PART OF PRA'S PATIENT-CENTRIC TRIAL DEVELOPMENT TOOLKIT

Rapid Trial Participation Burden Assessment

THE CENTER FOR RARE DISEASES

Acknowledgments

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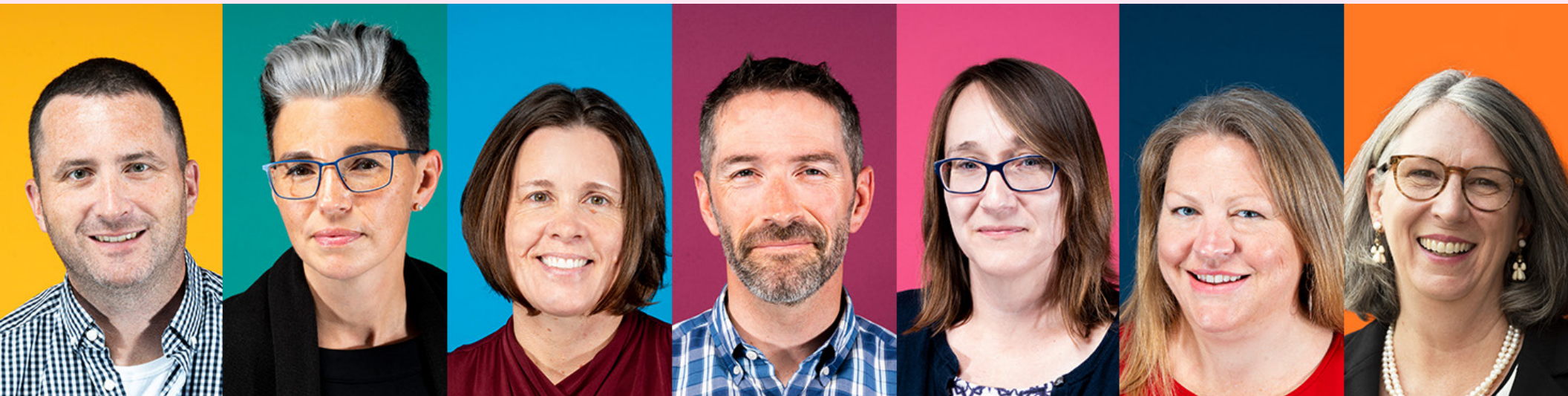

THE CENTER FOR RARE DISEASES

The Center for Rare Diseases at PRA Health Sciences has helped life sciences companies to implement more than 350 rare disease clinical trials.

We know from years of experience that one of the best ways to ensure the efficiency and successful implementation of a rare disease clinical trial is to **set participants up for success**. That begins with asking target patient communities how!

R A R E T O G E T H E R

Purpose

This tool was developed to help you, the Sponsor, to gather study-specific feedback directly from the patient community on aspects of your rare disease trial that may be challenging for study participants and may increase the **risk** of **recruitment failures, retention failures, protocol amendments**, and **trial delays**.

IMPORTANT

We strongly recommend working with Patient Advocacy Organizations (PAOs) that support your target trial population to send the survey you create to patients and caregivers. If you do not have existing relationships with PAO's, PRA's Patient Advocacy Strategy team can support your patient advocacy strategy throughout the trial design process.

Patient Burden Translates to Risk of Failures

Participating in a clinical trial takes an enormous effort from patients, caregivers, and their families. You can think of it as an endurance race that patients and families truly want to finish. Whether they can keep going to complete it depends a lot on how many obstacles in their way can be removed and how much assistance they have to overcome those that remain.

The only way to identify what aspects of a trial design or implementation may be "obstacles" that lead to failures is to **ask the patient community** for which the trial is intended. Once the risks (high-burden elements) are identified, the right mitigation strategies that can help trial participants *reach the finish line* can be developed.

This tool provides an easy to follow, structured method for gathering patient input that has been developed with the involvement of rare disease patients and caregivers. **The feedback obtained using this tool should be considered as a starting point only for further collaboration with patient communities to de-risk and support the success of a rare disease clinical trial.**

When to Use This Tool

There is no wrong time to seek out the perspective of patient communities. However, doing so as early as possible in your protocol/study development process will be especially efficient as it will help identify and troubleshoot risks before key decisions are finalized. Doing so leaves more options for risk mitigation or elimination open for consideration.

