MULTI-REGIONAL CLINICAL TRIALS

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

INCLUDING YOUNG PEOPLE IN RESEARCH: A TOOLKIT

Resources to facilitate & support inclusion of youth in research and research-related activities

Table of Contents

Instructions for Use and Intent of Materials

These tools, checklists, and considerations are offered to assist investigators, Institutional Review Boards (IRBs)/Ethics Committees (ECs), sponsors, and those working with children and adolescents to engage youth respectfully and thoughtfully throughout the lifecycle of a clinical trial and in all phases of product development. The toolkit offerings are intended to help guide researchers towards thoughtful engagement with young people who can speak to their experiences with clinical research. We urge users to give appropriate attention to gathering perspectives from participants who can properly represent key characteristics of the study's target population, including disease, age, or geographic distribution. We provide guidance on how to ensure that their perspectives are gathered, understood, appropriately weighted, and integrated in meaningful ways. These tools are offered as considerations, not mandates, and we expect that individuals will adapt them to their local context, inclusive of cultural humility, linguistic preferences, and the "ask" at hand. We also trust that constructive feedback will be provided to those who have participated in the activity as a way of respectfully closing the loop.

Voices of the Next Generation

Process Considerations for Pediatric Patient Engagement in Research and Research-Related Activities

Inclusion of the youth voice in pediatric product development and the clinical research lifecycle is both important and inspirational.

Case Study:

An 11-year-old patient was invited to be a panelist along with three adult researchers at a national conference. The youth panelist was enthusiastic about sharing her lived experience, and her guardian supported the youth's participation. She was excited, not intimidated, and felt that "she had a story to tell."

It quickly became clear that certain process and logistical considerations had not been anticipated for the involvement of a young person in this panel. As a confirmed speaker, she was entered into the conference database as a matter of course, without consideration of her age and status as a minor. She received multiple emails asking her for materials: identifying information, brief biography, headshot, and "learning objectives" for her talk. She was given the conference PowerPoint format and instructed on the time requirement to upload her slides. She was sent requests for permission to be recorded and to share the recording after presentation on the conference website. When she did not respond, she was sent emails that were increasingly directive and likely confusing to her. At no time was her guardian included on the email communications.

Special procedures for inclusion of pediatric participants in health research-related activities must be considered in, and developed in advance of, the activity.

Intent of materials:

We offer these tools, checklists, and considerations to assist investigators, IRB/EC boards, sponsors, and those working with young people to engage youth respectfully and thoughtfully, helping to ensure that their perspectives are gathered, offered, appropriately weighted, and integrated. We also trust that constructive feedback will be provided to those who have participated.

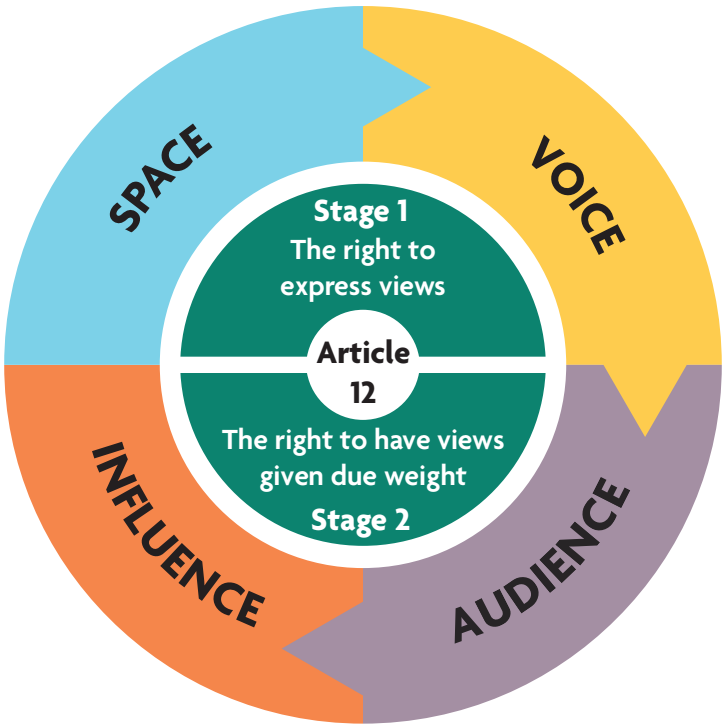
Talking to Young People:

How to Talk to Children and Adolescents about Clinical Research

The first step to respectful engagement and optimal communication with children and adolescents in the clinical research space is to set the stage for success.

The Lundy Model* describes 4 components that support a child's right to participate, express views and be heard, as laid out in Article 12 of the United Nations Convention on the RIghts of Children:

1. **Space** - this refers to an inclusive, safe environment that must be given to children to allow them to form and express their views. It goes beyond physical space to include the behavior and demeanor of researchers.
2. **Voice** - children need to be supported to understand their right to have and express views.
3. **Audience** - children's views must be heard and listened to.
4. **Influence** - this results when a space is created to give voice to children's input and the proper audiences receive and act on the information.



