The DEFINE study (DosE FIndiNg Extensions): Reporting Guidance for Early Phase Dose-Finding Trials: SPIRIT and CONSORT extensions

Participant Information Sheet

V1.0, 18th March 2022

We are inviting you to take part in a research study.

- We are inviting you to take part in a study called DEFINE (**D**os**E** **FI**ndi**N**g **E**xtensions) to improve the reporting of early phase dose-finding trials, by helping us decide on the important items that should be included in their protocols and reports of trial findings.
- Before you decide whether to take part, it is important that you understand why this research is being done and what it will involve.
- Please read the information in this sheet carefully. Please do not hesitate to contact us for more information or if you have any questions.
- It is your decision whether to take part or not. You are free to withdraw at any time.
- You will not be asked to take any drugs or treatment. We are only interested in your opinion on how to improve the guidelines for these types of trials.

A summary of the study

- There are two main sets of recommendations to help researchers plan and carry out clinical trials. These are called **SPIRIT** (Standard Protocol Items: Recommendations for Interventional Trials) and **CONSORT** (Consolidated Standards of Reporting Trials).
- You can find out more about **SPIRIT** and **CONSORT** using these links:
  https://www.spirit-statement.org/
  http://www.consort-statement.org/
- The aim of this study is to develop extensions to the **SPIRIT** and **CONSORT** guidelines to deal specifically with early phase dose-finding trials across all disease areas.
- Through a review of the literature and expert discussions, we have identified a list of potential items to be considered for dose-finding trials and would now like to gather your opinions on how important these items are, and whether there are further needs to be addressed.
- Your participation will help us identify items that should be incorporated into the guidance for producing high quality protocol content (SPIRIT-DEFINE) and high quality reporting of trial results (CONSORT-DEFINE) for dose-finding trials.

Contents

Contact information

Principal Investigator: Prof. Christina Yap
Christina.Yap@icr.ac.uk
Project Manager: Ms Aude Espinasse
Aude.espinasse@icr.ac.uk

Study email: DEFINE-icrctsu@icr.ac.uk

Further Information:

Project Website:

www.icr.ac.uk/DEFINEstudy

1 Why are we doing this study?

- Early phase dose-finding trials are carried out to check how safe new drugs and treatments are. They are often referred to as phase 1 or phase 1/2 trials. These dose-finding trials are a critical part of the therapeutic development process, and results from these trials need to be assessed accurately to ensure the selected doses and schedules are sufficiently safe and have promising results on treatment activity before progressing to subsequent (later phase) trials. Increasing use of more complex trial designs has meant that the requirement for good quality protocols and trial reporting to promote transparency and ensure reproducibility, are even more needed.
- Early phase dose-finding trials have specific design and analysis features, yet no clear guidelines exist to guide the reporting of these. A dose-finding SPIRIT and CONSORT extension will benefit the research community in supporting critical appraisal of these studies by all stakeholders, including researchers, funders, regulators, journal editors as well as the patient community.

2 Why am I being invited to take part?

You are being invited to take part in our research as you have been identified as a stakeholder in early phase dose-finding trials. To take part in this research, you must meet our inclusion criteria:
- Interest or experience in early phase dose-finding trials
- Ability to respond in the designated data collection period
- Regular access to a stable broadband internet connection.

3 Do I have to take part?

It is entirely up to you to decide whether you want to participate in this research. You are free to withdraw at any time by contacting DEFINE-icrctsu@icr.ac.uk. Please note that we may keep the data collected up to the point of withdrawals unless specifically requested, and provided it has not already been included in analysis.

4 What will I need to do if I take part in this research?

If you are interested in taking part, you will be invited to complete a Delphi survey. This will be done electronically, using an online platform called DelphiManager. No specialist software or installation is required, simply click on the link provided to be taken to the secure survey platform.

Delphi online survey
A Delphi survey is a multi-stage process designed to establish a group decision, or 'consensus'. To achieve this, a panel of experts (from different backgrounds) are asked to rate how important they think something is. In this case, we will ask you to rate the importance of a list of proposed items to be reported in the protocols (SPIRIT) and trial publications (CONSORT) of early phase dose-finding trials.

We anticipate 2 to 3 Delphi Survey rounds will be necessary. Each round will be open for approximately 4 weeks, and reminders will be sent weekly. You will be asked to rate the importance of the proposed items on a 9-point scale from not important to critically important. You will also have the option to explain your ratings, as well as suggest amendments or additional items to consider. It is expected that each round will take around 30 minutes.

