements

*This is a legal term and applies under exceptional conditions: Minors can become emancipated through certain actions, such as marriage
Guidance for Informed Consent and Assents for Paediatric Trials in Europe

– Country specificities in terms of one or two parent signatures

– Country specificities in terms of age of assent and consent

Guidance for Assent / Informed Consent Preparation

Age Groups
- 0<2 Years
- 2<6 Years
- 6<10 Years
- 10<18 Years

Assent / Informed Consent Guidance for Paediatric Clinical Trials with Medicinal Products in Europe
Developed by Enpr-EMA’s Working Group on Ethics

This document is intended to be used as an overview tool of the contents for assent/informed consent forms for all stakeholders (such as patients, sponsors and investigators) to support the conduct of high quality paediatric clinical trials in Europe across all paediatric age groups, from birth to less than 18 years of age.
Patients that use eConsent have a better understanding of the study purpose, risks, benefits, schedules, and their rights and responsibilities than patients using paper.

Reference - 2013 Independent validation study conducted by California Pacific Medical Center research Institute using Enroll®
• Assent and consent follow local jurisdictions regulations
• No harmonization on legal age of consent nor on assent age groups
• Integrity, honesty, and clarity are paramount in physician-patient and investigator-trial participant relationships regardless of age
• Cultural differences are to be taken into account
• Will econsent be the future process?
Thank you

For questions, please contact us:

CenterPediatricClinDev@prahs.com
Advancing International Pediatric Clinical Research

PART THREE

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

Guest Speaker
Dr. Haleema Saeed
Shaukat Khanum Memorial Cancer Hospital & Research Centre
Pakistan

This series is supported by an FDA Scientific Conference Grant.
Assent and Consent in the Field
Culture, Context and Respect

Haleema Saeed
Pediatric Hematology/Oncology
Shaukat Khanum Memorial Cancer Hospital and Research Center
Lahore, Pakistan
Perspective from Pakistan

• Developing middle income country
• Population of 242 million, 35% are children
• Limited clinical trials and research in pediatric patients
• National bio ethics committee and Pakistan medical counsel oversee and regulate research
• Consent by legal guardian required for those under 18 years
• No requirement for assent under law
Challenges in the Field - Language

• > 60 language
• No written form
• Lack of medical interpreters
Challenges in the Field - Family structure

- Variation in decision maker
- Family involvement in decision making
- Patriarchal family structure
Challenges in the Field – Autonomy vs. Paternalism

- Overall dependence on physician to make the decisions.
- Lack of education
- Trust in physicians

Challenges in the Field – Who to ask?

- Definition of legal guardian
- Desire to shield the patient from true picture

- Even in an adult population only 15% signed consent themselves

Challenges in the Field - Lack of Time, structure and resources

High burden of clinical work
Lack of support for data collection and management
Lack of structure

The Journey of clinical research in Pediatric oncology in Pakistan

• Establishment of a dedicated cancer hospital that organized annual meetings

• Start of Fellowship program and recognition of fellowship training by National body

• Establishment of National Society (PSPO)

• Grant from WHO to start National clinical Trial.

• 3 national level clinical trials approved by NBC

Conclusion

- There are many practical challenges to conducting ethical clinical research with appropriate informed consent and assent.
- These include cultural and language diversity, lack of clearly defined laws regarding assent, complex family structures and overly paternalistic society.
- Need to think outside the box to come up with culturally sensitive solutions.
Advancing International Pediatric Clinical Research

PART THREE

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

Guest Speaker
Dr. Ruben Cuttica
Hospitals General De Niño's
Pedro de Elizalde
Argentina

This series is supported by an FDA Scientific Conference Grant.
Assent and Consent In the Field: Culture, Context and Respect

Rubén J. Cuttica, MD, Prof.
Pediatric Rheumatology Consultant
Pediatric Rheumatology Unit
Hospital Pedro de Elizalde
Buenos Aires - ARGENTINA

cutticarj@yahoo.com.ar
HOSPITAL PEDRO DE ELIZALDE
Buenos Aires - Argentina

- Children’s general hospital
- All pediatric sub-specialties
- In and out-patient facilities
- Facilities for phase I to IV clinical trials
- Internal Review Board
- Teaching and Research Department
- Facilities to store biological samples
ARGENTINA