**Lundy Model of Participations, Lundy, L. (2007) 'Voice is not enough: conceptualising Article 12 of the United Nations Convention on the Rights of the Child' British Research Journal 33(6) 927-942.*

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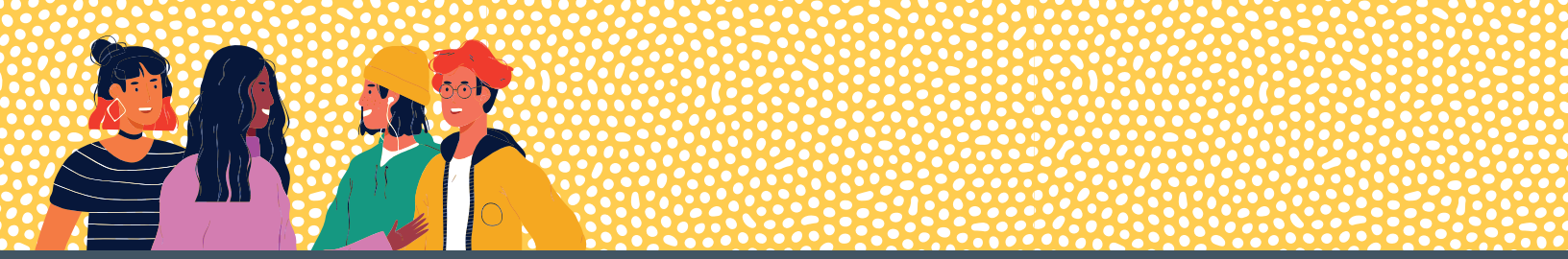


Count Me In:

Youth Assent and Parent/Guardian Permission Form for Research-Related Activities

Instructions

- This template is designed for organizations asking children and adolescents to contribute to activities other than direct participation in research, such as a conference, advisory group, video, or focus group.
- It is not to be used as an assent form for research participation.
- It is written for anyone over the age of approximately seven.
- Please note that the <<areas inside the arrows>> should be filled in with the appropriate text modified for the planned activity and the age of the child.
- When the form is printed or finalized, the arrows should be removed.
- The conversation to seek permission from the adult should occur before the conversation with the child/adolescent. Only if the parent/guardian gives permission should the young person be asked to participate.
- This form should NOT replace a conversation with the child/adolescent.
- The assent of the child or adolescent is required and should be documented.
- The parent or guardian must sign the permission form for the child's participation.*

**Certain exceptions may apply*

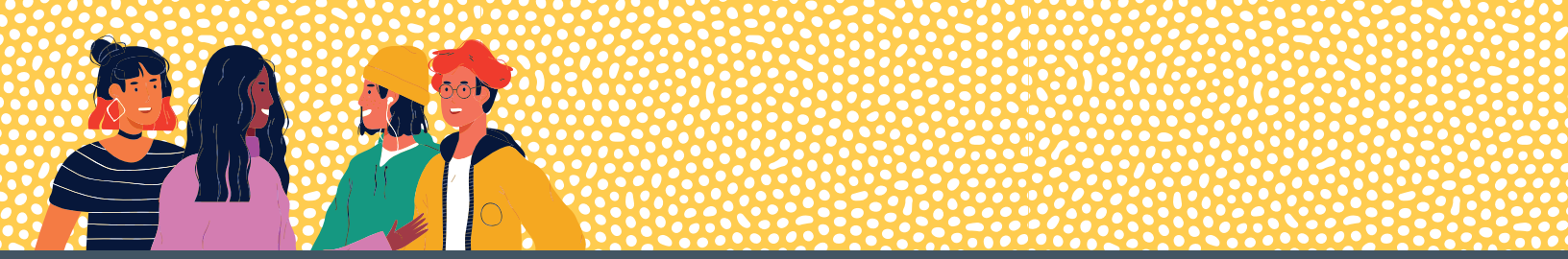
Below we include the Privacy Statement applicable to the MRCT Center and our affiliated institution. We recommend that you adapt this statement for your institution, organization, and location, and ensure it is consistent with regional, national, and local laws, regulations, and policies.

COUNT ME IN:

Your privacy is important to us. This Privacy Statement explains how the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard will collect, use, and share information about those who use our platform, access our newsletter, or receive communications from us. Learn More

Additional European Economic Area (EEA) privacy disclosures supplement the MRCT Center Privacy and Terms of Use. These disclosures apply only to how we collect, use, and share the Personal Data of individuals located in the EEA. Learn More

Mass General Brigham Website Privacy Statement



Part One: Parent/Guardian Permission for Minor Child to Participate

We ask permission to discuss <<activity>> at <<organization>> with your child. If you agree, your child will be asked to give assent to participate. The information in Part 2 below includes both the specifics of the activity and the information that will be shared with your child. Please read and review the entire form before you sign.

In brief:

<<Additional information about the requested activity>>

Please fill out and sign this form if you agree to allow your child to participate in <<activity>>. You will be given a copy of this form to keep after you have signed it.