How to Use This Tool to Create a Survey

Follow the instructions to create a patient-friendly, one-paragraph description of the study design/trial as an "introduction" for your survey

Create a second paragraph to explain how the information (data) from the survey will be used

For each survey, only select a maximum of 8-12 questions about the elements you suspect may be most difficult/relevant for intended participants

Create the survey questions by "filling in the blanks" with information relevant to the study design of your trial

Include the question "How easy or hard would this be for you?" and only include the multiple-choice options listed (easy, hard, impossible, not sure)

Include the further explanation prompt "Please tell us why:" with an *open text* field for each question

How To Use This Tool To Create a Survey (continued)

You can create the survey in whatever way is most appropriate for the target audience. Formats could include online survey platforms (e.g., SurveyMonkey), in a Word Document, or in the body of an email. The questions could also be asked in an interview

Do not change the question text or sequence (aside from filling in the blanks). The text and sequence are intentional and have been created and validated with rare disease patients/patient advocates

Do not change the rating scale in any way or eliminate it. This scale has been developed with patients/patient advocates, specifically for this tool. In the development of this tool, patients have emphasized that they should be the ones to specify how easy/hard something is, not to be told what is easy/hard for them

How To Get The Survey Out To Patients/Caregivers

The ideal way to get the survery out to patients is working with PAOs that advocate for the rare disease your trial is intended for. This approach is highly recommended by PRA's Center for Rare Diseases

Rare disease patient communities often have high levels of trust in and engagement with Patient Organizations that support them, and this translates to the best chance of patients coming across your survey and taking the time to answer it

If your company is not engaged with Patient Organizations or would like to work with a third party provider to run the survey for compliance considerations, PRA's Center for Rare Diseases can support you throughout the trial design process

Important Compliance Considerations

Do not brand the survey you create with your company logo. This is a form of qualitative market research and branding may classify it as "promotional material" which could prevent you from using it as intended and in compliance with the applicable codes and regulations in your country

Do follow your company's internal review process for public facing material before you use it

Make sure you are not collecting patient identifiable information. PRA's PAS team (or another third party) can assist in creating, distributing, and collecting feedback to ensure no patient identifiable information is collected

Adverse Events: If your company has commercial or clinical stage products, you will need to have an AE monitoring process in place for survey responses, as the "Please tell us why" field is open text and respondents could in theory write in an AE unprompted

QUESTIONS, COMMENTS, SUGGESTIONS ABOUT THIS TOOL?

Contact PRA's Center for Rare Diseases, Patient Advocacy Strategy team at **PRACenterforRareDiseases@prahs.com**

DISCLAIMER

PRA disclaims any liability related to your usage of this tool. PRA makes no guarantee as to the effectiveness of this tool or business decisions taken as a result of any review or usage of this tool. All liability related to use or misuse, whether personal or professional, by any party, is entirely disclaimed by PRA. By using this tool, you exempt PRA from any liability whatsoever related to your use of the tool.

Creating a Survey

About the Trial

Start by writing one plain language paragraph about the trial that provides framework and context:

About the study population – Specify the indication, including any alternative disease name commonly used by the patient community, plus any age or gender restrictions, if applicable.

About the trial drug – If the name or identifier of the investigational product is publicly available, provide that information. If the drug identity must remain blinded, consider including a plain language description of the mechanism of action.

About the intended disease-related health benefits – State which disease symptoms and/or change in disease course are specified in the study objectives, and what the "hoped for" benefits to patients would be.

About prior clinical development data – Provide the most relevant information from prior stages of development, such as safety outcomes from first-in-human studies, any efficacy information from prior stages of development, or even pre-clinical findings if this is an early phase trial.

About the value proposition of participation to the patient/caregiver – This would include information regarding open-label extension, if applicable, or duration of access to study drug during the treatment period. It could include altruistic value, as all study participants are taking an active role in developing new treatment options for their patient community.

About the Survey

About how data from responses will be used – Next, write a short paragraph about why you are seeking out this information (to try to make the trial as easy possible for patients and families) and what will be done with personal information (we strongly recommend that personal information is not requested, and that any identifiable information is destroyed once the survey responses have been analyzed).