47.000.000 Inhabitants  -  Surface 3 761 274 km²

3.081.550 in Buenos Aires City
17.875.743 (39%) living in Buenos Aires Province

60% european ancestry
ARGENTINA

39% younger than 24 y/o
55% is considered poor
median income less than 500 US$ /month
Mostly informal employment

Pandemia, isolation and uncertainty
Fear, anxiety and anguish

Severe Social and political struggle

This is the environment where we ask a patient and his family to participate in a clinical trial
## INFORMED CONSENT AND ASSENT ACCORDING TO CIVIL CODE IN ARGENTINA

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to &lt; 13</td>
<td>Informed Consent from at least one legal guardian + Informed Assent of the patient according to understanding.</td>
</tr>
<tr>
<td>13 to &lt; 16</td>
<td>Patient Informed Consent + Informed assent from at least one legal guardian <strong>in case of risk.</strong></td>
</tr>
<tr>
<td>16 to &lt; 18</td>
<td>Patient Informed Consent + Informed Assent of at least one legal guardian.</td>
</tr>
</tbody>
</table>
• Patient has some time to follow-up with the medical team.
• The first step is to explain what clinical research is and GCP in pediatric trials.
• Talk about why a patient may be admitted to the trial
• Talk about the current and trial treatment
• Talk about advantages, risks and uncertainties
• Informed consent form is given some time in advance to read it at home
• Set a new appointment to discuss about doubts and clarifications and finally make the decision to sign or not
KEYS TO A SUCCESSFUL INFORMED CONSENT

• Knowledge
• Time
• Dedication
• Privacy
• Quiet environment
• Clear explanations
• Sincerity
Advancing International Pediatric Clinical Research

ASSENT AND CONSENT IN THE FIELD: Culture, Context, and Respect

Guest Speaker
Dr. Muhammed Afolabi
London School of Hygiene & Tropical Medicine
England

This series is supported by an FDA Scientific Conference Grant.
Advancing international pediatric clinical research: Assent and consent in the field: culture, context, and respect

Muhammed Afolabi, MD, MPH, PhD, FWACP, FHEA, FFPH
Clinical Associate Professor
London School of Hygiene & Tropical Medicine, UK
28 June 2022
High preponderance of non-literate and functional illiterate populations

- 85% of juvenile criminals are functionally illiterate
- A child born to a non-literate mother is 50% less likely to survive past the age of 5 years.

Poverty: Illiteracy costs the economy USD $1 trillion each year: 2% of the GDP in developing nations, 1.2% of the GDP in emerging economies

Poor access to health care

Local languages exists in oral forms, no standardized writing formats, making translations & back-translations of ICF impractical

Large power differences between researchers and research participants

1. Poverty: Illiteracy costs the economy USD $1 trillion each year: 2% of the GDP in developing nations, 1.2% of the GDP in emerging economies

Speaking Book

Tell Your Story

Vaccines Save Children’s Lives (Wolof)
Language: Wolof
Country: Gambia
Topic: Immunization, vaccines
Sponsor: MRC BioInformatics Unit

Your Baby and Vaccines
Language: Wolof
Country: Gambia
Topic: Health Education, Immunization
Sponsor: Pfizer

https://youtu.be/TidUsnsOpgc
https://youtu.be/AMuX2DHlyfc
A multimedia consent tool for research participants in the Gambia: a randomized controlled trial

Muhammed Olanrewaju Afolabi, Nuala McGrath, Umberto D’Alessandro, Beate Kampmann, Egeruan B Imoukhuede, Raffaella Ravinetto, Neal Alexander, Heidi J Larson, Daniel Chandramohan & Kalifa Bojang
Many thanks!

- Webinar recording and slides will be posted in approximately one week
- Youth video will be also be available on YouTube
- We look forward to hearing from you
- Sign up for future webinar(s)
Thank you to our speakers, participants, and particularly the young people who shared their stories and taught us so much.

**International Children’s Advisory Network (iCAN),** producer of “Prioritizing Young People’s Voices in Clinical Research” video

All the youth who shared their time, expertise and stories with us from iCAN and Kids Barcelona
Please follow the MRCT Center

Thank you!