Have you read the assent form and this permission form or has it been read to you?

Yes_____ No_____

Have all of your questions about the form and the activity been answered?

Yes_____ No_____

Do you understand the activity your child is going to participate in?

Yes_____ No_____

Do you agree to allow your child to participate in this activity?

Yes_____ No_____

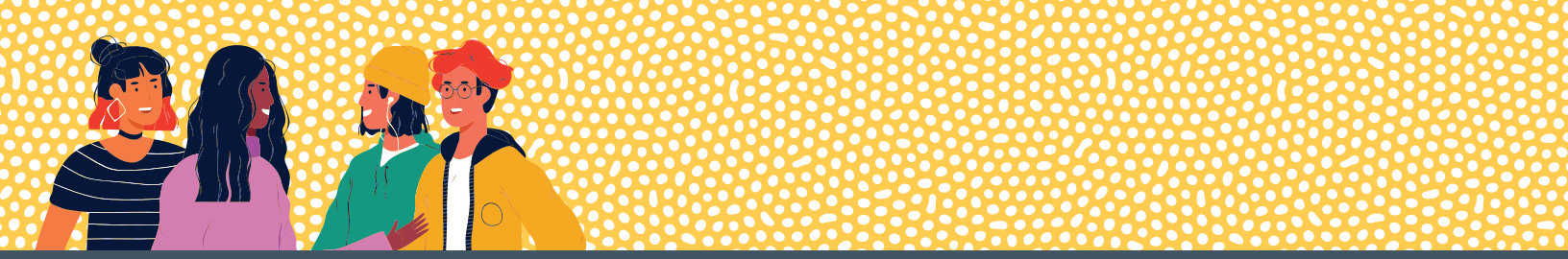
[Include any of the following questions that are applicable to the specific activity.]

Do you give us permission to audiotape your child's <<presentation, e.g.>>?

Yes_____ No_____

Do you give us permission to videotape your child's <<presentation, e.g.>>??

Yes_____ No_____



Do you give us permission to use your child's photo?

Yes_____ No_____

Do you give us permission to use your child's <<audio/video/photo>> responses in other professional settings, such as <<list settings>> for educational purposes?

Yes_____ No_____

Do you give us permission to give your child a <<payment/in-kind gift/gift>> for your child's participation?

Yes_____ No_____

Name of Child Participant (please print): _____

Name of Parent or Legal Guardian (please print): _____

Signature of Parent or Legal Guardian: _____

Date: _____

I have been given a copy of this permission form.

Yes_____ No_____

Name of investigator/staff/interviewer (please print): _____

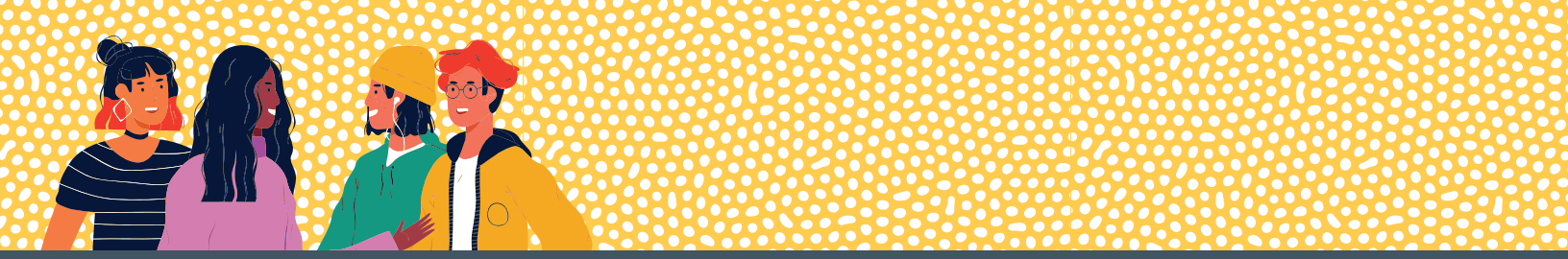
Signature of Interviewer: _____

Date: _____

Staff interviewer notes:

If parent/guardian says yes to photo, detail in what way the photo will be used:_____

Other:



Part Two: Information Sheet for Youth

What Are We Asking?

We are asking you to join us and participate in this <<conference, advisory group, video, or focus group>>.

This sheet talks about the <<conference, advisory group, video, or focus group>> and the choices that you have. We want you to ask us any questions that you have, at any time.

Important things to know:

- You decide if you want to participate.
- You can say 'No', or you can say 'Yes'.
- No one will be upset if you say 'No'.
- It's ok to change your mind.
- You can say 'No' at anytime.
- We will thank you no matter what you decide!

Why are we doing this <<conference, advisory group, video, or focus group>>?

