National Cancer Strategy 2017-2026: Defining a Therapeutic Trial

Contents

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Version	Date	Amendment	Approved By
1	13/09/2022		NCCP

National Cancer Control Programme

1. Summary

The National Cancer Strategy 2017-2026[1] includes a key performance indicators (KPI) to measure therapeutic clinical trial enrolment but does not provide an explicit definition of a therapeutic clinical trial.

The NCCP reviewed the Irish and International clinical trial definitions as well as the definitions for clinical trials included in European cancer centre accreditation models and is proposing the inclusion of the following in the Cancer Strategy definition rather than restrict the definition to interventional trials only:

- All studies with ethical approval[2]
- Studies can be non-interventional, interventional or diagnostic studies [3]
- Biobank collections are excluded

This approach would assign a broad definition to the term included in the National Cancer Strategy 2017-2026, including both interventional trials and non-interventional trials. It aligns with the European Cancer Centre Certification Programme[4] definition and overlaps with the OECI Accreditation & Designation Programme[5] definition. This definition will also allow for the National Cancer Information System (NCIS)[6] to be utilised without development as a data collection tool.

2. Background

The National Cancer Strategy 2017-2026 aims to develop a culture in the cancer care system that values research for the benefit of patients, and is supportive of those who engage in it. The Strategy recognises that cancer clinical trials should be a core activity of the NCCP designated cancer centres. The Strategy also highlights that it is important to grow and support integrated translational and clinical trial infrastructure; with the aim of enrolling 6% of patients with cancer on "therapeutic clinical trials" annually and has included a related key performance indicators (KPI).

The Strategy does not provide an explicit definition of a "therapeutic clinical trial", therefore, as a first step in operationalising this KPI, there is need to define which clinical trials are to be included.

[1] Department of Health National Cancer Strategy 2017-2026 https://assets.gov.ie/9315/6f1592a09583421baa87de3a7e9cb619.pdf
[2] Scientific approval as well as formal identification of a Principal Investigator should be included during the ethics process
[3] This includes cohort-based observational biomarker driven studies provided that there is a formal Principal Investigator role linked to it
[4] http://ecc-cert.org/european-cancer-centre/
[5] Background (oeci.eu)
[6] NCIS - About the National Cancer Information System
https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/projects/mocisproject.html

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Version	Date	Amendment	Approved By
1	13/09/2022		NCCP

For optimal data quality, and in order to minimise any burden on resources, the required data should be collected as part of routine service delivery and possible data sources should be considered. Therefore, alignment of the definition, in so far as possible, with existing data collection tools, such as the National Cancer Information System (NCIS), and existing European accreditation systems is desirable.

This document explores possible definitions of a "therapeutic trial" for the purposes of operationalising the Cancer Strategies clinical trial KPI.

3. Definition of a "Therapeutic Trial"

While there appears to be no standardised definition of a therapeutic trial, it seems reasonable to conclude that a therapeutic trial involves providing a therapy (treatment) to a patient to study its impact.

Taken at its most literal sense this could refer solely to interventional trials whereby pre-defined interventions (medication, surgery, radiation or device) are studied to determine their effectiveness. However it may also be reasonable, and sensible, to include non-interventional studies as they may also include the study of a therapeutic intervention. The main difference being that the intervention is not necessarily pre-defined.

Neither of the main accreditation standards in Europe, discussed in more detail below, use the term therapeutic trial, but both include both interventional and non-interventional trials when calculating clinical trial participation. There is also variation in the definition of a clinical trial used by Irish and International organisations as can be seen in Appendix 1.

4. Data Collection - The National Cancer Information System

Roll out is underway of the National Cancer Information Stem (NCIS) [7], which records information about a patient's cancer case, diagnosis and treatment in a single longitudinal record. NCIS will be implemented in all public hospitals providing cancer services.