Questions About Screening

INSTRUCTIONS FOR SPONSOR	PARTICIPANT QUESTION	RATING	FURTHER EXPLANATION
	If you had to...	**How easy or hard would it be for you?**	**Please tell us why:**
Contentious I/E Criteria List any I/E criteria that are under the participant control that may pose a risk to recruitment. Repeat the question for each of these criterion, eg, stable background medication, lab values, clinical features such as biopsy, imaging results, genetic testing…	Have/be_____to get into the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Washout Period List the drugs/products and the timeframe	Stop taking _____for _____before you could try to get into the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Screening Visits List the number of screening visits	Spend _____days/hours doing medical tests at a medical center to find out if you can get into the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Re-Screening List the re-screening policy	Have only _____try/tries to get into the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Travel If it's very likely that participants will have to travel a long distance to get screened… list that here	Travel more than _____ hours for medical tests to see if you can get into the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Labs/tests *they* have to schedule and organize within a set window of time List the labs or tests in which participants would have to make their own arrangements. Repeat the question for every lab/test	Make arrangements to get _____ test done in _____ days/weeks/ months at your local laboratories to find out if you can get into the trial	○ Easy ○ Hard ○ Impossible ○ Not sure	
Placebo/Control Drug If the trial is placebo… explain what odds the person would have to live with…	Stay in the trial without knowing if you're getting a placebo or the trial drug… given that your chances of ending up with either are _____ in or _____ %	○ Easy ○ Hard ○ Impossible ○ Not sure	
Limits to person's options If participation limits the person's treatment options or excludes them from many future studies (eg, gene therapy), mention that here	Give up the ability to _____ for (time/duration) _____ if you take part in this trial	○ Easy ○ Hard ○ Impossible ○ Not sure	

Questions About Travel

INSTRUCTIONS FOR SPONSOR	PARTICIPANT QUESTION	RATING	FURTHER EXPLANATION
	If you had to...	**How easy or hard would it be for you?**	**Please tell us why:**
Travel How far does the person likely have to travel for each visit?	Travel more than _____ hours each time you have to go to the hospital during the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Expenses – Incidentals Considering asking participants to pay expenses and wait for reimbursement?	Pay for your costs of travel (such as gas, food, rental car, hotel) yourself upfront, send in receipts, and wait to get paid back later	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Mobility Equipment If you're not sure whether you might need to provide mobility equipment	Use only the equipment you already have to help you get to the trial hospital	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Travel – Caregiver Support If you're not sure whether patients would want to bring a caregiver or caregivers would need a second caregiver to come along	**Patient:** Travel to the hospital on your own without anyone to support me **Caregiver:** Travel with the patient by myself without another person to help you both	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Overnight Visits List the number of overnight visits in the protocol and how long for each overnight visit (e.g. 24 hrs.) List the number of overnight visits (or number of nights in a row) in the protocol	Stay overnight for hospital tests _____ (#) times during the trial	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Expenses – Childcare If it's likely that people would have to pay for child care	Arrange and pay for child care/ babysitting while away from home	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Expenses – Virtual Is the participant going to have to do lengthy calls/video calls/download and use apps on their own phone…	Use your own phone and internet to _____ (participate in long calls with the trial staff, download an app, fill out questionnaires…) that would use up phone data or minutes	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

Questions About Visits & Assessments

INSTRUCTIONS FOR SPONSOR	PARTICIPANT QUESTION	RATING	FURTHER EXPLANATION
	If you had to...	**How easy or hard would it be for you?**	**Please tell us why:**
Missing Work Fill in number of days (or half days) of work that a person might miss if they're employed and have to do visits (in person or virtual from home) during working hours	Miss _____ days (or half days) of work for each visit to the hospital/research site/online visit	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Unfamiliar Medical Team	Visits a different hospital than your normal one with a different medical team	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Difficult Tests/Procedures Fill in the test/procedures that may be unfamiliar, or that patients might generally want to avoid doing if they can, such as organ biopsy or MRI or Lumbar Puncture **Ask the question for each difficult test/procedure**	Do _____ (test/procedure) _____ (number of times) which would mean _____ (negative aspect) _____	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Test Side Effects Fill in side effects related to tests that may interfere with day-to-day activities for participants. Example: fasting, eye dilatation	Experience _____ (expected side effect) here, _____ (frequency, duration here)	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Test Mix Acceptance Enter the combination of tests suspected of being 'too much' in one visit/timeframe	Do _____ (test/procedure #1), _____ (test/procedure #2) and _____ (test/procedure #3…) in _____ (time frame here, e.g. the same visit, one week…)	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Waiting Fill in an 'approximate' time that participants might have to physically be on site/at hospital	Spend _____ hours at the hospital to get all the tests done	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Sitting Still During Tests Fill in approximately how long the participate might have to sit still for questions/assessments…. This can be really difficult for children and for adults depending on the features of their conditions	Sit still for _____ (hrs./a long time) while answering questions or waiting	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Accessibility Support for Visits	**Patient:** Get around between different departments at the hospital on your own without any help **Caregiver:** Help the patient get around between different departments at the hospital by yourself without another person to help you both	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Wi-Fi Access at Site Fill in hours or days that participants would spend at the hospital/research site potentially without good Wi-Fi access. (Participants often rely on Wi-Fi to conduct remote learning, keep kids occupied during wait times, to do work or tend to other responsibilities)	Spend _____ hours/day at the hospital with no access to Wi-Fi or poor quality Wi-Fi	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