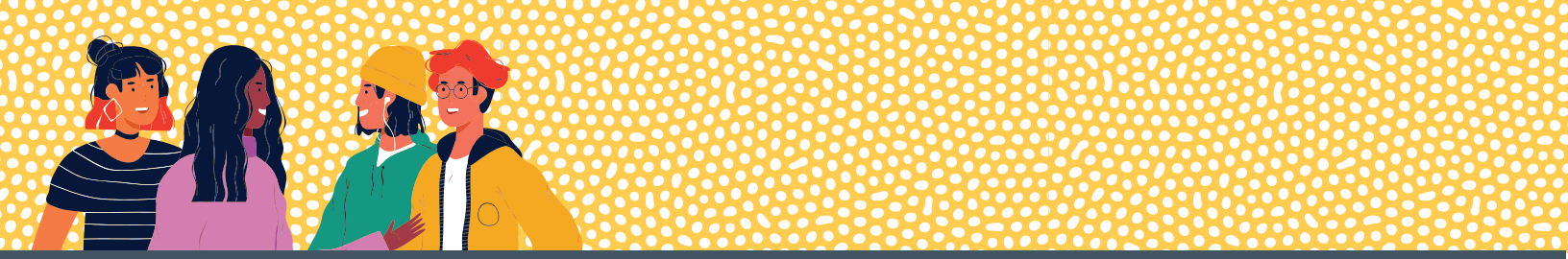
We are doing this to find out more about <<additional information about this activity>>.

What happens if I say yes?

- We will ask you questions about <<your experience as a XX, how you feel as a XX>>.
- Then you will say your answers.
- Recording: We will <<record your voice and face / record just your voice>>.
- <<Other>>
- It will take about <<minutes/hours>>.
- In order to get ready, we will <<talk to you before the day>>.

What happens if I say no?

- Nothing! You can say **NO** at any time.



Could bad things happen if I say yes?

- Some of the questions might be hard to answer or make you uncomfortable. You don't have to answer any question you don't want to.
- It will take up some of your personal time if you decide to do this.

Will I be paid to do this?

- <<Yes, you will be paid to participate.>>
- <<No, you will not be paid to participate.>>
- <<To thank you for participating, we would like to give you XX>>.

Why would I say yes?

- Your experience might help others.
- It might be fun, and you might learn something.
- <<You may have the chance to be recorded and others will hear your thoughts and opinions.>>

Remember:

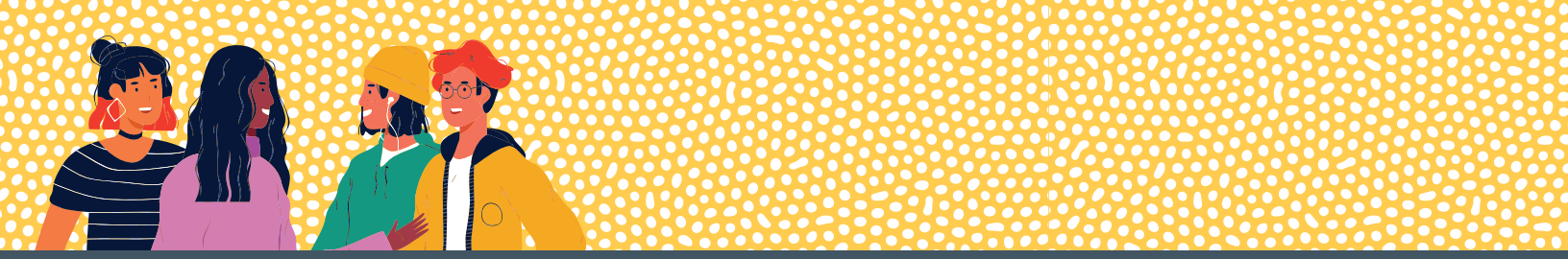
- You can ask us any questions at any time.
- Take the time you need to make your choice.

What's next?

- If you decide you want to do this <<XX>> after we talk, please write your name below.
- We will write our name too. This shows that we talked and that you want to take part.

Contact Information

This <<activity>> is being organized by <<name>> at <<organization>>. <<Her/his/their>> phone number is <<phone number>> and e-mail is <<email>>. If you have any questions about the <<activity.>> you can call, text, or e-mail to ask them.



Part Three: Statement of Youth Agreement to Participate

(May be read by or to the participant. Once adult permission has been obtained, we recommend making the following a conversation with the young person.)

We want to make sure you understand that you have been asked to participate as a <<speaker/focus group member, interviewee, etc.>> about <<topic>>. You have been able to ask any questions about the <<activity>> and your questions have been answered.