NCIS includes the C37 Cancer Centre application which can capture clinical trial participation with reporting aligned to the ECC Certification Programme. There is also potential to capture more detailed information about the nature of trial recruitment, e.g. patients screened but not enrolled. The NCCP have consulted with Cancer Trials Ireland (CTI) and the Health Research Board (HRB) to ascertain what information is already being collected. NCCP have also consulted with the NCIS

[7] NCIS - About the National Cancer Information System
https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/projects/mocisproject.html

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vendor, who have indicated that recruitment information, aligned with CTI and HRB, will likely be collectable following some development.

While NCIS would not be the sole or required means for collecting data, the provision of a nationally configured platform to collate and report on this information will assist hospitals in data collection and help improve data quality.

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Version	Date	Amendment	Approved By
1	13/09/2022		NCCP

5. Cancer Accreditation Systems – Clinical Trial Definitions

The two main Cancer Centre Accreditation Programmes in Europe[8], The ECC Certification Programme[9] and the OECI Accreditation & Designation Programme[10], require reporting on trial involvement.

Both accreditation standards require the proportion of patients enrolled in trials to be reported, however they differ in their definition of a clinical trial for inclusion as outlined below. More detail on the data definitions of the accreditation models are included in Appendix 2.

5.1. ECC Clinical Trial Definition

The ECC provides a broad definition of clinical trials

- All studies with ethical approval
- Studies can be non-interventional, interventional or diagnostic studies
- Biobank collections are excluded

As noted above NCIS provides a report that aligns with this ECC definition. Patients are logged as participating in a clinical trial in their tumour documentation. A report can then be generated which includes all patients participating in an ethically approved study with a study inclusion date during the reporting period.

5.2. OECI Clinical Trial Definition

The OECI clinical trial reporting requirements are somewhat more complex than ECC, however the definition of trials is similar.

- Prospective Phase 1, 2 and 3 clinical trials containing one *or* more interventions in diagnosis, treatment, follow-up or rehabilitation.
    - Interventional means that the study contains one or more defined actions aiming to improve diagnosis, care or outcome.
- Studies may be single arm or multi-arm.
- Cohort-based observational biomarker-driven studies can be included, provided that they concern studies with a formal Principal Investigator role from the centre, and are approved by scientific and ethical review committees.
- Patients included in clinical quality or registry studies are **excluded**.

[8] One of the flagship initiatives of Europe's Beating Cancer Plan is the establishment by 2025 of an EU Network linking recognised National Comprehensive Cancer Centre's in every Member State to facilitate quality-assured diagnosis and treatment, including training, research and clinical trials across the EU[8].

[9] http://ecc-cert.org/european-cancer-centre/

[10] Background (oeci.eu)

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NCIS does not have specific functionality for complying with OECI reporting requirements. It may be possible to include more specific data points to achieve this, however this would be challenging and requires agreement as to the specific fields and additional configuration.

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Appendix 1 – Clinical Trial Definitions

The table in this appendix provides trial definitions from other organisations. This is a sample list therefore is not exhaustive.

World Health Organisation here	**A clinical trial** is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials may also be referred to as interventional trials. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.
Health Research Board (here)	**A clinical trial** is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.
ICH E6 (R2) Good clinical practice (here)	**Clinical trial/study** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.
Clinical trials.gov[11] (here)	A clinical study involves research using human volunteers (also called participants) that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials (also called interventional studies) and observational studies. **Clinical Trials** - In a clinical trial, participants receive specific interventions according to the research plan or protocol created by the investigators. These interventions may be medical products, such as drugs or devices; procedures; or changes to participants' behaviour, such as diet. Clinical trials may compare a new medical approach to a standard one that is already available, to a placebo that contains no active ingredients, or to no intervention. Some clinical trials compare interventions that are already available to each other. **Observational Studies** - In an observational study, investigators assess health outcomes in groups of participants according to a research plan or protocol. Participants may receive interventions (which can include medical products such as drugs or devices) or procedures as part of their routine medical care, but participants are not assigned to specific interventions by the investigator (as in a clinical trial). For example, investigators may observe a group of older adults to learn more about the effects of different lifestyles on cardiac health.