In subsequent round(s), you will receive a summary of the overall scores along with your own score, and you will be able to change or maintain your ratings from the previous round. Low scoring items may be dropped between rounds.

Items having reached pre-defined ratings thresholds will be considered for inclusion in the Dose-Finding SPIRIT and CONSORT extension.

Proposed key dates:

Delphi Survey Round 1: March – April 2022

Delphi Survey Round 2: May – June 2022

Delphi Survey Round 3 (if needed): July – August 2022

Please note these dates may change subject to the progress of the study. You will be informed by email of the launch of each subsequent survey round.

5 What are the possible benefits and disadvantages of taking part?

There will be no direct benefit to you from taking part in this research, but your contribution will help a range of people interested in assessing health care interventions to improve the way in which research is conducted and evaluate the merit of specific research trials.

We would like to acknowledge those who contribute to the CONSORT guidelines by completing the Delphi survey. We plan to report the names of the Delphi participants as an appendix to our reports. We will ask you after the final Delphi questionnaire if you would like to be included in the list of contributors. We will make it clear that participation in the Delphi does not necessarily mean agreement with the final guidance and that participants had a range of views. If you would prefer to not be included in the list of names, that is fine as well. On completion of all rounds, a certificate will be provided for your records.

There are no anticipated risks in taking part in the study. No potentially sensitive information will be collected, and data will be shared anonymously.There will be the option to save and return to the survey to reduce time burden.

6 General information about how the research is conducted

How will confidentiality be maintained?

The Institute of Cancer Research is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Liverpool provides the DelphiManager software used to collect the data and will act as the data processor. Following closure of the Delphi Survey, the data collected will be archived by the University of Liverpool for a minimum of 5 years, according to the current data protection legislation.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

All information collected about you during the study will be kept strictly confidential. When you join the study, your full name, email address, stakeholder category and broad geographical region (from pre-specified lists) will be collected. All information about you will be stored securely and accessible only to the research team members. It will be treated as strictly confidential and nothing that might identify you will be revealed to any third party. With your permission, we may keep your contact details so we can get in touch if there is any relevant future research that you may be interested in taking part in or to be informed of the results of the study. If you do not wish for your contact details to be kept for a copy of the study results to be sent to you or to be contacted about future research, these will also be disposed of securely at the end of the study.

You can find out more about how we use your information at www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/transparency or by contacting DEFINE-icrctsu@icr.ac.uk.

What if there is a problem?

If you have any concern about any aspects of the project, please speak to the project Manager Ms Aude Espinasse or the Principal Investigator Professor Christina Yap who will do their best to answer your query.

If you remain unhappy and wish to complain formally, you can do this by contacting the Institute of Cancer Research/Royal Marsden Joint Committee for Clinical Research. Please quote ref no: CCR5460

Committee for Clinical Research
Research & Development
The Royal Marsden NHS Foundation Trust
203 Fulham Rd, Chelsea,
London SW3 6JJ

Email: R&D-CCR <RDCCR@rmh.nhs.uk>

What will happen to the results of the study?

At the end of the study the results will be published in scientific medical journals and presented at conferences. The resulting Dose-Finding SPIRIT and CONSORT extension will be published on the EQUATOR (Enhancing the Quality and Transparency of Health Research) website: (https://www.equator-network.org/) to enable free and widely available sharing of the guidance. Although you will not be identified in any publication or linked to any data published, we intend to acknowledge the Delphi Survey participants as stated above. We will ask you for your permission to do so.

Who is organising and funding the research?

The project is being undertaken by an international group of early phase trials specialists and methodologists led by Professor Christina Yap (please see full list on the project website) and coordinated by the Institute of Cancer Research Clinical Trial and Statistics Unit. CONSORT-DEFINE is funded through the UKRI Medical Research Council and National Institute for Health Research (MRC–NIHR) Methodology Research Programme grant (grant no. MR/T044934/1). SPIRIT-DEFINE does not receive any external financial support.

Who has reviewed the project?

The study has been assessed for risk and approved by the study sponsor's Committee for Clinical Research. The Heath Research Authority has been consulted and confirmed Research Ethics Approval is not required

What do I have to do now?

Please follow the link provided to access the Delphi survey platform. This will take you to the registration and consent page.

Thank you for taking the time to consider participating in this project