My questions have been answered. Yes_____ No_____

I agree to participate in the activity. Yes_____ No_____

I have been given a copy of this form. Yes_____ No_____

Name (please print): _____

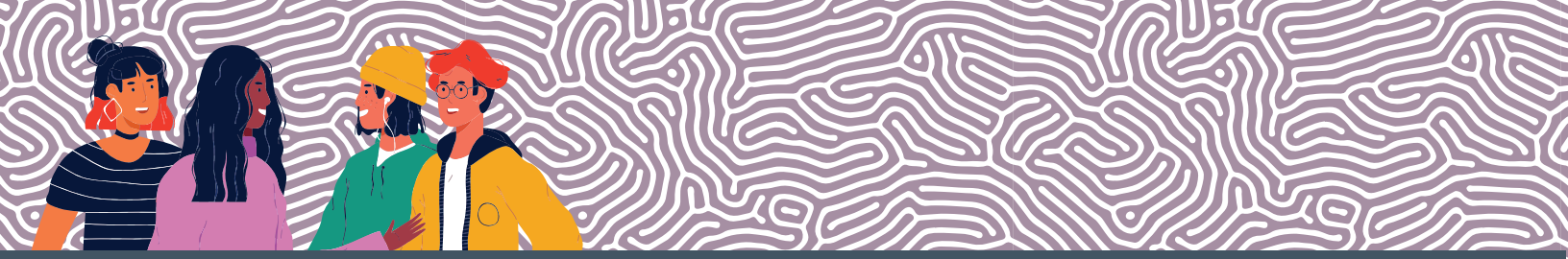
Signature of child: _____ Date: _____

or

Oral agreement of child (Please check):_____

Staff Presenter Name (print): _____

Staff Presenter Signature: _____ Date: _____



Initiating the Conversation with Children/Adolescents, their Parents/Guardians, and Caregivers

The questions below are offered as a general guide to use in developing questions to explore with children and adolescents, their parent(s), guardians, or other caregivers. It is not intended to be prescriptive but rather to help stimulate consideration and adaptation to the specific context.

Part 1: Questions Relevant to Understanding the Disease Impact and Barriers to Trial Participation

What is the **impact of the disease** on the patient/family?

By "impact" we mean effect on the patient's quality of life and ability to function, including at home, at school and extra-curricular activities, and at work, as well as their ability to sleep and take part in daily activities. The impact of disease on family/others also shapes youth experience of the disease.

Which symptoms are most troublesome to the patients? to parents/caregivers?

What endpoints/outcomes matter most to patients? to parents/caregivers?

How important are the <<primary and key secondary endpoints>> to the patients and caregivers? to the population?

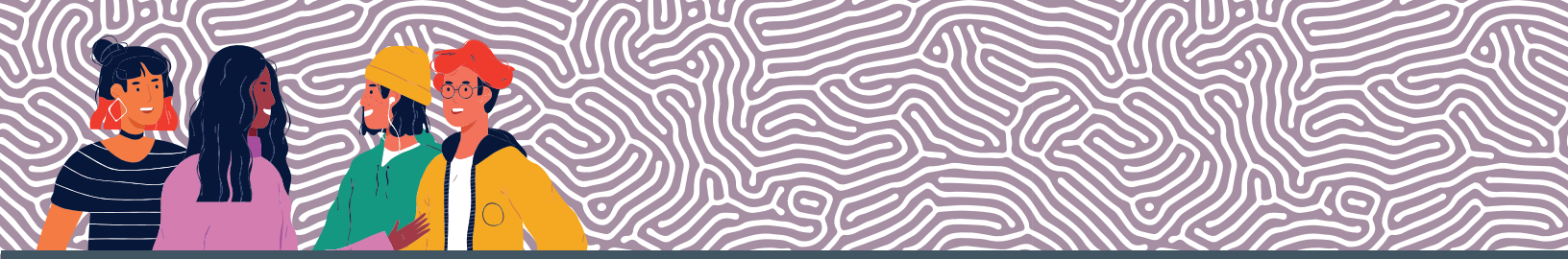
What are the patient's and what are the parent's/caregiver's worries about the future and their disease progression?

What are the patient's and what are the parent's/caregiver's perspectives about their treatment options?

Are the options understood/satisfactory/sufficient? If not, explore further.

Are there treatment needs or side effects that are not covered or considered?

Other?



Part 2: Considerations Relevant to Understanding the Patient Community

Describe how the trial sponsor is currently engaged with patient communities for this indication. If not engaged, please detail reasons.

What are the 'shared objectives' or 'jointly held priorities' between trial sponsor and patient groups?

What stands out about the science, portfolio, trial, approach, or engagement plan? The investigators may need feedback on the components that are attractive or interesting, as well as the components that are problematic or off-putting.

How will the sponsor team share trial impact, changes, results, and updates with the community and other stakeholders?

Who are the key influencer(s) or advocate(s) in online patient communities?

Part 3: Questions Related to Patients and Parents/Guardians Finding a Relevant Trial

How do patients/parents/guardians find a trial that may be meaningful and relevant to them?