[11] Clinicaltrials.gov is a database of privately and publicly funded clinical studies conducted around the world and is managed by the US National Library of Medicine

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Appendix 2 - Cancer Accreditation and calculation of patient enrolment in clinical trials

This appendix includes more specific information on the two main European Cancer Accreditation Standards approach to clinical trial measurement.

Both accreditation standards require the proportion of patients enrolled in trials to be reported, however they differ in the frequency of reporting and target enrolment. The language used to describe the numerator and denominator definitions vary but are essentially the same.

Comparison of the ECC and OECI Accreditation Programmes for the calculation of study rate

KPI	ECC	OECI
Target Study Rate	≥ 5% for each tumour entity[12]	No target rate specified
Reporting Frequency	Annually	Every five years (an index year is chosen)
Numerator	Number of centre's patients recruited per Index Year	Number of patients included into clinical trials
Denominator	No of Primary Cases attending the centre per Index Year	Number of newly treated cancer patients in the index year

ECC Definitions

ECC Numerator: Number of centre's patients recruited per Index Year

- The Numerator is the number of patients, diagnosed with a given tumour entity, who consent to participate in Clinical Trials within the Index Year.
- Only patients recruited for studies with ethical approval count as participants.
- Non/interventional/diagnostic studies are recognised as clinical trials.
- Biobank collections are excluded.
- Patients can be counted once for each study. The relevant date is the date of patient consent.
- Patients in palliative and adjuvant situations can be counted, no limitation as to stages.
- Patients who are recruited for a number of studies, in parallel, can be counted more than once.
- Patients in the follow-up of a study no longer count towards the study rate.
- All study patients can be counted when calculating the study rate (proportion of study patients in relation to all the Centre's primary cases), i.e., the Numerator is **not** a subset of the Denominator.

[12] For a Paediatric Cancer Centre, the target Study Rate is >90% of all patients attending the centre for treatment

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ECC denominator: No. of Primary Cases attending the centre per Index Year

- The definition of a Primary Case is specific for each diagnosis and can be found in the Catalogue of Requirements, e.g., and can be the date of initial diagnosis or the date of first presentation for treatment at the cancer centre.
- Primary cases refer to patients and not patient stays/surgeries.
- Double counting of patients is allowed in certain circumstances, e.g., if a patient is diagnosed with bilateral breast cancer in the Index Year, they can be counted as two primary cases within that year. However, if they are diagnosed with a new breast cancer, in an already diseased breast, this is not counted as a New Primary in that breast.

OECI Definitions

OECI Numerator: Number of patients included into clinical trials

- The number of patients with a cancer diagnosis included in prospective Phase 1, 2 and 3 clinical trials containing one *or* more interventions in diagnosis, treatment, follow-up or rehabilitation.
- Interventional means that the study contains one or more defined actions aiming to improve diagnosis, care or outcome.
- Studies may be single arm or multi-arm.
- Participants in cohort-based observational biomarker-driven studies can also be included in the number forming the percentage for Designation, provided that they concern studies with a formal PI role from the centre, and approved by scientific and ethical review committees.
- Patients included in clinical quality or registry studies are **excluded** from the Designation percentage.

OECI denominator: Number of newly treated cancer patients in the index year[13]

- The number of patients with a diagnosis of cancer who are treated for the first time in the cancer centre/institute in the index year for a particular cancer, regardless of the date and place of the initial diagnosis.
- Treated means that the patient has gone through cancer directed treatment, regardless of type.
- Newly treated means the patient has never been treated before in the cancer centre/institute for the same cancer.
- According to this definition: a patient with a new (second or subsequent) cancer should be counted again; but a patient with a recurrent disease previously treated in the centre/institute should not be counted. The number of patients is counted, not the number of visits.

[13] OECI A&D Manual v3.0 2019, Quantitative Questionnaire, Chapter 2, Quality Reporting, General Numbers section 2.1.1.2 Cancer Patients newly treated in the index year, available at https://www.oeci.eu/accreditation/Page.aspx?name=MANUAL_3

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- All study patients can be counted when calculating the study rate (proportion of study patients in relation to all the Centre's new cancer cases), i.e., the Numerator is **not** a subset of the Denominator.

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