	If you had to...	How easy or hard would it be for you?	Please tell us why:
Daily Diary Depending on the type of diary, use the relevant question. Ex. eDiary, paper diary	Complete a short survey on your (mobile phone/computer-paper) every day	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Wearables over 24 hours Fill in the type of wearable device that would be required	Wear _____ device on your _____ for 24 hrs. a day, _____	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
Visible Wearables Fill in the type of wearable device and where it is placed on the body (some people may be uncomfortable with it being seen by others	Wear _____ device on your _____ which would be visible to those around you	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

Questions About Treatment Period

INSTRUCTIONS FOR SPONSOR	PARTICIPANT QUESTION	RATING	FURTHER EXPLANATION
	If you had to...	**How easy or hard would it be for you?**	**Please tell us why:**
IP Side Effects Fill in potentially burdensome side effects that could make managing day-to-day life more difficult for patients/caregivers	Experience _____ (expected side effect) here, _____ (frequency, duration here)	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
IP Self-Administration Fill in the tasks for compounding and administering the trial drug at home if applicable	Prepare the drug dose at home by _____ and give it to yourself/ the patient	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	
IP Equipment Needed Fill in the equipment needed that you are assuming participants already have and do not plan to provide (calculator, special sippy cup, etc)	Use your own _____ (equipment/ device) for_____ (task required)	◯ Easy ◯ Hard ◯ Impossible ◯ Not sure	

Example Survey

Thank you for participating in this survey!

This survey is meant to be completed by individuals with **RARE DISEASE** disease who are 18 years or older. **SPONSOR** is looking to begin a phase 3 clinical trial to assess the efficacy of **RDRUG1** in stopping disease progression in individuals with **RARE DISEASE** disease. Previous clinical trials with **RDRUG1** have shown safety and efficacy in the studied populations.

The information gathered from this survey will be used in developing the protocol that will be used in our Phase 3 clinical trial. **SPONSOR** is committed to doing what we can to make participation in this clinical trial as easy as possible for patients and caregivers. This study will include an open label extension, which means everyone who participates in the clinical trial may be eligible to continue to receive active treatment for an extended period of time.

Thank you for your time filling out this survey. Your insight and answers will help us to create the best version of the clinical trial we can.

Please place an X in the box that you feel most accurately reflects your feeling about how easy or hard each question would be. Please also tell us why you made the selection you did. The more information you are able to provide, the more we will understand how to make our clinical trial easier for people to participate!

	EASY	HARD	IMPOSSIBLE	NOT SURE	Please tell us why
1. If you had to stop taking pain medication for 2 weeks before you could try to get into the trial, how easy or hard would that be for you?					

	EASY	HARD	IMPOSSIBLE	NOT SURE	Please tell us why
2. If you had to spend 8 hours doing medical tests at a medical center to find out if you qualify for the trial, how easy or hard would that be for you?					
3. While participating in the trial, if you had to pay for your costs of travel (such as gas, food, rental car, hotel) yourself upfront, send in receipts, and wait to get paid back later, how easy or hard would that be for you?					
4. While participating in the trial, if you had to stay overnight for hospital tests a total of 8 times during the trial, how easy or hard would that be for you?					
5. While participating in the trial, if you had to use your own phone and internet (for long calls with the trial staff, downloading an app, filling out questionnaires) that would use up phone data or minutes, how easy or hard would that be for you?					

	EASY	HARD	IMPOSSIBLE	NOT SURE	Please tell us why
6. While participating in the trial, if you had to miss 2 days of work for each visit to the hospital/ research site, how easy or hard would that be for you?					
7. While participating in the trial, if you had to visit a different hospital than your normal one and with a different medical team, how easy or hard would this be for you?					
8. While participating in the trial, if you had to do an MRI eight times, which would mean having to lay flat and still for a prolonged period of time, how easy or hard would that be for you?					