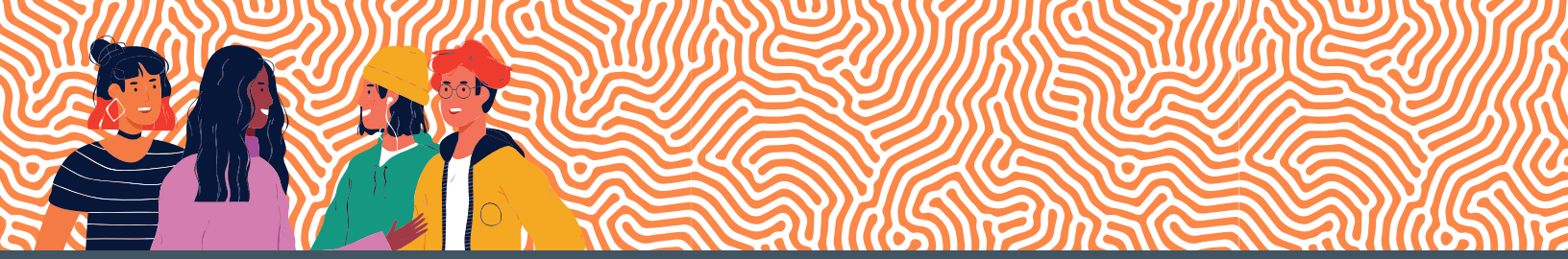
How do they usually access healthcare information?

Who is actively helping patients, and parents/caregivers on behalf of patients, get access to healthcare?

From whom do patients/parents/caregivers want to hear about clinical trials, disease information, and treatment options?

How could investigators raise awareness of the trial to groups who would find it relevant?

What are the needs in terms of information/understanding? What should patient and parent/caregiver educational material look like?



Youth Engagement Throughout the Drug Development Lifecycle

Children and adolescents can provide feedback throughout the lifecycle of a clinical trial and in all phases of product development. The table below lists some of ways in which the youth perspective may be helpful.

Phase of Study & Product Development	Areas for Consideration
Prioritization of Research	» Unmet medical needs » Patient experience, standard of care, and burden of disease » Prioritization of development efforts within a disease for novel agents across and within classes of products
Preclinical Through Clinical Trials	» Disease, symptomatology » Unmet medical needs » Indications for study (study questions) » Risk tolerance » Suitable study endpoints » Formulation considerations (route, palatability, acceptability) » Convenience » Burden of administration
Protocol Design	» Study design » Risk tolerance » Study population » Eligibility criteria » Protocol acceptability (use of placebo, standard of care) » Study duration » Frequency of research procedures » Readability of patient education, recruitment, instruction materials » Recruitment methods and communication channels » Readability of informed consent/assent » Input into digital technologies » Input into hybrid and decentralized trial design

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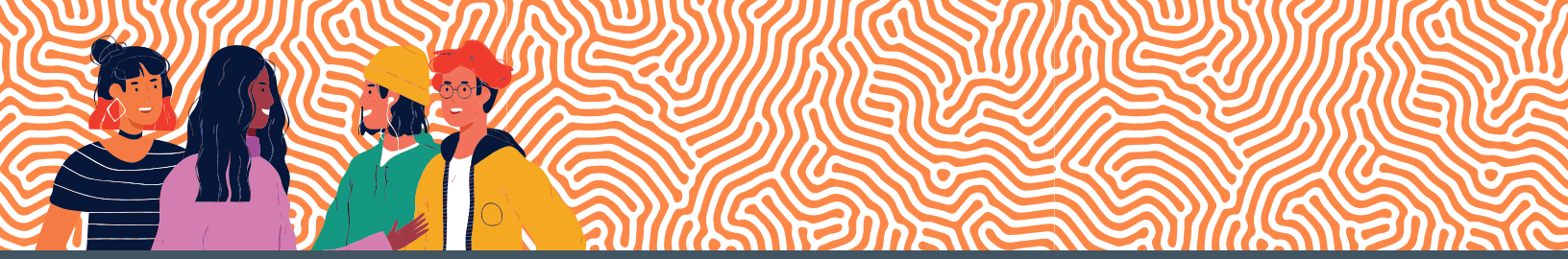
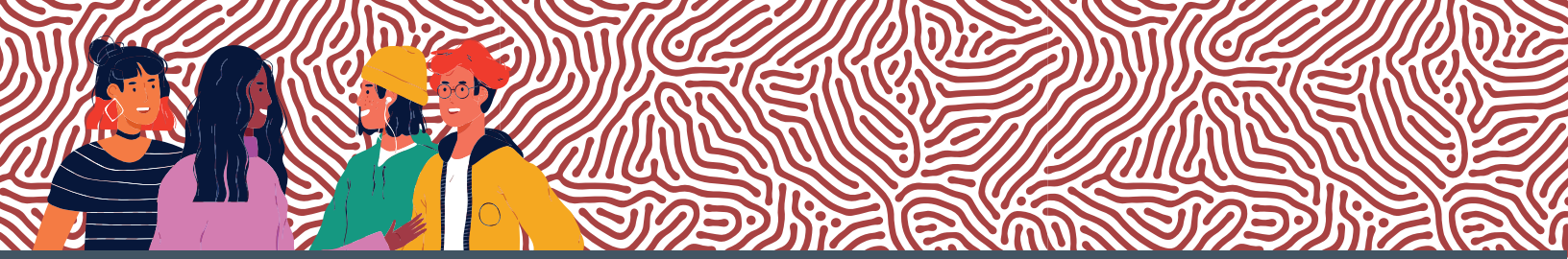


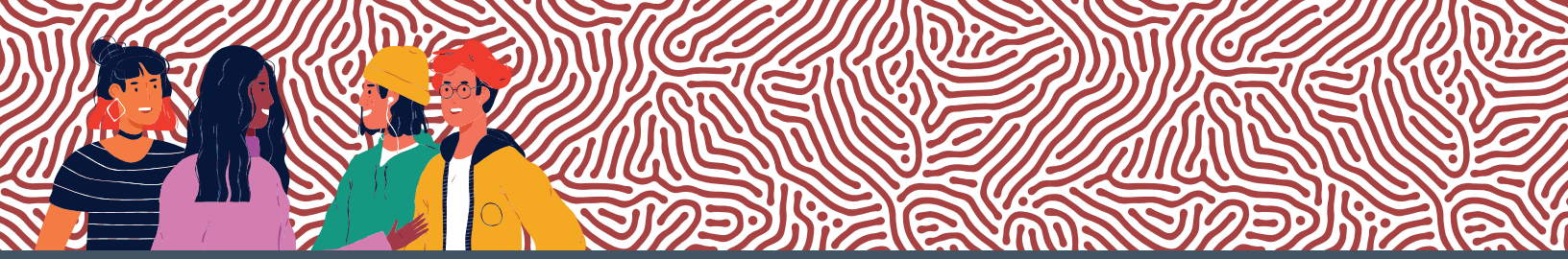
Phase of Study & Product Development	Areas for Consideration
Institutional Review Board (IRB)/Research Ethics Committee (REC) Review	» Risk tolerance » Insights into benefit/risk assessment » Commentary or input to protocol in advance of submission » Informed consent/assent documents and procedural instructions
During Study Conduct	» Advise on patient recruitment and retention » Communicate merits of a study » Input into adverse events » Help understand participant feedback and complaints » Respond to investigator questions and concerns
Study Completion	» Help interpret study results » Test readability of plain language summary » Suggest communication modalities to involved communities » Identify future opportunities for study



Considerations to Aid Decisions Around Youth Engagement

Children and adolescents can provide feedback in many aspects across the lifecycle of a clinical trial and in product development. The table below lists some of ways in which the youth perspective may be helpful.

Part 1: Considerations When Identifying & Selecting Youth for Patient Engagement Activities and Matching with Researchers	
Community characteristics, including: ◇ historical contact with researchers ◇ where research is being conducted ◇ the target population	◇ who stands to benefit from the research ◇ cultural and linguistic considerations ◇ other, as appropriate
Youth characteristics, including: ◇ biological age ◇ emotional/cognitive/developmental stage ◇ disease status ◇ time needed to tend to health maintenance	◇ school/family/job & extracurricular activity obligations ◇ assent of youth; consent of parent/ guardian/caregiver ◇ ability to use technology or accommodate logistics of trial design
Researcher characteristics, including: ◇ cultural congruence ◇ cultural humility	◇ linguistic abilities ◇ experience working with youth
Communications/outreach considerations, including: ◇ age appropriateness of materials ◇ cultural and linguistic relevance	◇ ease of access to technology ◇ use of social media
Select resources to inform further considerations: ◇ https://www.ema.europa.eu/en/news/involving-young-people-ema-activities ◇ https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/principles-involvement-young-patients/consumers-within-ema-activities_en.pdf	



Part 2: Considerations to Support Youth Engagement

When obtaining assent, consider:

- age and maturity of youth
- cognitive capabilities
- cultural and linguistic considerations
- verbal vs written assent

What type of activity the youth participant is most comfortable engaging in, for example:

- individual interview
- focus group
- conference presentation
- material review

Do the logistics of the activity allow for youth to participate easily and comfortably? Consider:

- location accessible by public transportation or parking available
- potential conflicts with other responsibilities like school, work, other
- will parent/caregiver be present?
- duration of engagement. e.g., one-off vs weekly meeting for 2 months
- compensation and/or reimbursement for expenses for youth and parent/ caregiver

What steps are needed to complete the requested activity? For example:

- phone calls
- prep meetings
- photos
- slides
- video recording
- specific technology needs, e.g. zoom
- practice sessions
- wifi connection

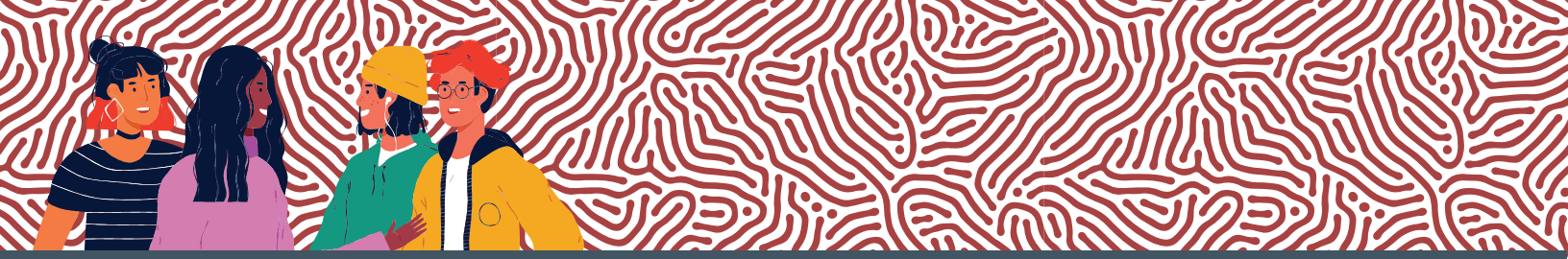
What are the possible risks, discomforts, or inconveniences?

- may be uncomfortable talking about some topics
- confidentiality concerns
- time away from friends/activities

How will concerns be mitigated?

- clear explanation of intended use of data collected
- clear explanation of how confidentiality will be maintained (if applicable)

Other?



Part 3: Considerations for Sponsors in Understanding the Community Landscape

What is already known about the disease/the patient population/the questions at hand?

What can be borrowed from existing literature/patient gathered data that is relevant to this effort?

What is the overall strategy for this data collection activity?

What are the aims of this data collection activity?

What are the current questions to be answered in this data collection activity?

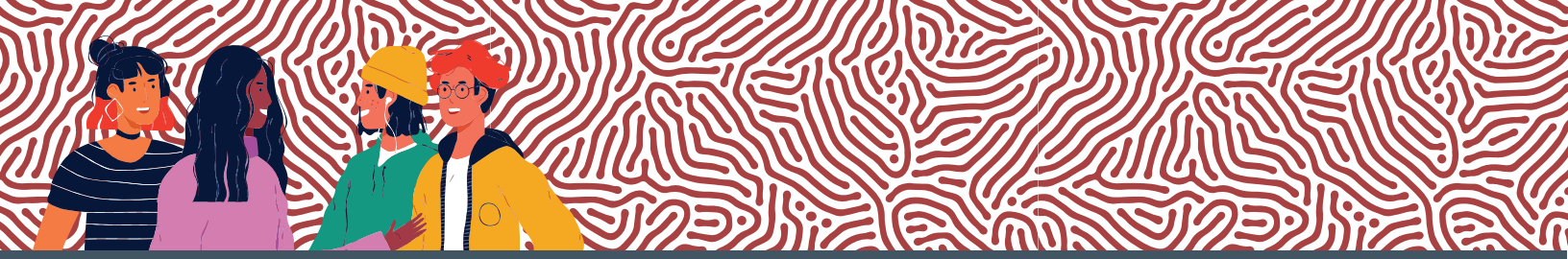
How will the insights gathered be used?

- Patient-friendly trial design - considerations include access barriers; burdens associated with participation; patient "friendliness" of device, assessment procedures; other
- Choice of endpoints - ensure that the data being collected will inform endpoint development & the unmet needs from patient perspective
- Patients' views/insights on acceptability of benefit-risk trade-off issues (e.g., acceptability of a drug which offers strong benefits at expense of rare but serious risks)
- Expected impact of the patient/participant engagement strategy in development program and whether patient experience data informs clinical trial design
- What will be done with the data collected? Ensure that a feedback loop is part of the initial strategy
- Anticipated value by stakeholder (patients, carers, patient organizations, etc)

What are the outputs?

- Key question for patient community
- Patient engagement strategy
- Decision on patient engagement activities to conduct
- Timing of engagement
- Feedback loop

Other?



Part 4: Considerations for Reporting Data to, and Working with, Involved Stakeholders Regarding Youth Engagement

Maintain transparency

Maintain awareness of the ever-changing landscape of working with children

- Kids will not participate like adults throughout the drug development lifecycle (children age)
- Many pediatric diseases or disorders are age-specific and the child and the caregivers' opinions change as the child matures

Institutional Review Boards/Ethics Committees:

- What was done? What was considered? How was engagement approached? Other?
- Create a checklist for use at **continuing review** that demonstrates what patient data collection activities were conducted and if the patient perspective was provided (within the protocol); if not, provide support for that decision
- Create a form for the IRB to use to ask what they did with the information they received to ensure/promote transparency
- Include pediatric patients/families on IRBs (and other boards)

Regulators:

- Normalize expectations regarding the kind of information needed
- Standardize the expectation that patient perspective data adds value and that it differs at various stages in the process
- Ensure that appropriate weight given to young person's voice

Industry:

- Build patient engagement into the process
- Avoid redundancies

Investigators (academic/industry/government)—adhere to same standards and expectations

- Conduct an inventory of patient reported outcomes (PROs) for common pediatric indications
- Assemble multi-stakeholder groups to define areas of need
- Develop an efficient strategy to develop tools where there is a need
- Cultivate interest from regulators re: common/universal patient reported outcomes
- Promote utilization of existing Young Persons Advisory Group (YPAG) networks, such as the European YPAG Network (eYPAGnet)

Acknowledgements

Our heartfelt thanks to all the wise young people - and the adults who care for them - who have partnered with us in this effort. You shared your insights and wisdom with us and taught us the things we need to know to do this work with honesty, integrity, and compassion. This would not have been possible without you.